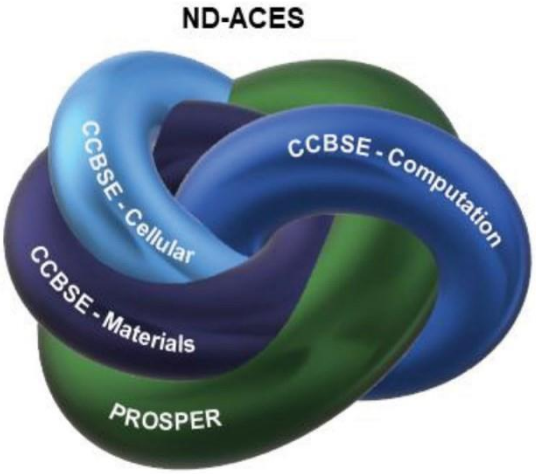
NSF EPSCoR RII Track-1 Strategic Plan 2020-2025



ND-ACES: New Discoveries in the Advanced Interface of Computation, Engineering, and Science

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Principal Investigator/Project Director: Kelly A. Rusch, Ph.D., P.E., BCEE

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ND EPSCoR

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Executive Summary

North Dakota (ND) EPSCoR's Strategic Plan details the conceptual, programmatic, and management framework for successfully accomplishing the goals of ND-ACES (New Discoveries in the Advanced Interface of Computation, Engineering, and Science), ND's National Science Foundation (NSF) Research Infrastructure Improvement (RII) Track-1 Cooperative Agreement. ND-ACES is a $24M five-year (July 1, 2020 – June 30, 2025) federal ($20M)/state ($4M) partnership led by principal investigator (PI) and project director (PD) Kelly A. Rusch, Ph.D., PE, BCEE (Executive Director – ND EPSCoR and Professor – Department of Civil and Environmental Engineering, North Dakota State University [NDSU]). The Co-PIs are John Mihelich, Ph.D., Interim Vice President for Research and Economic Development, University of North Dakota (UND), and Jean Ostrom-Blonigen, Ph.D., CPA, Project Administrator, ND EPSCoR.

ND-ACES capitalizes on and supports the continued growth in research capacity and capability at the two research universities (RUs; NDSU and UND), one master's college/university (MCU; Minot State University [MiSU]), three primarily undergraduate institutions (PUIs; Dickinson State University [DSU], Mayville State University [MaSU], and Valley City State University [VCSU]), and three of the five tribal colleges/universities (TCUs; Cankdeska Cikana Community College [CCCC], Nueta Hidatsa Sahnish College [NHSC], and Turtle Mountain Community College [TMCC]). ND-ACES will catalyze ND's research and computing capabilities by leveraging prior and new investments to create knowledge that expands ND's bioscience research, capacity, and expertise through the collaborative work of personnel at the above nine institutions within a unified Center for Cellular Biointerfaces in Science and Engineering (CCBSE). The CCBSE, co-led by Mark Hoffmann, Ph.D. (UND [Colin K. Combs served in this capacity at UND from July 1, 2020 – June 30, 2022]) and Kalpana S. Katti, Ph.D., F. AIMBE (NDSU), has three integrated Pillars of scientific inquiry: 1) Materials Design at Biointerfaces; 2) Cellular Systems at the Materials Interface; and, 3) Computation, Machine Learning, and Predictive Modeling.

The impact and reach of ND-ACES' research efforts/intellectual merit are enhanced via the simultaneous and linked broader impact efforts of the Promoting Sustainable Partnerships in Education and Research (PROSPER) team. PROSPER activities span each of the nine institutions listed above, and a fourth TCU (Sitting Bull College [SBC]). The goals of these efforts will be achieved through the establishment of diverse and sustainable STEM education and professional development pathways and expanded bioscience partnerships and internships designed to enhance success in future federal funding and support the transformation of research into practical use via trained personnel and new products. PROSPER will also expand underserved (i.e., rural, inner city, or low income) and underrepresented (i.e., American Indians, Alaska Natives, Blacks, Hispanics, women, or persons with disabilities) participation, and inform the residents of ND.

Vision and Mission

Vision

ND-ACES will be the Northern Plain's leading scientific and educational driver in new and sustainable biosciences technologies; particularly in knowledge and translational activities in biointerfaces related to cancer progression and metastasis.

Mission

ND-ACES will contribute to cancer research in ways that have state, national, and international ramifications and underpin sustainable activities for a trained and diverse workforce and informed populace and lead to future efforts focused on new therapeutic solutions (beyond the scope of this effort).

Introduction

Description

ND-ACES builds university-based scientific and translational research capacity and capability at nine of 10 participating institutions: two research universities (RUs), one master's college/ university (MCU), three primarily undergraduate institutions (PUIs), and three tribal colleges/ universities (TCUs) to help drive the continued growth of the state's emerging biosciences ecosystem. Senior personnel from these institutions (Appendix A) contributed to strategic planning activities (Appendix B) and have developed a living framework to work collaboratively (Appendix C) on the ND-ACES activities identified in the Project Implementation section of this Strategic Plan. A glossary of acronyms is included as Appendix D.

Within the Center for Cellular Biointerfaces in Science and Engineering (CCBSE), researchers across nine participating institutions will use computational modeling to garner an improved interdisciplinary understanding of biological and engineered materials biointerfaces; expand expertise in novel cellular growth and analysis paradigms for mimicking the *in vivo* environment; catalyze research/computing capabilities; and, support the translation of research into use through products, partnerships, and collaborations with various stakeholders.

The reach and sustainability of CCBSE will be enhanced through a series of broader impact efforts by participants (Appendix A) at all 10 participating institutions (Appendix E) organized within the Promoting Sustainable Partnerships within Education and Research (PROSPER) network. Through PROSPER, ND-ACES provides diverse and sustainable STEM education and professional development pathways and expanded bioscience partnerships and internships designed to increase success in future federal funding and support the translation of research into use, broaden underserved (particularly rural and/or low-income students) and underrepresented (particularly American Indians, Hispanics, women, or persons with disabilities) participation, and inform ND's citizens.

Overarching Goal

The goal of North Dakota's RII Track-1 effort, New Discoveries in the Advanced Interface of Computation, Engineering, and Science (ND-ACES) is to build greater capacity to facilitate innovation within ND's bioscience sector in sustainable fundamental, applied, and translational research as well as broaden participation and economic engagement beyond commodities. Specifically, ND-ACES' research will expand ND's familiarity, expertise, and research capacity related to the growth of breast and prostate cancer cells that mimic primary and metastatic tumors. ND-ACES will expand bioscience capacity by leveraging current and new investments that lead to new knowledge and increase ND's competitiveness. Success in this arena will help diversify the state's economy beyond the boom and bust agriculture and oil (commodity) sectors.

ND-ACES Alignment with North Dakota's Science and Technology Plan (S&T Plan)

ND's S&T Plan (Appendix F) identifies bioscience as an emerging area of critical importance for RU research emphases and addresses state priorities for economic growth. Prior to the submission of this NSF RII Track-1, the ND EPSCoR State Steering Committee (Appendix A) reviewed and confirmed the relevance of the S&T Plan to the ND-ACES research and they will continue to make recommendations regarding future focus areas. ND-ACES is poised to dramatically enhance success in building capacity for bioscience research in ND and sustaining innovative science in the state. ND-ACES, through efforts at the RUs, MCU, PUIs, and TCUs,

enables the capacity-building that helps transition the CCBSE into a mature entity for research innovation. This effort includes shaping the expertise and capabilities in research and development areas that align with federal priorities while addressing the sustainability of important growth areas for the state.

The CCBSE addresses the potential for biosciences research growth in ND and will build capacity for innovative research that focuses on specific Strategies detailed in the state's S&T Plan by calling for investments in the emerging biotechnologies sector (Strategy 1.A.1.iii); associated support for the development of a "biosciences/biomedical" research corridor in the Red River Valley, where both of the RUs are located (Strategy 1.A.1.vi); expanded support across ND for materials science research (Strategy 1.A.1.vii); increased state investments in advanced scientific computing and visualization (Strategies 1.A.5; 2.B.1, 2.B.6, 4.B); support and expansion of infrastructure in key research and development areas (Strategy 2); continued support for the Grand Challenge areas of NDSU (healthy populations and vital communities) and UND (human health and big data) (Strategy 1.B); and, increased academic partnerships with the private sector (Strategy 3). Further, the S&T Plan identifies activities to produce and retain STEM graduates who are "technically skilled and business-wise" (Strategy 4). CCBSE capitalizes on recent industry and medical sector growth, which points to the tremendous potential the bioscience sector holds for North Dakota.

PROSPER provides for real-time understanding of STEM needs at the MCU/PUIs/TCUs (Strategy 4.A.1); STEM pathway programs between the MCU/PUIs/TCUs and RUs (Strategy 4.A.2); additional research experiences for undergraduates (Strategy 4.A.3); cyberinfrastructure (CI) interns (Strategies 4.B.1 and 2), and increased awareness of the state's innovation ecosystem to improve economic diversification and quality of life for citizens (Strategy 5). The state, along with the North Dakota University System (NDUS) and the North Dakota Association of Tribal Colleges (NDATC), have identified the critical need for STEM education and workforce development (EWD). PROSPER is fully integrated with CCBSE and will synergistically help build a tech-savvy workforce through diverse bioscience/STEM education and professional development pathways; broaden participation by underrepresented and underserved populations; sustain impact through the translation of research into the private and medical sector; and promote awareness among ND’s residents.

Primary Organizational Partners and Their Roles

The CCBSE is co-led by NDSU University Distinguished Professor Kalpana S. Katti, Ph.D., F. AIMBE and UND Chester Fritz Distinguished Professor Mark Hoffmann, Ph.D. The CCBSE is fully integrated across three research Pillars: 1) Materials Design at Biointerfaces; 2) Cellular Systems at the Materials Interface; and, 3) Computation, Machine Learning, and Predictive Modeling. Each CCBSE Pillar is also co-led by a NDSU and UND researcher. Collectively, the CCBSE Pillars will support the expansion of bioscience research capacity and advanced understanding of the biochemistry and cell biology of cancer cells and tumors (primary metastasis sites).

PROSPER provides education and experiences designed to build a diverse workforce, enhance partnerships and collaborations with various stakeholders, and inform the residents of ND. The four components of PROSPER are: 1) Education and Workforce Development; 2) Broadening Participation; 3) Partnerships and Collaborations; and, 4) Communication and Dissemination.

ND-ACES funds the intellectual merit efforts of the CCBSE and the fully integrated corresponding broader impact efforts of PROSPER across the 10 organizational partners as

outlined in Table 1. For additional details, including the names and the locations of senior personnel, see Appendix A. For a map of campus locations, see Appendix E.

Table 1. Location of Senior Personnel and their Primary ND-ACES' Role

Name of Institution	Type of Institution	Location	PI / Co-PIs	CCBSE Senior Personnel	PROSPER Senior Personnel
Cankdeska Cikana Community College (CCCC)	TCU	Fort Totten		2	1 (same person)
Dickinson State University (DSU)	PUI	Dickinson		1	
Mayville State University (MaSU)	PUI	Mayville		1	
Minot State University (MiSU)	MCU	Minot		1	
North Dakota State University (NDSU)	RU	Fargo	2	12	3*
Nueta Hidatsa Sahnish College (NHSC)	TCU	New Town		1	1 (same person)
Sitting Bull College (SBC)	TCU	Fort Yates			1
Turtle Mountain Community College (TMCC)	TCU	Belcourt		1	1 (same person)
University of North Dakota (UND)	RU	Grand Forks	1	10	4
Valley City State University (VCSU)	PUI	Valley City		2	

**The three NDSU PROSPER Personnel are ND EPSCoR Staff.*

Expected Benefits of Project to the Jurisdiction and to the Jurisdiction's Academic Research and Education Infrastructure

Achieving ND-ACES' vision, mission, and overarching goal requires the collective expertise of existing faculty researchers, critical investment by each RU in two new faculty hires, the purchase of additional equipment at three ND campuses (by the ND EPSCoR State Office in the year preceding this agreement), access to institutional resources at all participating institutions, and input from scientific and industry partners. ND-ACES builds on ND's strong history of fostering technology/knowledge-based development, moving university-based intellectual property into the private sector, creating higher-paying technology-based jobs, and nurturing university-industry relationships and its continued commitment to data infrastructure.

In fall 2017, the RUs began a joint biomedical engineering graduate degree program (eight M.S. graduates and 12 current M.S. students), an important pool of students for potential incorporation into CCBSE research and workforce development efforts. Both RUs have research foci in health (biosciences/biomedical) and infrastructure (data analytics/societal infrastructure). NDSU's commitment to health-related bioscience research includes the recent hiring of seven faculty in biomedical engineering-sensors and 3D printing, materials/ mechanobiology, computational biology, cancer biology, polymer science, and computational

chemistry (the last two were hired under ND's pervious Track-1 cooperative agreement, INSPIRE-ND, OIA #1355466) and the recent support of eight graduate students in biointerfaces fields. NDSU also invested in the Center for Computationally Assisted Science and Technology (CCAST) by increasing its footprint, procuring additional equipment, recruiting one research facilitator (FY18), and supporting (through ND EPSCoR) four Ph.D. cyberinfrastructure (CI) interns. In 2020, NDSU received an award from NSF for the acquisition of a high-performance computing system for scientific research and education. UND has committed to developing its capacity in data analytics, machine learning (ML), artificial intelligence (AI), and deep learning. UND's School of Medicine has invested in the growth of cellular expertise through three recent hires in cancer cell biology and the establishment of a clinical and translational research center (IDeA; Dakota Cancer Collaborative on Translational Activity-includes NDSU). UND has also hired faculty in integrative systems biology and computational materials chemistry and recently expanded its Computational Research Center (CRC).

The ND-ACES logic model (Table 2) outlines how the investments ND-ACES makes in existing and new personnel, high performance computing (HPC)/cyberinfrastructure (CI) systems, workforce, and partnerships will drive outcomes and create lasting jurisdictional impact. Key investments include equipment purchased by the ND EPSCoR State Office prior to the start of the award (from state, non-match dollars) and NDSU and UND's commitment to provide the funding necessary to hire two new faculty associated with the CCBSE Materials Design at Biointerfaces Pillar (a need identified in the proposal development and outlined in more detail within the response to NSF's programmatic terms and conditions located in Appendix G). ND-ACES investments provide the ability to conduct new research and outreach activities (outlined in the Project Implementation section of this document) designed to produce short-term outcomes within the five years of this RII Track-1 cooperative agreement. These efforts have been carefully designed to provide longer-term outcomes with sustained jurisdictional impacts that will help ND expand its economy and reach beyond commodity-based investments.

As will be demonstrated within the ND-ACES annual report to NSF, the ND-ACES milestone activities and metrics (outlined in the Project Implementation section) provide a pathway to ND-ACES outcomes that produce changes in the knowledge and capacities of the state (Table 2, CCBSE outcomes) and sustained positive impacts and growth as a result of these changes (Table 2, long-term outcomes). The outcomes of ND-ACES are the beneficial impacts on ND that will affect sustainable engagement, inform stakeholders, support ND's growing biosciences sector, and advance the development of a skilled workforce. The short- and long-term outcomes summarized within the ND-ACES logic model will improve the local economy for the citizens of ND, leading to jurisdictional impacts within the Northern Plains' growing biosciences sector.

Jurisdiction-wide impacts will be the result of the achievement of short-term and long-term outcomes all along the education and workforce continuum. ND-ACES will prepare the Northern Plains to be a leader in new and supportable biosciences technological developments. This commercial growth will impact the state by providing expanded workforce opportunities in a new industry.

Table 2. ND-ACES Logic Model

	Investments	Activities	Participants	Outcomes Short (5Yrs)	Outcomes Long (10Yrs)	Jurisdiction Impact
Faculty/Research	Project Personnel, 2 new materials science faculty – 1 at each RU, and 2019 ND EPSCoR State Office laboratory equipment purchases at NDSU and VCSU	Synthesize, characterize materials; define 3D cell-matrix mechanisms; create large-scale cellular modeling; expand AI/ML expertise; report updates on research	Collaboration of ND-ACES team, seed grant awardees, joint RU biomedical/ engineering and other students, EAB, State Steering, medical/ health community	Create new knowledge that expands ND's bioscience research, capacity, and expertise; catalyze ND's research/ computing capabilities; increase success in federal funding; support translation of research into use; inform citizens	Effect sustainable engagement and support of project participants Inform local/ national research and stakeholder, community, and public Expanded use of HPC/CI in PUI/MCU/TCU research and education Foster the ongoing development of a skilled, diverse workforce Positively impact state economy Supply research outcomes for growing/ new bioscience ventures and partners	Northern Plains leader in new and sustainable biosciences technology advances Sustainable, competent, and diverse state biosciences and bio-technology workforce from A.A. through Ph.D. Growing economic sector in bioscience industry with new partners, growing businesses, and expanded workforce opportunity
HPC/CI	Project HPC investments, including 2019 ND EPSCoR State Office HPC/CI system purchases at both RUs	Train researchers, build state-wide access to equipment/HPC/ CI systems	ND-ACES, new CI facilitators at RUs, and CI campus staff			
Workforce	Commitments made to bioscience/ STEM education and developing a diverse workforce pool	Strengthen bio-science/STEM ecosystem through mentoring; teacher professional development in rural/tribal/ underserved; training in research; NATURE; student teaching	Senior ND-ACES faculty to mentor early career faculty, graduate/ undergraduate students; rural/ underserved/ tribal K-12 teachers	Establish diverse and sustainable bioscience/ STEM education and professional development pathways; seek to broaden the participation of under-represented communities		
Partnerships	Investing in partnerships	Leverage/ recruit partners to expand research impact; add contract/ collaborative opportunities, and internships	ND-ACES personnel and ND/regional industry/ medical partners	Impact beyond the project with partnerships and expanded internships		
	Communication and assessment throughout all elements					

Project Implementation

ND-ACES personnel (Appendix A) will work collaboratively (Figure 1) within and across the three CCBSE research Pillars (Materials Design at Biointerfaces; Cellular Systems at the Materials Interface; and Computation, Machine Learning, and Predictive Modeling; and the four PROSPER broader impact components (Education and Workforce Development, Broadening Participation, Partnerships and Collaborations, and Communication and Dissemination). The RU HPCs, shown between the CCBSE and PROSPER groups are instrumental to the operational work conducted within the Computational Approaches Pillar; have training/outreach responsibilities to the MCU, PUIs, and TCUs; and, will play a role in expanding the STEM pathway of several students through the hiring of CI interns.

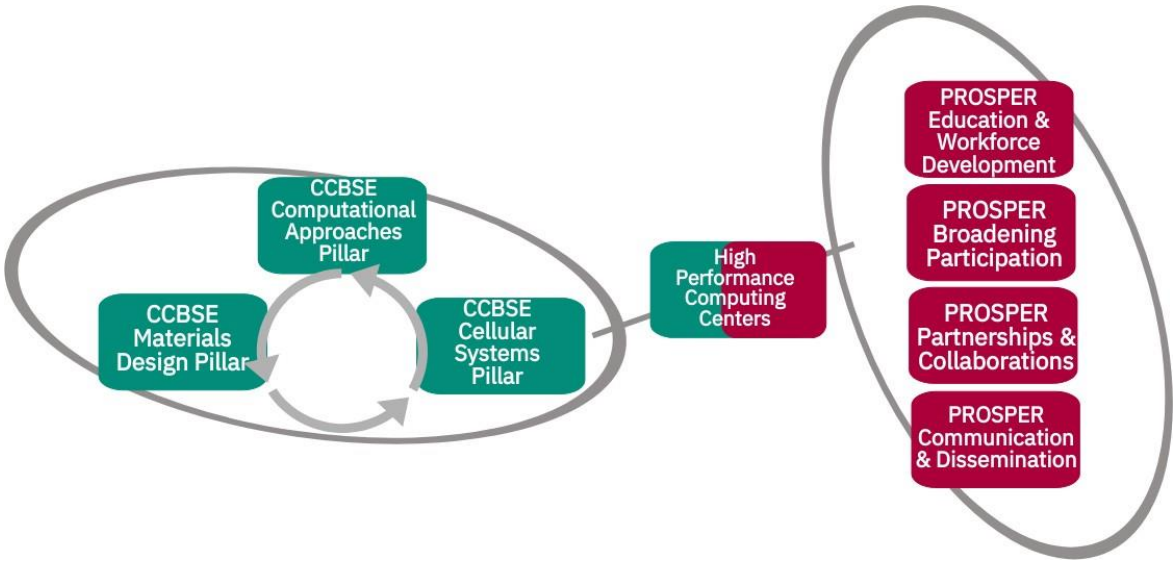


Figure 1. Interrelationships of CCBSE and PROSPER Personnel

The ND-ACES overall work plan will be implemented along five integrated tracks:

1) Interdisciplinary and transdisciplinary research in biointerfaces (the interface between engineered and biological materials) that uses advanced research computing as a conduit for intellectual and translational advances.
2) Workforce training and broadened participation programming at all campuses to support North Dakota's biosciences industry.
3) Regional industry and medical entity partnerships that facilitate bioscience sector sustainability.
4) Advanced research computing to increase North Dakota researchers' expertise, with the research universities serving as solution providers.
5) Elevated public understanding of the economic impact of growing North Dakota's biosciences sector through strategic research investments as a result of data-sharing, communication, and outreach.

CCBSE Implementation

The CCBSE activities link to ND-ACES tracks 1, 2, 3, and 4 and support the center's core goal of expanded bioscience research capacity in improved soft tissue and bone-mimetic scaffolds and models that create and increase the knowledge and advanced understanding of the biochemistry and cell biology of cancer cells and tumors. To broaden application of the foundational knowledge gained on metastasized cancer/tumors, the team, led by K. Katti (NDSU) and M. Hoffmann (UND [previously C. Combs [July 1, 2020 – June 30, 2022]), will pursue developmental research to increase capacity and knowledge in the area of nanoparticle-based delivery systems (secondary goal; links to ND- ACES tracks 1, 2, 3, and 4). This secondary goal will provide a solid foundation for the future development of new therapeutic solutions (mid- to long-term outcome; not in the scope of this proposal) to address bone metastasized cancer. The CCBSE researchers collaborate across multiple disciplines of materials science engineering, cellular biology, and scientific computing.

The CCBSE goals will be reached by employing five Strategies:

1) Construct innovative 3D biocompatible structures of hard and soft tissues (core goal).
2) Design novel cell culture paradigms to accurately model *in vivo* tumor cell biology (core goal).
3) Provide a fundamental understanding of biointerfaces that adapts to biomedical and biotechnology research and translates to industry (core and secondary goals).
4) Use iterative computational learning to establish models capable of predicting cell responses on 3D biointerfaces (core goal).
5) Develop an understanding of polymer nanoparticles as a surrogate for vascular transport of effector molecules (secondary goal).

Each Pillar has a set of Pillar-specific goals and objectives, which when successfully addressed will lead to achieving CCBSE's core and secondary goals. CCBSE's success will be enabled by old and new investments, multidisciplinary coordination among nine institutions, and transdisciplinary growth of expertise and research capacity across three research Pillars: 1) Materials Design at Biointerfaces (hereto forth called Materials Design Pillar); 2) Cellular Systems at Materials Interfaces (hereto forth called Cellular Systems Pillar); and, 3) Computation, Machine Learning, and Predictive Modeling (hereto forth called Computational Approaches Pillar).

CCBSE Materials Design Pillar

The Materials Design Pillar is co-led by Sanku Mallik (NDSU) and Julia Zhao (UND). Team members include: Austin Allard (TMCC), Mikhail Bobylev (MiSU), Guodong Du (UND), Khwaja Hossain (MaSU), Kalpana Katti (NDSU), Mike Parker (CCCC), Mohi Quadir (NDSU), and Brent Voels (CCCC). Two new materials science faculty were identified at the proposal stage as necessary to the project (Table 2). UND has hired Binglin Sui, Assistant Professor, Chemistry, while NDSU will begin its search in fall 2021 (see Appendix G for additional details).

This group is focused on designing bio-inspired materials (hard and soft tissue) as platforms for the growth of cancer cells in the primary tumor site (soft tissue) and a metastatic bone site (hard tissue). The three goals of this Pillar are outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 3). The goals emphasize the foundational design principles of tissue-mimetic materials and nanoparticles. The results from the Cellular Systems Pillar and the Computational Approaches Pillar will allow iterative

improvement of the design principles for the materials research under this Pillar. Hence, the goals for the Materials Design Pillar are not hypothesis-driven.

This team will use three Tactics aligned with CCBSE Strategies 1, 3, 4, and 5 to successfully meet its Pillar-specific goals and objectives: 1) design novel soft materials that mimic tissues through layered chitosan-alginate systems (primary site of cancer) and hard materials that mimic bone through amino acid modified clays (secondary site - metastatic; Strategy 1); 2) develop a system for vascular surrogacy in 3D cocultures (Strategy 5); and, 3) integrate with the Cellular Systems Pillar (via G. Du and K. Katti) and the Computational Approaches Pillar (via W. Xia) teams to produce a high throughput format for rational design of increasingly functional materials (Strategies 3 and 4).

The workflow will follow an iterative cycle: 1) biosimilar and biocompatible materials will be selected for hard and soft tissue matrix designs; 2) polymer nanoparticles will be designed for vascular-like transport of effector molecules into the dense 3D cell cultures; 3) scaffolds and polymeric nanoparticles will be delivered to the Cellular Systems Pillar for assessing the effects of released effector molecules on the heterogeneous 3D culture phenotypes for comparison to *in vivo* growth (studies from literature); 4) Cellular Systems Pillar feedback will be integrated with computation predictions; and, 5) predictive model output from the Computational Approaches Pillar will direct modifications for specific material pore size, shape, organization, elasticity, and degradability over time for subsequent iterations.

Materials Design Pillar Goal 1.1: The team will develop porous bone-mimetic scaffolds to create interfaces with breast and prostate cancer cells and collaborate with the Cellular Systems Pillar to study the effects of the materials using cell phenotyping. Specifically, this goal is the selection of optimal hard materials as porous bone-mimetic scaffolds.

- **Materials Design Pillar Objective 1.1a:** Nanoclays with added amino acids will also be investigated to affect cellular adhesion and interaction. Molecular dynamic (MD) simulations by the Computational Approaches Pillar will identify amino acids for use in material modification, and an intercalated clay-polymer scaffold will be fabricated in various formulations to better mimic bone tissue. Thus, the objective will be to design and optimize nanoclays polymer composite scaffolds to enable a more authentic bone mimetic environment.
    - Supporting Activity:
        - Prepare nanoclay scaffolds incorporating a variety of amino acids, seek optimal impacts on the growth of cancer spheroids.
        - Assist non-RU campuses in the administration and development of necessary compliance protocols (institutional biosafety committee, materials transfer agreements, etc.) ***[Approved by NSF 7/28/21]***

- **Materials Design Pillar Objective 1.1b:** Sequential seeding of mesenchymal stem cells and cancer cells on the scaffolds will be followed by cellular phenotype characterization to enable mimicking of the secondary site of cancer. Thus, the objective will be to characterize the scaffolds and demonstrate cancer cell growth.
    - Supporting Activity:
        - Prepare the scaffolds, culture breast and prostate cancer cells, give to the Cellular Systems Pillar to genotype and test with polymer nanoparticles.

Materials Design Pillar Goal 1.2: The team will develop soft, polymeric scaffolds for the growth of prostate and breast cancer cells. Scaffold mechanics will be optimized using steered molecular dynamics (SMD) modeling efforts of the Computation team to help optimize the stress-strain characteristics of the scaffold material. As a result, the combined model outputs will inform the modulation of the concentrations of chitosan, (Chi) sodium alginate (Alg), and polygalactouronic acid (pgA) to achieve characteristics that support cancer cell cultures and enable the mechanical stability of the scaffold system. Specifically, this goal is the selection of optimal polymeric materials as soft tissue-mimetic scaffolds.

- **Materials Design Pillar Objective 1.2a:** The team will initially focus on preparing two 3D scaffold systems: 1) tailored multilayers of ChiAlg gel-like structures and Chi-PgA and 2) polycaprolactone (PCL) electrospun fibers with the ChiAlg hydrogels. Thus, the objective will be to design and optimize soft polymeric scaffolds by altering composition and based on feedback from the Cellular Systems Pillar.

    - Supporting Activity:
        - Prepare new soft scaffolds from Chi, Alg, and PgA and characterize the new scaffolds to determine optimal polymer composition, ratio, and preparation protocol for future design
        - Assist non-RU campuses in the administration and development of necessary compliance protocols (institutional biosafety committee [IBC], materials transfer agreements [MTAs], etc.) ***[Approved by NSF 7/28/21]***

- **Materials Design Pillar Objective 1.2b:** Seeding of cancer cells on the scaffolds will be followed by cellular phenotype characterization to enable mimicking of the primary site of cancer and demonstrate optimal cancer cell growth. Thus, the objective will be to mimic primary cancer site in an *in vitro* setting.

    - Supporting Activity:
        - Determine mechanical properties and cell viability in the optimized hard and soft scaffolds. Then, analyze gene expression profiles to demonstrate primary tumor formation and testing of selected nanoparticles.
        - Assist non-RU campuses in the administration and development of necessary compliance protocols (institutional biosafety committee [IBC], materials transfer agreements [MTAs], etc.) ***[Approved by NSF 7/28/21]***

Materials Design Pillar Goal 1.3: The team will prepare polymersomes responsive to the hypoxic microenvironment of the 3D cultures of the cancer cells, and development of polymer-based fluorescent nanoparticles for cancer cell imaging. In collaboration with the Cellular Systems Pillar, the developed nanomaterials will be used to investigate the biochemical changes and apoptosis of the cancer stem cells in the hypoxic niches of the 3D cultures after exposure to a gene transcription (small organic molecule) inhibitor to inhibit the stemness.

- **Materials Design Pillar Objective 1.3a:** Design and develop stimuli-responsive polymeric materials as nanocarriers.

    - Supporting Activities:
        - Investigation of pH responsive properties for the identified polymers including their responsive time, sensitivity and conditions.

        - Test the developed nanomaterials biocompatibility including toxicity, incubation time, nanoparticle concentration etc.
        - Application of the nanoparticles to cell culture.

- **Materials Design Pillar Objective 1.3b:** Design and develop silicon quantum dots (QDs) and polymer-QDs hybrids for bioimaging.

    - Supporting Activities:
        - Selection of the best precursor and chemical reaction pathway for making silicon quantum dots.
        - Testing of a few polymers, whose emission wavelengths overlap with the excitation wavelengths of the silicon quantum dots, hybridization feasibility with the silicon quantum dots.
        - Incubation of the developed silicon quantum dots and the hybrids of polymer-SiQDs with cancer cells and test their fluorescence imaging.

- **Materials Design Pillar Objective 1.3c:** Design and test polymer nanoparticles for vascular surrogacy for use in 3D cocultures.

    - Supporting Activities:
        - Design, preparation, and testing of hypoxia-responsive polymer nanoparticles on the hard and soft scaffolds, determine biochemical effects on the cancer cells.
        - Design, preparation, and testing of pH-responsive polymer nanoparticles on the hard and soft scaffolds, determine biochemical effects on the cancer cells.

Table 3. Materials Design Pillar Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

CCBSE RESEARCH GOALS: Materials Design Pillar						
Goal 1.1: Selection of optimal hard materials as porous bone-mimetic scaffolds • **Objective 1.1a: Design and optimize nanoclay scaffolds** • **Objective 1.1b: Characterize the scaffolds and demonstrate cancer cell growth**						
Objective 1.1a	**Specific milestones**					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: Prepare nanoclay scaffolds with amino acids for cancer cell growth	Prepare scaffolds based on prior studies	Optimize amino acid structure based on modeling, the loading amount, prepare two additional scaffolds, provide scaffolds to nanomaterials sub-group and Cellular Systems Pillar	Provide feedback to the Computational Approaches Pillar, optimize scaffold materials, provide the scaffolds for nanomaterials testing	Continue to prepare the optimized scaffold, provide them to Cellular Systems Pillar	Continue to prepare the optimized scaffold	Lead: **K. Katti,** Co-lead: G. Du, W. Xia, (Computational Approaches Pillar liaison), New Hire at NDSU ***[Responsibility change approved by NSF 9/8/21]***
Activity 2: Assist non-RU campuses involved in Activity 1 with compliance protocols ***[Metric change approved by NSF on 7/28/21]***	Assist with the initiation of conversations between non-RU faculty and RU campuses for the administration of necessary compliance protocols (IBC, MTAs)	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Leads: **K. Katti, M. Hoffmann, S. Mallik, J. Zhao** ***[Responsibility change approved by NSF on 5/16/22]***

Objective 1.1b	Specific milestones					
	Year 1	Year 2	Year 3	Year 4	Year 5	Responsible parties
Activity 1: Characterize the scaffolds and culture of breast and prostate cancer cells	Mechanical characterization, biocompatibility testing, nanomechanics, metastatic breast and prostate growth	Continue with characterization, optimize cell spheroid growth, nanomechanics	Optimize scaffold and cancer cell growth conditions, nanomechanics	Continue to prepare the optimized scaffolds with cancer cells and patient-derived samples	Continue to prepare the optimized scaffolds with cancer cells and patient-derived samples	Lead: **K. Katti** Co-lead: G. Du, W. Xia (Computational Approaches Pillar liaison), New Hire at NDSU ***[Responsibility change approved by NSF 9/8/21]***

Goal 1.2: Selection of optimal polymeric materials as soft tissue-mimetic scaffolds

- **Objective 1.2a: Design and optimize soft polymeric scaffolds**
- **Objective 1.2b: Characterize the scaffolds and demonstrate cancer cell growth**

Objective 1.2a	Specific milestones					
	Year 1	Year 2	Year 3	Year 4	Year 5	Responsible parties
Activity 1: Prepare soft scaffolds from Chi, Alg, and PgA, characterize the scaffolds	Prepare soft material scaffolds from two polymers	Optimize the scaffolds by altering the polymer composition and molecular weights, provide feedback to Computational Approaches Pillar and scaffolds for nanomaterials testing and Cellular Systems Pillar	Based on the feedback from the Computational Approaches and Cellular Systems Pillars optimize scaffold materials, provide scaffolds for nanomaterials testing and Cellular Systems Pillar	Continue to prepare the optimized scaffolds, provide scaffolds for nanomaterials testing and Cellular Systems Pillar	Continue to prepare the optimized scaffolds, provide scaffolds for nanomaterials testing and Cellular Systems Pillar	Lead: **K. Katti, K. Hossain** Co-leads: M. Quadir, B. Voels, M. Parker, A. Allard, W. Xia (Computational Approaches Pillar liaison)

Activity 2: Assist non-RU campuses involved in Activity 1 with compliance protocols ***[Metric change approved by NSF on 7/28/22]***	Assist with the initiation of conversations between non-RU faculty and RU campuses for the administration of necessary compliance protocols (IBC, MTAs)	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Leads: **K. Katti, M. Hoffmann, S. Mallik, J. Zhao** ***[Responsibility change approved by NSF on 5/16/22}***
Objective 1.2b	**Specific milestones**					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: Determine mechanical properties, cell viability in the scaffolds, analyze gene expression profiles	Mechanical characterization, nanomechanics, biocompatibility testing, breast and prostate cancer cell growth	Continue with characterization, optimize tumoroid growth, nanomechanics	Optimize scaffold and cancer cell growth conditions, nanomechanics	Continue to prepare the optimized scaffolds with cancer cells	Continue to prepare the optimized scaffolds with cancer cells	Lead: **K. Katti** Co-lead: G. Du, M. Quadir, K. Hossain, W. Xia (Computational Approaches Pillar liaison)
Activity 2: Assist non-RU campuses involved in Activity 1 with compliance protocols ***[Metric change approved by NSF on 7/28/21]***	Assist with the initiation of conversations between non-RU faculty and RU campuses for the administration of necessary compliance protocols (IBC, MTAs)	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Leads: **K. Katti, M. Hoffman n, S. Mallik, J. Zhao** ***[Responsibility change approved by NSF 5/16/22***

Goal 1.3: Develop a system for vascular surrogacy in 3D co-cultures

- **Objective 1.3a: Design and develop stimuli-responsive polymeric materials as nanocarriers**
- **Objective 1.3b: Design and develop silicon quantum dots (QDs) and polymer-QDs hybrids for bioimaging**
- **Objective 1.3c: Design and test polymer nanoparticles for vascular surrogacy**

Objective 1.3a	**Specific milestones**					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: Investigate pH responsive properties	Identify poly(silyl ether)s as pH-responsive materials	Modify and improve polymer structure and nanoparticles (NPs) properties	Make light-responsive polymeric materials for controlled release and optimize NPs fabrication	Prepare lanthanide binding polymeric materials and fabricate NPs	Prepare multi-responsive polymeric materials and fabricate NPs	Lead: **G. Du** Co-leads: J. Zhao, C. Combs, B. Sui ***[Responsibility change approved by NSF 7/28/21]***
Activity 2: Test biocompatibility	Fabricate and characterize NPs	Test toxicity of the polymers and NPs	Test the cell survival rate when the light-responsive polymer	Test biocompatibility of the lanthanide binding polymer NPs	Evaluate polymer-NPs biocompatibility *in vitro*	Lead: **G. Du** Co-leads: J. Zhao, C. Combs, B. Sui ***[Responsibility change approved by NSF 7/28/21]***
Activity 3: Examine cell culture usage		Determine optimal hard and soft scaffolds in *in vitro* studies	Determine optimal cancer cell identification using the polymer NPs in 3D cells	Image 3D hard and soft scaffolds using the prepared NPs	Determine cellular applications of the NPs in soft and hard scaffolds	Lead: **G. Du** Co-leads: J. Zhao, C. Combs, B. Sui ***[Responsibility change approved by NSF 7/28/21]***

Objective 1.3b	Specific milestones					
	Year 1	Year 2	Year 3	Year 4	Year 5	Responsible parties
Activity 1: Selection of the best precursor	Selection of precursors for making silicon quantum dots (QDs)	Modify quantum dot surface through chemical reactions	Selection of polymer to improve quantum dot's quantum yield	Making quantum dot and polymer hybrids	Prepare the optimized hybrid of quantum dots-polymer in 3D scaffold	Lead: **J. Zhao** Co-leads: G. Du, C. Combs, B. Sui ***[Responsibility change approved by NSF on 7/28/21]***
Activity 2: Testing feasibility	Optimization of QD's optical signals in cancer cells	Test toxicity and biocompatibility of the QDs	Test the selected polymers in bioimaging	Test the biocompatibility of hybrids in 3D cell Culture	Identification of intra cellular reactions using the hybrids in soft and hard scaffold	Lead: **J. Zhao** Co-leads: G. Du, C. Combs, B. Sui ***[Responsibility change approved by NSF on 7/28/21]***
Activity 3: Cancer cells imaging	Application of the QDs in cancer cell imaging	Application of the QDs for cancer cell identification	Application of the polymers in cancer cell imaging	Application of the hybrids in 3D cell culture	Application of the hybrids in 3D cell culture	Lead: **J. Zhao** Co-leads: G. Du, C. Combs, B. Sui ***[Responsibility change approved by NSF on 7/28/21]***

Objective 1.3c	Specific milestones					
	Year 1	Year 2	Year 3	Year 4	Year 5	Responsible parties
Activity 1: Design, preparation, and testing of hypoxia-responsive polymer nanoparticles	Synthesize a set of diblock copolymers	Optimize release properties of anticancer drugs using cancer cells on hard and soft material scaffolds	Select the optimal nanoparticle, demonstrate tumor targeting and tumor penetration on the hard and soft material scaffolds	Determine the effects of the released drugs on the cancer cells, mechanistic studies	Based on the mechanistic studies, select and demonstrate the efficacy of the optimal variant	Lead: **S. Mallik** Co-leads: M. Bobylev, K. Katti, G. Du ***[Responsibility change approved by NSF on 9/8/21]***
Activity 2: Design, preparation, and testing of pH-responsive polymer nanoparticles	Synthesize a set of triblock copolymers with conjugated anticancer drugs	Optimize pH-mediated release of the anticancer drugs	Select the optimal nanoparticle, demonstrate tumor targeting and penetration on the hard and soft scaffolds	Mechanistic studies on the pH-triggered drug release from polymer backbone, cellular effects of the released drugs	Based on the mechanistic studies, select and demonstrate the efficacy of the optimal variant	Lead: **M. Quadir** Co-leads: S. Mallik, K. Katti, G. Du~~, New Hire at NDSU~~ ***[Approved by NSF 9/8/21]***

Across this Pillar	Milestone metrics for Materials Design Pillar				
	Year 1	Year 2	Year 3	Year 4	Year 5
Objective 1.1a ***[Metric change approved by NSF on 9/8/21]***	Prepare 3 different biocompatible scaffolds	Develop 2 nanoclay scaffolds incorporating the amino acids and evaluate additional one hard scaffold	Select one optimal scaffold (critical)	Prepare enough scaffolds for the other Pillars and for Materials Design Pillar Goal 3	Prepare enough scaffolds for the other Pillars and for Materials Design Pillar Goal 3
Objective 1.1b	Complete characterizations on the scaffolds prepared in 1.1a. Demonstrate growth of MCF7 and PC3a cells	Demonstrate growth of MDA-MB-231 and PC3 cells and compare with MCF 7 and PC3a cells	Demonstrate tumoroid formation (critical)	Time evaluation of tumor growth on optimized scaffolds	The tumors on the scaffold are genetically and morphologically similar

Objective 1.2a	Prepare 3 different biocompatible scaffolds	Prepare 3 different biocompatible scaffolds	Select 1 optimal scaffold (critical)	Prepare enough scaffolds for the other Pillars and for Materials Design Pillar Goal 3 (nanomaterials testing)	Prepare enough scaffolds for the other Pillars and for Materials Design Pillar Goal 3
Objective 1.2b	Complete characterizations on the scaffolds prepared in 1.1a Demonstrate growth of MCF7 and PC3a cells	Demonstrate growth of MDA-MB-231 and PC3 cells and compare with MCF 7 and PCa	Demonstrate tumoroid formation (critical)	Time evaluation of tumor growth on optimized scaffolds	The tumors on the scaffold are genetically and morphologically similar
Objective 1.3a	Prepare 5 different PSEs and characterize nanoparticles	Demonstrate drug release in the tumoroids cells in scaffolds	The nanoparticles release drugs within desirable time in scaffolds (critical)	Prepare 3 different polymers, demonstrate imaging in the tumor cells in 3D scaffolds	Released drugs kill majority of cancer cells in scaffold/models
Objective 1.3b	QDs with stable signal in cells	Demonstrate good biocompatibility with cancer cell lines	Identify two polymers (critical)	Make two polymer-SiQD hybrids	Demonstrate optimized imaging
Objective 1.3c	Prepare 3 polymers with different hypoxia-responsive units, characterize nanoparticles	Prepare two additional polymers, demonstrate drug release in the tumoroids on hard and soft scaffolds	The nanoparticles release drugs within 2 hours in the hard and soft scaffolds (critical)	Release drugs kill at least 80% of the breast and prostate cancer cells on the scaffolds (critical)	Released drugs kill at least 80% of the cancer cells in the patient-derived model
	Prepare 3 polymers, characterize nanoparticles	Demonstrate drug release in the tumoroids on hard and soft scaffolds	The nanoparticles release drugs within 2 hours in the hard and soft scaffolds (critical)	Release drugs kill at least 80% of the breast and prostate cancer cells on the scaffolds (critical)	Released drugs kill at least 80% of the cancer cells in the patient-derived model

Across this Pillar	**Anticipated Outcomes of Materials Design Pillar**	
	Short-term (5 Years) (changes in knowledge or capacities)	**Long-term (10 Years) (changes in actions or conditions)**
Goal 1.1	Create new knowledge that expands ND's bioscience research, capacity, and expertise; increase success in federal funding; support translation of research into use.	Effect sustainable engagement and support of project participants; foster the ongoing development of a skilled, diverse workforce.

Goal 1.2	Create new knowledge that expands ND's bioscience research, capacity, and expertise; increase success in federal funding; support translation of research into use.	Effect sustainable engagement and support of project participants; foster the ongoing development of a skilled, diverse workforce.
Goal 1.3	Create new knowledge that expands ND's bioscience research, capacity, and expertise; increase success in federal funding; support translation of research into use.	Effect sustainable engagement and support of project participants; foster the ongoing development of a skilled, diverse workforce.
Overall Outcomes	Increase success in federal funding; support translation of research into use.	Supply research outcomes for growing/new bioscience ventures and partners; positively impact state economy

CCBSE Cellular Systems Pillar

The Cellular Systems Pillar is co-led by Archana Dhasarathy (UND) and John Wilkinson (NDSU). Team members include: Colin Combs (UND), Nicholas Galt (VCSU), Amanda Haage (UND), Kerry Hartman (NHSC), Kalpana Katti (NDSU), Jiha Kim (NDSU), and Hilde van Gijssel (VCSU).

This group is focused on increasing the capacity and expertise of the CCBSE researchers in basic and translational use of *in vivo*-like 3D cell cultures, which will ultimately (long-term outcome) allow the team to partner with regional health care providers to serve as a resource for personalized medicine approaches to cancer. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 4). The goal empathizes the creation of innovative models of heterogeneous, multi-cell 3D research cultures using multiple soft and hard material scaffolds designed by the Materials Design Pillar (via G. Du and K. Katti) and refined by the Computational Approaches Pillar (via M. Hoffmann ***[Approved by NSF 7/28/21]****).* Hence, the goals for the Cellular Systems Pillar are not hypothesis-driven.

This team will use three Tactics aligned with CCBSE Strategies 2, 3, and 4 to successfully meet its objectives: 1) validate multiple soft and hard tissue scaffolds as appropriate for *in vivo*-like 3D cultures (Strategy 2); 2) generate heterogeneous multicellular 3D cultures with improved *in vivo*-like tissue by sequential addition of cell types (macrophages, fibroblasts, etc.) with the cancer cell lines (Strategy 3); and, 3) model patient-derived organoid (PDO) systems and compare with the commonly used and commercially available mouse patient-derived xenograft (PDX) systems to develop a high throughput system that combines materials and modeling to create an improved culture paradigm for human *in vivo* relevance (Strategy 4).

The workflow will initially focus on prostate and breast cancer cell lines grown in both soft and hard tissue biomaterial scaffolds is designed to grow different cell types and tuned to optimize adhesion, porosity, and stiffness or evaluation of cellular response. These tests will allow better definition of the role of biointerfaces and 3D structures including those of a hypoxic nature, on complex multi-cell behaviors such as *in vitro* cell growth and differentiation, cancer growth/ metastatic progression, and multicellular tissue engineering. Research will then focus on creating innovative models of heterogeneous, multi-cell 3D research cultures using multiple soft and hard material scaffolds designed by the Materials Design Pillar and refined by the Computational Approaches Pillar.

Cellular Systems Pillar Goal 2.1: The team will use various biomaterial formulations (test scaffolds) developed by the Materials Design Pillar to develop a robust pipeline for both morphometric and molecular analysis for the purpose of validating whether characteristics of the test scaffolds are biocompatible and can be used to answer fundamental questions about cancer cells' behavior in response to different microenvironmental inputs. Then, using systematic analysis, the team will determine which materials have the most potential for high throughput content testing and, in conjunction with the Computational Approaches Pillar feed computation-driven models to optimize the materials design of the scaffolds. Specifically, this goal is to create innovative models of heterogeneous, multi-cell 3D research cultures.

- **Cellular Systems Pillar Objective 2.1:** Increase CCBSE capacity/expertise in basic and translational use of *in vivo*-like 3D cell cultures, which will ultimately (long-term outcome) allow the team to partner with regional health care providers to serve as a resource for personalized medicine approaches to cancer.

- Supporting Activities:
  - Validate multiple soft and hard tissue scaffolds as appropriate for *in vivo*-like 3D cultures, breast/prostate cancer monocultures.
  - Generate heterogeneous multicellular 3D cultures with improved *in vivo*-like tissue by sequential addition of cell types (macro-phages, fibroblasts, etc.) with the cancer cell lines.
  - Model patient-derived organoid (PDO) systems and compare with the commonly used and commercially available mouse PDX systems to develop a high throughput system that combines materials and modeling to create an improved culture paradigm for human *in vivo* relevance.
  - Assist non-RU campuses in the administration and development of necessary compliance protocols (institutional biosafety committee, materials transfer agreements, etc.)

Table 4. Cellular Systems Pillar Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

CCBSE RESEARCH GOAL: Cellular Systems Pillar						
Goal 2.1: Create innovative models of heterogeneous, multi-cell 3D research cultures • **Objective 2.1: Increase CCBSE capacity/expertise in basic and translational use of *in vivo*-like 3D cell cultures**						
Objective 2.1	**Specific milestones**					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: Validate multiple soft and hard tissue scaffolds	Standardize validation protocols using existing materials and compare to 2D culture Create protocol database Establish common reagent database Preliminary validation of 1st generation materials (viability, hypoxic responses, EMT/MET status) Submit data to Materials Design Pillar and Computational Approaches Pillar	Secondary validation of 1st generation materials (migration, adhesion, surface contact analysis) Preliminary validation of 2nd generation materials (viability, hypoxic responses, EMT/MET status) Update SOPs and reagents database Submit data to Materials Design Pillar and Computational Approaches Pillar	Tertiary validation of 1st generation materials (focal adhesion, migration, Transcriptomics) Secondary validation of 2nd generation materials (migration, adhesion, surface contact analysis) Update SOPs and reagents database Nanomaterial delivery assessment Submit data to Materials Design Pillar and	Quaternary validation of 1st generation materials (chromatin accessibility and modification assays) Tertiary analysis of 2nd generation materials Nanomaterial delivery assessment Submit data to Materials Design Pillar and Computational Approaches Pillar Update SOPs and reagents database	Quaternary validation of 2nd generation materials (chromatin accessibility and modification assays) Nanomaterial delivery assessment Submit data to Materials Design Pillar and Computational Approaches Pillar Update SOPs and reagents database	Leads: **A. Dhasarathy, J. Wilkinson** Co-leads: C. Combs, G. Du, (Materials Design Pillar liaison), K. Hartman; K. Katti, A. Haage, H. van Gijssel, M. Hoffmann (Computational Approaches Pillar liaison) ***[Responsibility changes approved by NSF on 7/28/21]***

			Computational Approaches Pillar			
Activity 2: Generate heterogeneous multicellular 3D cultures with improved *in vivo*-like tissue	Establishment of viable co-culture conditions of tumor cell lines and macrophages or fibroblasts Preliminary validation of 1st generation materials (viability, hypoxic responses, EMT/MET status) Data exchange with Materials Design Pillar and Computational Approaches Pillar Create protocol database Establish common reagent database Submit data to Materials Design Pillar and Computational Approaches Pillar	Comparison of co-cultures to tumors Establishment and maintenance of inter-cell contact sites between seeded populations Morphometric analysis Submit data to Materials Design Pillar and Computational Approaches Pillar Update SOPs and reagents database	Continued establishment and maintenance of inter-cell contact sites between seeded populations (via microscopic evaluation) Continued Morphometric analysis Submit data to Materials Design Pillar and Computational Approaches Pillar Update SOPs and reagents database	TAM analysis Gene expression profiling Nanocarrier assessments Continued Submit data to Materials Design Pillar and Computational Approaches Pillar Update SOPs and reagents database	Continued gene expression profiling Continued Nanocarrier assessments, including interruption of TAM/TAF/Cancer cell interactions Submit data to Materials Design Pillar and Computational Approaches Pillar Update SOPs and reagents database	Leads: **C. Combs, J. Wilkinson, A. Haage, N. Galt, G. Du,** (Materials Design Pillar liaison), **K. Katti, M. Hoffmann** ***[Approved by NSF 7/28/21],*** (Computational Approaches Pillar liaison) ***[Responsibility changes approved by NSF on 7/28/21]***

Activity 3: Develop a high throughput system that combines materials and modeling to create an improved culture paradigm for human *in vivo* relevance	Procure and maintain PDX models of breast and prostate cancer from commercial sources. Isolation of PDX tumors and establishment of growth as organoids (XOs) in culture Preliminary comparisons of XO tissues using viability assessments, and determination of phenotypes between 2D, scaffold, and *in vivo* maintenance conditions Establish clinical partnerships to obtain additional patient materials for organoid establishment Submit data to Materials Design and Computational Approaches Pillars	Detailed analysis of XO tissues in maintaining viability and proliferative capacity of explanted tissue when maintained upon the next-generation scaffolds. Establishing long-term (greater than 1 month) viable patient-derived organoid (PDO) lines. Optimization of standard procedures as needed Preliminary PDO assessments and testing success in maintaining viability and proliferative capacity of explanted tissue (greater than 1 month) when maintained upon the next-generation scaffolds Submit data to Materials Design	Continued XO explant grafting and comparison between scaffold and *in vivo* phenotypes Hypoxia-acidification analysis of XO scaffold cultures XO growth in the absence and presence of TAM/TAF seeding, comparative growth analysis Detailed analysis of PDO tissues in maintaining viability and proliferative capacity of explanted tissue when maintained upon the next-generation scaffolds Submit data to Materials Design and Computational Approaches Pillars Update SOPs and reagents database	Continued TAM/TAF seeding and comparative analysis of XO behavior to purified cell cultures Preliminary assessment of nanocarrier mediated pharmacologic interventions on TAMs-PDO communication Continued organoid assessments and testing success in maintaining viability and proliferative capacity of explanted tissue (greater than 1 month) when maintained upon the next-generation scaffolds Microenvironment assessments of XO and PDO scaffold cultures Submit data to Materials Design and Computational Approaches Pillars	Gene expression profiling comparisons of XO/PDO cultures to *in vivo* growth conditions Continued assessment of nanocarrier mediated pharmacologic interventions on TAMs-PDO communication Submit data to Materials Design and Computational Approaches Pillars Update SOPs and reagents database	Leads: **J. Kim, J. Wilkinson, C. Combs, A. Haage, H. van Gijssel**

	Update SOPs and reagents database	Pillar and Computational Approaches Pillar Update SOPs and reagents database		Update SOPs and reagents database		
Activity 4: Assist non-RU campuses involved in Activity 1 with compliance protocols ***[Metric changes approved by NSF on 7/28/21]***	Assist with the initiation of conversations between non-RU faculty and RU campuses for the administration of necessary compliance protocols (IBC, MTAs)	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Ensure that all necessary compliance protocols are in place at the non-RU campuses	Leads: **K. Katti, C. Combs, A. Dhasarathy, J. Wilkinson**

Across this Pillar	**Milestone metrics for Cellular Systems Pillar**				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**

Objective 2.1	Activity 1: Validation SOP creation using existing materials and 2D culture Protocol database creation based on validation Reagent database creation based on validation Completion of preliminary evaluation of provided first generation materials (baseline viability and growth, initial hypoxic response and EMT/MET signatures) e.g., 85% similar to 2D and matrigel cultures	Activity 1: Completion of secondary validation on provided 1st generation materials Completion of preliminary validation on provided 2nd generation materials Continued data exchange with Materials Design and Computational Approaches Pillars	Activity 1: Completion of tertiary validation, provided 1st generation materials Completion of secondary validation, provided 2nd generation materials Completion of preliminary nanomaterial delivery assessments Continued data exchange with Materials Design and Computational Approaches Pillars	Activity 1: Completion of quaternary validation, provided 1st generation materials Completion of tertiary validation, provided 2nd generation materials Completion of secondary nanomaterial delivery assessments Continued data exchange with Materials Design and Computational Approaches Pillars	Activity 1: Completion of quaternary validation, provided 2nd generation materials Completion of tertiary nanomaterial delivery assessments Continued data exchange with Materials Design Pillar and Computational Approaches Pillar

	Data exchange with Materials Design and Computational Approaches Pillars				
	<u>Activity 2:</u> A protocol for growth of multi-cellular cultures on provided hard and soft 1st generation materials	<u>Activity 2:</u> An optimized co-culture protocol for growth on provided hard and soft 1st generation materials A co-culture protocol for growth on provided hard and soft 2nd generation materials Establish phenotype marker criteria (e.g., morphology and proteins) for co-cultures on provided hard and soft 1st generation materials to compare to *in vivo* tumors	<u>Activity 2:</u> An optimized co-culture protocol for growth on provided hard and soft 2nd generation materials Establish phenotype marker criteria (e.g., morphology and proteins) for co-cultures on provided hard and soft 2nd generation materials to compare to *in vivo* tumors Protocol for nanocarrier design and drug delivery to 3D-cultures	<u>Activity 2:</u> Optimized protocol for nanocarrier design and drug delivery to 3D-cultures Genomic and transcriptomic characterization of co-cultures on hard and soft materials	<u>Activity 2:</u> Demonstration of nanocarrier-mediated drug delivery effects on co-culture viability and the established cellular phenotype markers Genomic and transcriptomic characterization of nanocarrier-mediated drug delivery to co-cultures on hard and soft materials
	Continued data exchange with Materials Design and Computational Approaches Pillars	Continued data exchange with Materials Design and Computational Approaches Pillars	Continued data exchange with Materials Design and Computational Approaches Pillars	Continued data exchange with Materials Design and Computational Approaches Pillars	Continued data exchange with Materials Design and Computational Approaches Pillars

	Activity 3: Successful establishment of PDX colonies as source of test materials Establishment and maintenance of PDX explant tissues (XOs) in scaffold cultures with greater than 1-month viability Development of standard protocols for sustained growth of XO tissues on next generation material scaffolds Continued data exchange with Materials Design and Computational Approaches Pillars	Activity 3: Complex Analysis of phenotypic criteria indicating XO tissues on scaffolds exhibit growth and gene expression characteristics similar to *in vivo* conditions Faster and more efficient growth of XO tissues under scaffold conditions when compared to *in vivo* maintenance Successful growth of PDO on the next-generation scaffolds Continued data exchange with Materials Design and Computational Approaches Pillars	Activity 3: Response to hypoxia/acidification by XO/scaffolds that mimics the *in vivo* tumor environment Development of a standard protocol for successful co-culture of XO with TAM/TAF on scaffolds Complex Analysis of phenotypic criteria indicating PDO tissues on scaffolds exhibit growth and gene expression characteristics similar to *in vivo* conditions Faster and more efficient growth of PDO tissues under scaffold conditions when compared to *in vivo* maintenance Continued data exchange with Materials Design and Computational Approaches Pillars	Activity 3: Successful long-term culture of PDO with TAM/TAF on scaffolds Presentation of miniature tumor microenvironment by PDO/TAM/TAF on scaffolds that is similar to TME of PDX tumor Continued data exchange with Materials Design Pillar and Computational Approaches Pillar	Activity 3: Changes in PDO/scaffold growth behavior, genetics, and morphology upon the intervention of TAM-PDO communication Presentation of drug resistance characteristics by explanted tumoroids that maintain similar properties to those observed *in vivo* Continued data exchange with Materials Design Pillar and Computational Approaches Pillar

Across this Pillar	Anticipated Outcomes of Cellular Systems Pillar	
	Short-term (5 Years) **(changes in knowledge or capacities)**	**Long-term (10 Years)** **(changes in actions or conditions)**
Goal 2.1	We will establish an interdisciplinary collaborative team across the state engaging faculty, graduate, and undergraduate students at NDSU, UND, the PUIs, and TCUs focused on developing our expertise in use of cell line and patient-based organoid cultures.	The established interdisciplinary partnerships will expand to include faculty, industry, and institutions beyond the initial ND-ACES. New programs, departments, or centers will formalize based upon the established expertise.
Overall Outcomes	Create new knowledge that expands ND's bioscience research, capacity, and expertise; catalyze ND's research/ computing capabilities; increase success in federal funding; support translation of research into use; inform citizens; establish diverse and sustainable bioscience/STEM education and professional development pathways; seek to broaden underserved participation; and impact beyond the project with partnerships and expanded internships.	Effect sustainable engagement and support of project participants; inform local/national research and stakeholder community, and public; expanded use of HPC/CI in PUI/MCU/TCU research and education; foster the ongoing development of a skilled, diverse workforce; positively impact state economy; supply research outcomes for growing/new bioscience ventures and partners.

CCBSE Computational Approaches Pillar

The Computational Approaches Pillar is co-led by Dinesh Katti (NDSU) and Deniz Cakir (UND ***[Approved by NSF 5/16/22]***)). Team members include: Marcus Fries (DSU ***[Approved by NSF 8/27/21***]), Mark Hoffmann (UND), Svetlana Kilina (NDSU), Trung Bao Le (NDSU), Lu Liu (NDSU), Yen Lee Loh (UND ***[Approved by NSF 5/16/22]***), and Wenjie Xia (NDSU). Support for this Pillar will come from the high-performance computing centers at NDSU (Khang Hoang ***[Approved by NSF 2/18/21]***) and UND (Aaron Bergstrom).

This group is focused on developing computational predictive models to provide useful design rules for creating biointerfaces. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 5). The goal emphasizes the development of an *in-silico* platform to predict tumor growth through the enhancement of connected learning, knowledge, and application across multiscale modeling, machine learning platforms, and experimental biomaterials and cellular data.

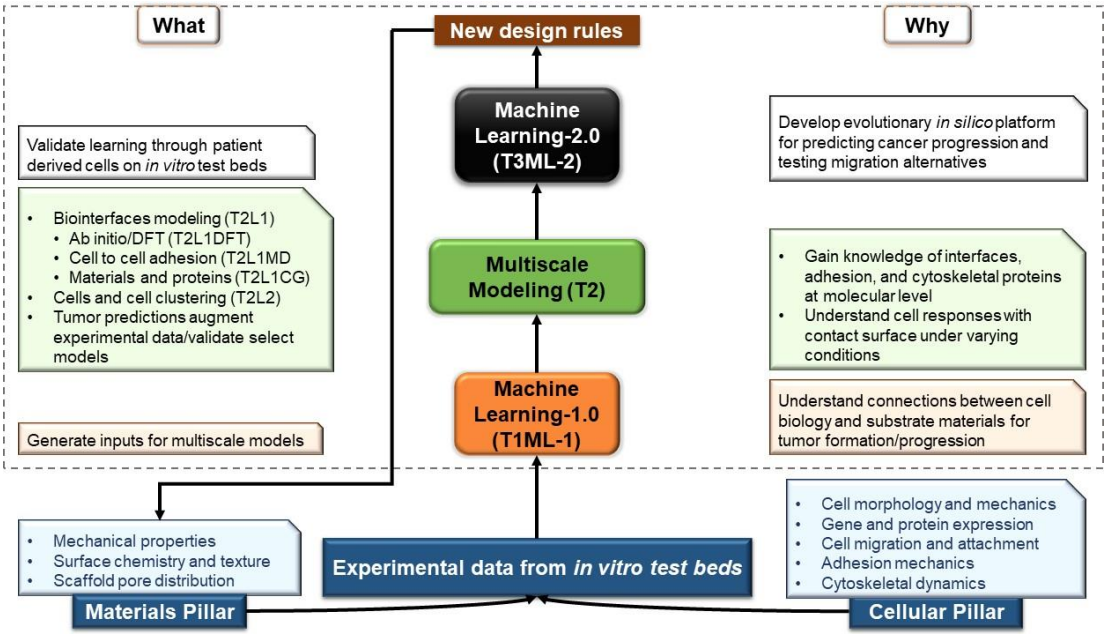


Figure 2. Iterative Tactics of Computational Approaches Pillar

This team will use four interdependent Tactics (Figure 2) aligned with CCBSE Strategies 1, 3, and 4 to successfully meet the objective of the Pillar. *Due to the intricate interdependencies of these Tactics, the activity milestones in this section are presented with additional detail*:

1) Machine learning-1 (T1ML-1) to understand connections between cellular biology and substrate materials.
2) Multiscale modeling (T2 is further delineated in the next paragraph) from nano- to macroscale.
3) Machine learning-2 (T3ML-2) that will use the data from T1ML-1 and T2 to develop the *in-silico* platform.
4) Computationally-driven materials design (T4).

The workflow will follow an iterative cycle (Figure 2) informed by the Materials Design Pillar (via W. Xia) and Cellular Systems Pillar (via M. Hoffmann ***[Approved by NSF 7/28/21]***). The Pillars will in turn be informed, via a reciprocal cycle of modeling of the cancer progression from the initial stages of cell attachment (primary site), to tumor formation, migration to secondary site

(metastasis), and growth in *in vitro* testing. The computationally created design rules can provide fundamental information to enhance the predictability of the cellular responses to various material surfaces and characteristics. The team, assisted by CI personnel, will build a collaborative research framework and proof-of-concept machine learning platform trained by experimental data gathered from cancer cell behavior on soft and hard tissue testbeds and computer simulations, resulting in multiscale models to predict disease progression.

Computational Approaches Pillar Goal 3.1: Conduct interdisciplinary/transdisciplinary research in biointerfaces (the interface between engineered and biological materials) that uses advanced research computing as a conduit for intellectual and translational advances. Specifically, this goal is the development and enhancement of computational approaches in the prediction of breast and prostate cancer tumor growth.

- **Computational Approaches Pillar Objective Pillar 3.1**: Enhance connected learning, knowledge, and application across multiscale modeling, machine learning platforms, and experimental biomaterials and cellular data, which will result in an evolutionary in-silico platform to predict tumor growth.
    - Supporting Activities:
        - Machine learning to understand connections between cellular biology and substrate materials based on experimental data.
        - Multiscale modeling from nano- to macroscale (Materials Design Pillar).
        - Multiscale modeling from nano- to macroscale (Cellular Systems Pillar).
        - Machine learning that will use data to develop the in-silico platform.
        - Design rules.

Table 5. Computational Approaches Pillar Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

CCBSE RESEARCH GOAL: Computational Approaches Pillar						
Goal 3.1: Develop and enhance computational approaches in the prediction of breast and prostate cancer tumor growth • **Objective 3.1: Create an evolutionary in-silico platform to predict tumor growth**						
Objective 3.1	**Specific milestones**					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: Machine learning to understand cellular and materials connections	C7-ML Bone Site Image recognition of cancer cells and bone cells based on existing databases and validate with 2D experiments	C7-ML Bone Site Image recognition of cell migration, clustering and tumor formation Role of material formulation on cellular growth in 3D	C7-ML Bone Site Identification of patterns in gene, protein expressions and other assay data and their relationship to tumor formation. Role of material properties formulation on cellular growth in 3D			Leads: C7-**L. Liu;** C8-**Y.L. Loh** ***[Responsibility change approved by NSF 5/16/22}***
	C8-ML Primary Site Image recognition of cancer cells from other cells in tissues from databases and validate with 2D experiments	C8-ML Primary Site Image recognition and prediction of cell migration, clustering and tumor formation Role of material formulation on cellular growth in 3D	C8-ML Primary Site Identification of patterns in gene, protein expressions and other assay data and their relationship to tumor formation Role of material properties			

			formulation on cellular growth in 3D and prediction of optimal properties			
[Mitigation change approved by NSF 8/27/21]		Build Machine learning capacity at a PUI and determine Y3-5 PUI researcher activity	Build Machine learning capacity at a PUI. Actively collaborate with ML researchers at NDSU and/or UND for image recognition of cell migration, clustering, and breast cancer tumor formation. Identify the role of material formulation on cellular growth in 2D	Identification of patterns in the gene, protein expressions, and other assay data and their relationship to breast cancer tumor formation. Role of material properties formulation on cellular growth in 2D		Lead: **M. Fries**, D. Katti, M. Hoffmann, L. Liu, Y.L. Loh ***[Responsibility change approved by NSF on 5/16/22]***
Activity 2: Multiscale modeling with Materials Design Pillar	M1-Ab-initio/DFT 10 unnatural amino acids-evaluation of partial charges. Evaluation of interactions with clay composite. Evaluation of interactions with two polymers	M1-Ab-initio/DFT Computational evaluation of additional/designer modifier molecules Evaluation of interactions with clay composite Evaluation of interactions with two polymers	M1-Ab-initio/DFT Computational evaluation of additional/ designer modifier molecules Evaluation of interactions with clay composite Evaluation of interactions with two polymers			Leads: M1 & M2-**M. Hoffmann**; M3 & M5-**D. Katti** M4-**W. Xia**; M6-**T. Le** ***[Responsibility change approved by NSF on 7/28/21]***

	M2-Ab-initio/DFT MD model for primary site composite: evaluation of partial charges and binding sites	M2-Ab-initio/DFT MD model for primary site composite with up to three formulations and densities: evaluation of partial charges and binding sites	M2-Ab-initio/DFT MD model for primary site composite with up to three additional formulations and densities: evaluation of partial charges and binding sites			
	M3-Molecular Dynamics MD and SMD simulations of existing PCN: Evaluation of mechanical properties at the molecular scale	M3-Molecular Dynamics MD and SMD simulations of PCNs using second candidate amino acid: Evaluation of mechanical properties at the molecular scale	M3-Molecular Dynamics MD and SMD simulations of PCNs using third candidate amino acid: Evaluation of mechanical properties at the molecular scale			
	M4-Coarse Graining Development of CG model for PCN and evaluation of mechanical properties	M4-Coarse Graining Development of CG model for PCN with second candidate amino acid with varying polymer characteristics	M4-Coarse Graining Development of CG model for PCN with third candidate amino acid with varying polymer characteristics			
	M5-Finite Element Modeling FEM model of PCN and evaluating constitutive responses	M5-Finite Element Modeling FEM model of PCN with second candidate amino acid. Evaluating constitutive responses	M5-Finite Element Modeling FEM model of PCN with third candidate amino acid. Evaluating constitutive responses			

	M6-Computational Fluid Dynamics CFD models for scaffolds with degradation	M6-Computational Fluid Dynamics CFD models for scaffolds with new formulations, synthesis parameters and degradation characteristics	M6-Computational Fluid Dynamics CFD models for scaffolds with new formulations, synthesis parameters and degradation characteristics			
Activity 3: Multiscale modeling with Cellular Systems Pillar	C1-Ab-initio/DFT Bone site Identification and characterization of Integrin domains interacting with clay. Identification and characterization of a representative Integrin- domains interacting with polymer. Evaluating the charge redistribution/ transfer over the substrate-protein interface	C1-Ab-initio/DFT Bone site Identification and characterization of cell-cell adhesion molecule (E-Cadherin) domains at cadherin junctions and at the cell anchor site	C1-Ab-initio/DFT Bone site Identification and characterization of representative Integrins (covering 4 classes)- domains interacting with clay Identification and characterization of representative Integrins (covering 4 classes)- domains interacting with polymer. Evaluating the charge redistribution/ transfer over the substrate-protein interface	C1-Ab-initio/DFT Bone site Identification and characterization of additional Integrins (covering 4 classes)- domains interacting with clay Identification and characterization of six additional Integrins (covering 4 classes)- domains interacting with polymer. Evaluating the charge redistribution/ transfer over the substrate-protein interface	C1-Ab-initio/DFT Bone site Studies on the influence of various ions on the adhesion of integrins with clay. Studies on the influence of various ions on the adhesion of integrins with polymers. Evaluating the charge redistribution/ transfer over the substrate-protein interface	C1-**S. Kilina;** C2-**D. Cakir;** C3, C5 & C11-**D. Katti;** C4, C9-**W. Xia;**

	C2-Ab-initio/DFT Primary site Identification and characterization of a representative Integrin- domains interacting with polymers 1 and 2. Identification and characterization of Integrin domain interacting with composites. Evaluating the charge redistribution/transfer over the substrate-protein interface	C2-Ab-initio/DFT Primary site Identification and characterization of cell-cell adhesion molecule (E-Cadherin) domains at cadherin junctions and at the cell anchor site.	C2-Ab-initio/DFT Primary site Identification and characterization of representative Integrins (covering 4 classes)- domains interacting with polymers 1 and 2 Identification and characterization of representative Integrins (covering 4 classes)- domains interacting with composites. Evaluating the charge redistribution/ transfer over the substrate-protein interface	C2-Ab-initio/DFT Primary site Identification and characterization of additional Integrins (covering 4 classes) - domains interacting with polymers 1 and 2 Identification and characterization of additional Integrins (covering 4 classes)- domains interacting with composites. Evaluating the charge redistribution/ transfer over the substrate-protein interface	C2-Ab-initio/DFT Primary site Studies on the influence of various ions on the adhesion of integrins with polymers. Evaluating the charge redistribution/ transfer over the substrate-protein interface	C6-**T. Le** C10-**M. Hoffmann** ***[Responsibility change approved by NSF 7/28/21]***
	C3-Molecular Dynamics Mechanics of Actin and actin dynamics Model construction of representative Integrin	C3-Molecular Dynamics Mechanics of Actin and actin dynamics with polymerization/depolymerization genes. Mechanics of representative Integrin on PCN and polymers	C3,C9,C10-Molecular Dynamics Mechanics of E-Cadherin junctions Mechanics of representative Integrin molecules on PCN and polymers	C3, C9, C10-Molecular Dynamics Mechanics of additional Integrin molecules on PCN and polymers		

	C4-Coarse Graining CG model of multiple integrins with PCN: evaluation of the mechanics of the interphase	4-Coarse Graining CG model of multiple integrins with primary site polymers: evaluation of the mechanics of the interphase	C4-Coarse Graining CG model of six integrins with bone site and primary site polymers: evaluation of the mechanics of the interphase	C4-Coarse Graining CG model of additional six integrins with bone site and primary site polymers: evaluation of the mechanics of the interphase	
	C5-Finite Element Modeling Development of cancer cell model on PCN	C5-Finite Element Modeling Simulations of experiments to evaluate cell substrate adhesion	C5-Finite Element Modeling Simulations of experiments to evaluate cell substrate adhesion, incorporating actin properties from MD and updated properties of interphase obtained from CG, to develop continuum adhesion models. Development of FEM models for Cell-Cell adhesion		
				C11-Multibody dynamics simulations integrated with Finite Element Modeling Modeling of cell migration on substrates	C11-Multibody dynamics simulations integrated with Finite Element Modeling Modeling of cell clustering on substrates

	C6-Computational Fluid Dynamics CFD models for scaffolds with cellular growth of MSCs	C6-Computational Fluid Dynamics CFD models for scaffolds with cellular growth of MSCs cocultured with prostate cancer cells	C6-Computational Fluid Dynamics CFD models for scaffolds with cellular growth of MSCs cocultured with breast cancer cells	C6-Computational Fluid Dynamics Parametric studies on scaffold and bioreactor geometry using CFD models with cellular growth of MSCs cocultured with prostate and breast cancer cells to aid in the development of scaffold pore geometry and bioreactors	C6-Computational Fluid Dynamics CFD models and simulations for cell transport to and through scaffolds to mimic cancer cell adhesion during metastasis	
Activity 4: Machine learning to develop the in-silico platform			C12, C14, C15, C16, C18-ML Bone Site Development and training of ML system with cancer progression (cell-cell adhesion and cell-substrate adhesion) data, biointerface parameters from multiscale modeling and experimental data (images and gene/protein expressions, material properties) from Cellular Systems Pillar and Materials Design Pillar	C12, C14, C15, C16, C18-ML Bone Site Training of ML system with cancer progression (cell-cell adhesion and cell-substrate adhesion) data, tumor formation data, biointerface parameters from multiscale modeling and experimental data (images and gene/protein expressions, material properties) from Cellular Systems Pillar and Materials Design Pillar (e.g., material properties, surface characteristics, chemistry, porosity,	C12, C14, C15, C16, C18-ML Bone Site Additional training of ML system with cancer progression (cell-cell adhesion and cell-substrate adhesion) data, tumor formation data, biointerface parameters from multiscale modeling and experimental data (images and gene/protein expressions, material properties) from Cellular Systems and Materials Design Pillars. Evaluate accuracy of predictions with	C12-**L. Liu** (lead); C13-**Y.L. Loh** (lead); C14-**W. Xia** ***[Responsibility change approved by NSF on 5/16/22]***

				3D confinement, adhesion proteins, interacting protein domains, ECM characteristic). Evaluate accuracy of predictions with separate datasets	separate datasets	
			C13, C14, C15, C16, C18-ML Primary Site Development and training of ML system with cancer progression (cell-cell adhesion and cell-substrate adhesion) data, biointerface parameters from multiscale modeling and experimental data from Cellular Systems and Materials Design Pillars	C13, C14, C15, C16, C18-ML Primary Site Training of ML system with cancer progression (cell- cell adhesion and cell-substrate adhesion) data, tumor formation data, biointerface parameters from multiscale modeling and experimental data from Cellular Systems and Materials Design Pillars. Evaluate accuracy of predictions with separate datasets	C13, C14, C15, C16, C18-ML Primary Site Additional training of ML system with cancer progression (cell-cell adhesion and cell-substrate adhesion) data, tumor formation data, biointerface parameters from multiscale modeling and experimental data from Cellular Systems and Materials Design Pillars. Evaluate accuracy of predictions with separate datasets	C15-**M. Hoffmann**; C16-**D. Katti;** C18-**T. Le** ***[Responsibility change approved by NSF on 7/28/21]***

[Metric change approved by NSF 8/27/21]					Primary site: Development and training of ML system with cancer progression (cell-cell adhesion and cell-substrate adhesion) data, biointerface parameters from multiscale modeling and experimental data from Cellular Systems and Materials Design Pillars	Lead: **M. Fries**, D. Katti, M. Hoffmann, L. Liu, Y.L. Loh
Activity 5: Design Rules				C17, C12, C13, C14, C15, C16, C18- Formulation of draft design rules for materials and scaffolds Interrogating the ML system to develop design rules for materials and scaffolds used for cancer progression experiments	C17, C12, C13, C14, C15, C16, C18- Formulation of updated design rules for materials and scaffolds Interrogating the ML system along with feedback from experiments using rules from previous iteration to develop design rules for materials and scaffolds used for cancer progression experiments	C12-**L. Liu;** C13-**Y.L. Loh;** C14-**W. Xia** C15-**M. Hoffmann***;* C16-**D. Katti;** C17- All Pillar and science leads C18-**T. Le** ***[Responsibility changes approved by NSF on 7/28/21 and 5/16/22]***

Across this Pillar	Milestone metrics for Computational Approaches Pillar				
	Year 1	Year 2	Year 3	Year 4	Year 5
Objective 3.1	Activity 1: Bone site - Classification Accuracy >=0.4 Primary site - Datasets generation from composite data sources for ML model training & identification of best performing ML algorithms for image recognition of the 4 types of cancer cells on bone stem cells Activity 2: M1-Ab-initio/DFT-Obtain binding interface information at the atomistic level M2-Ab-initio/DFT - Building atomistic models to understand interfaces M3-Molecular Dynamics - Successful model development	Activity 1: Bone site - Classification Accuracy >=0.5 Primary site - 1) Datasets generation for the cellular growth-material formulation using data from experimentalists and other collaborators Identification of high performing ML algorithms on image recognition for cell migration and clustering Activity 2: M1-Ab-initio/DFT - Obtain binding interface information at the atomistic level M2-Ab-initio/DFT - Building atomistic models to understand interfaces M3-Molecular Dynamics - Successful model development; compare mechanical properties with nanoindentation with results within an order of magnitude	Activity 1: Bone site – Classification Accuracy >=0.6 Primary site - Determination of patterns & optimal properties via ML Activity 2: M1-Ab-initio/DFT - Obtain binding interface information at the atomistic level M2-Ab-initio/DFT - Building atomistic models to understand interfaces M3-Molecular Dynamics - Successful model development; compare mechanical properties with nanoindentation with results within an order of magnitude		

	M4-Coarse Graining - CG model of clay developed; CG model of polymer developed; CG force field validated	M4-Coarse Graining - CG model of clay developed; CG model of PCN developed; CG force field validated	M4-Coarse Graining - CG model of clay developed; CG model of PCN developed; CG force field validated		
	M5-Finite Element Modeling - Successful model development	M5-Finite Element Modeling - Successful model development. Elastic modulus within an order of magnitude of nanoindentation/ macroscale experiments	M5-Finite Element Modeling - Successful model development. Elastic modulus within an order of magnitude of nanoindentation/ macroscale experiments		
	M6-Deterministic models for degrading scaffold under shear flows developed; Rate of degrading validated	M6-Computational Fluid Dynamics - Range of model parameters for degradable scaffold established; Models for cell interaction and migration developed	M6-Computational Fluid Dynamics - Multi-resolution CFD model for scaffold developed; Local distribution of shear stresses in complex geometries validated		
	Activity 3: C1-Ab-initio/DFT Bone site - Creation of reduced models for integrin domains, nanoclays, and polymers	Activity 3: C1-Ab-initio/DFT Bone site - Validation and improvement of reduced models for nanoclays and polymers interacting with Integrin domains	Activity 3: C1-Ab-initio/DFT Bone site	Activity 3: C1-Ab-initio/DFT Bone site	Activity 3: C1-Ab-initio/DFT Bone site

	C2-Ab-initio/DFT - Building atomistic models to model bio-interfaces	C2-Ab-initio/DFT - Building atomistic models to represent/model bio-interfaces	C2-Ab-initio/DFT Primary site - Building atomistic models to model bio interfaces	C2-Ab-initio/DFT Primary site	C2-Ab-initio/DFT Primary site - Building atomistic models to represent/model bio-interfaces
	C3-Molecular Dynamics - Successful model development of actin and integrin. Obtaining mechanical properties of actin from SMD	C3-Molecular Dynamics - Successful model development of actin and depolymerization genes; integrin on surfaces; Obtaining mechanical properties of actin and integrin from SMD	C3, C9, C10-Molecular Dynamics - Determine the mechanical properties of E-Cadherin junctions; Determine the mechanical properties of the integrin molecules on PCN and polymers	C3, C9, C10-Molecular Dynamics - Determine the mechanical properties of the additional six integrin molecules on PCN and polymers	C11-Multibody dynamics simulations integrated with Finite Element Modeling - Successful development of multibody dynamics simulations model for cell migration
	C4-Coarse Graining - CG model of integrins developed; Integrins-PCN interfacial interactions captured by CG modeling	C4-Coarse Graining – Continued	C4-Coarse Graining - Mechanical properties of interphases obtained with CG modeling for six integrins and varying interfacial design parameters	C4-Coarse Graining - Mechanical properties of interphases obtained with CG modeling for additional six integrins with extended interfacial design parameters	
	C5-Finite Element Modeling - Successful development of FEM cell model	C5-Finite Element Modeling –Successful development of FEM cell model on substrate; incorporation of adhesion parameters from C1 through C4; calibration with experiments	C5-Finite Element Modeling - Successful development of FEM cell model on substrate and Cell-Cell adhesion model; incorporation of adhesion parameters from C1 through C4; calibration with experiments		

	C6-Computational Fluid Dynamics - Continuum representation of actin networks in cell membrane developed; Cell adhesion model developed and validated	C6-Computational Fluid Dynamics - Models for cell migration on a clay substrate developed and validated	C6-Computational Fluid Dynamics - CFD simulations of flows around groups of cancer cells populated on a substrate	C6-Computational Fluid Dynamics - Using measures such as cell density and alignment to validate CFD models for cellular migration on the surface of scaffold	C6-Computational Fluid Dynamics - Full-scale simulation of cell migration in a bio-reactor. Resolution provides from millimeter to micrometer (three order of magnitudes). Flow distribution and shear stresses will be provided in all pores of the scaffold
			Activity 4: C12, C14, C15, C16, C18-ML Bone Site - Obtain the knowledge to construct preliminary rules of designing new scaffold materials for bone site. Classification Accuracy >=0.6	Activity 4: C12, C14, C15, C16, C18-ML Bone Site - Obtain the knowledge to construct fundamental rules of designing new scaffold materials for bone site; Classification Accuracy >=0.7; Generate simulated datasets under perturbed conditions and use those datasets to build ML models for cell migration; ML predictive models derived; ML model predictions validated against modeling and experiments	Activity 4: C12, C14, C15, C16, C18-ML Bone Site - Accuracy >=0.8; ML predictive models derived; ML model predictions validated against modeling and experiments; obtain the knowledge to construct fundamental rules of designing new scaffold materials for bone site

			C13, C14, C15, C16, C18-ML Primary Site - Obtain the knowledge to construct preliminary rules of designing new scaffold materials for primary site. Statistical and reduced order models will be developed to predict where cancer cells migrate and grow	C12, C14, C15, C16, C18-ML Bone Site - ML predictive models derived; ML model predictions validated against modeling and experiments; obtain the knowledge to construct fundamental rules of designing new scaffold materials for bone site C13, C14, C15, C16, C18-ML Primary Site - ML predictive models derived; ML model predictions validated against modeling and experiments; obtain the knowledge to construct fundamental rules of designing new scaffold materials for primary site <u>Activity 5</u>: C17, C12, C13, C14, C15, C16, C18- Parameter-structure-property relationships drawn for design of materials; optimized design parameters identified; develop design rules (geometry, material properties) for fluid flows in degradable scaffolds	C13, C14, C15, C16, C18-ML Primary Site - Accuracy >=0.8; ML predictive models derived; ML model predictions validated against modeling and experiments; obtain the knowledge to construct fundamental rules of designing new scaffold materials for primary site <u>Activity 5</u>: C17, C12, C13, C14, C15, C16, C18- Formulation of updated design rules for materials and scaffolds - Parameter-structure-property relationships refined for design of materials; materials design parameters finalized; validate design rules and establish optimized ranges of parameters

Across this Pillar	Anticipated Outcomes of Computational Approaches Pillar	
	Short-term (5 Years) **(changes in knowledge or capacities)**	**Long-term (10 Years)** **(changes in actions or conditions)**
Goal 3.1	Build capacity - researchers and students in computational areas of multiscale modeling and machine learning targeted towards biomedical research. Development of robust computational models spanning multiple length scales for tissue engineered scaffolds and cells seeded on scaffolds. This will lead to enhanced understanding of cell adhesion mechanisms on materials and the understanding of mechanisms that influence mechanical properties of materials and scaffolds. Development of ML tools/processes to predict cellular behavior on tissue engineering materials and scaffolds leading to proof of concept for using ML for predicting cancer progression in *in vitro* systems.	Increased workforce in the region trained in leveraging computations for discoveries and design in biomedical fields. Increased graduate student enrollment in programs such as biomedical engineering, materials and nanotechnology, computer science with research focus in biomedical areas. New research center(s) such as ERCs, MERSECs focused on translational biomedical research driven by computations. Support biomedical companies (startups and existing) with technologies, IP and workforce. Collaborate with physicians to validate and revise predictive models and findings with patient data for potential deployment for real world applications.
Overall Outcomes	Enhanced understanding of biointerfaces via computations and their role on cellular response and development of design rules for materials design.	Predictive tools for cancer progression.

CCBSE - Overall Summary

As previously stated, the core goal of the CCBSE is to expand bioscience research capacity in improved soft tissue and bone-mimetic scaffolds and models that create and increase the knowledge and advanced understanding of the biochemistry and cell biology of cancer cells and tumors. This goal will be accomplished through the successful completion of the Materials Design Pillar, Cellular Systems Pillar, and Computational Approaches Pillar metrics outlined above in Tables 3, 4, and 5. Additional CCBSE outcomes that will be obtained through the combined efforts of the three Pillars are outlined in Table 6. Success of the core goal lays the foundation for the secondary goal to increase capacity and knowledge in the area of nanoparticle-based delivery systems by pursuing developmental research, which is a long-term goal for the CCBSE and not a part of the ND-ACES project.

Table 6. CCBSE Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

CCBSE RESEARCH: Overall					
Core Goal: Expand bioscience research capacity in improved soft tissue and bone-mimetic scaffolds and models that create and increase the knowledge and advanced understanding of the biochemistry and cell biology of cancer cells and tumors					
CCBSE Strategies	**Specific milestones**				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Strategy 1: Construct innovative 3D biocompatible structures of hard and soft tissues	Successful completion of Materials Design and Computational Approaches Pillar Y1 activities and metrics	Successful completion of Materials Design and Computational Approaches Pillar Y2 activities and metrics	Successful completion of Materials Design and Computational Approaches Pillar Y3 activities and metrics	Successful completion of Materials Design and Computational Approaches Pillar Y4 activities and metrics	Successful completion of Materials Design and Computational Approaches Pillar Y5 activities, objectives, and goals
Strategy 2: Design novel cell culture paradigms to accurately model *in vivo* tumor cell biology	Successful completion of Cellular Systems Pillar Y1 activities and metrics	Successful completion of Cellular Systems Pillar Y2 activities and metrics	Successful completion of Cellular Systems Pillar Y3 activities and metrics	Successful completion of Cellular Systems Pillar Y4 activities and metrics	Successful completion of Cellular Systems Pillar Y1 activities Y5 activities, objectives, and goals
Strategy 3: Provide a fundamental understanding of biointerfaces that adapts to biomedical and biotechnology research and translates to industry	Successful completion of Materials Design, Cellular Systems, and Computational Approaches Pillar Y1 activities and metrics	Successful completion of Materials Design, Cellular Systems, and Computational Approaches Pillar Y2 activities and metrics	Successful completion of Materials Design, Cellular Systems, and Computational Approaches Pillar Y3 activities and metrics	Successful completion of Materials Design, Cellular Systems, and Computational Approaches Pillar Y4 activities and metrics	Successful completion of Materials Design, Cellular Systems, and Computational Approaches Pillar Y5 activities, objectives, and goals
Strategy 4: Use iterative computational learning to establish models capable of	Successful completion of Materials Design, Cellular Systems, and Computational	Successful completion of Materials Design, Cellular Systems, and Computational	Successful completion of Materials Design, Cellular Systems, and Computational	Successful completion of Materials Design, Cellular Systems, and Computational	Successful completion of Materials Design, Cellular Systems, and Computational

predicting cell responses on 3D biointerfaces	Approaches Pillar Y1 activities and metrics	Approaches Pillar Y2 activities and metrics	Approaches Pillar Y3 activities and metrics	Approaches Pillar Y4 activities and metrics	Approaches Pillar Y5 activities, objectives, and goals
Secondary Goal: Increase capacity and knowledge in the area of nanoparticle-based delivery systems by pursuing developmental research					
CCBSE Strategies	**Specific Milestones**				
	Year 1	Year 2	Year 3	Year 4	Year 5
Strategy 4: Use iterative computational learning to establish models capable of predicting cell responses on 3D biointerfaces	Outside the scope of ND-ACES. However, knowledge gained in ND-ACES (Years 1-5) will serve as the basis for this long-term strategy				
Strategy 5: Develop an understanding of polymer nanoparticles as a surrogate for vascular transport of effector molecules	Outside the scope of ND-ACES				

Overall milestone metrics for CCCBSE, in addition to those outlined in Tables 3, 4, and 5	
Number of new hires	2
Total number of peer-review publications	140
Number of collaborative products/outputs (one senior author from two or more ND-ACES institutions) ***[Metric change approved by NSF on 5/16/22]***	70
Total number of conference presentations by CCBSE senior personnel	90
Total number of submitted research proposals (PI/Co-PI from two or more ND-ACES institutions)	50
Number of submitted collaborative proposals	25

Number of CAREER proposals submitted	2-4
Total external research funding (million $) – 5-year total is cumulative	$25M
Number of projects funded with private sector partners	12
Number of graduate students trained (some may be counted in multiple years)	140
Number of conference presentations by graduate students (oral and poster)	120
Number of undergraduate students trained (some may be counted in multiple years)	70
Number of conference presentations by undergraduate students (oral and poster)	80
Seed Funding: seed funding support of $60,000 in Translational Research Initiative Project and an additional $101,655 in other research opportunity support – 5-year total is cumulative	$161,655
Number of CCBSE research participant meetings (to be scheduled monthly)	50-60

Across the CCBSE	Anticipated Outcomes of CCBSE	
	Short-term (5 Years) (changes in knowledge or capacities)	Long-term (10 Years) (changes in actions or conditions)
Meet CCBSE's Core Goal	Create new knowledge that expands ND's bioscience research, capacity, and expertise; catalyze ND's research/ computing capabilities; increase success in federal funding; support the translation of research into use; and have impact beyond the project with partnerships and expanded internships.	Effect sustainable engagement and support of project participants and supply research outcomes for growing/new bioscience ventures and partners.

PROSPER Implementation

Expanding North Dakota's emerging biosciences capacity through a STEM-enabled, well-trained workforce positions ND-ACES as North Dakota's leading scientific and educational resource and will signify successful completion of this important work. PROSPER efforts incorporate both faculty and students at all 10 participating institutions in collaborative research (and one institution, SBC, has chosen to focus solely on outreach), early career development, education enhancement, and outreach to increase the abilities of early career faculty, increase advanced scientific computing capabilities, and broaden the participation and number of STEM undergraduate and graduate students. North Dakota's K-12 sectors are also crucial to a sustainable ND STEM pathway; thus, another key component will be education and outreach in rural and tribal K-12 schools. Teachers, particularly those in grades 6-12, will engage in professional development activities where they will learn about tools to expose and engage their students in biosciences inquiry. Additionally, to bring the new knowledge and companion products to industry, focused activities will build or expand on existing collaborative industry/medical partnerships. Finally, a suite of communication activities will engage, inform, and educate ND stakeholders and citizens, as well as national audiences about ND-ACES scientific and outreach efforts. PROSPER is comprised of four sections/elements: 1) Education and Workforce Development; 2) Broadening Participation; 3) Partnerships and Collaborations; and, 3) Communication and Dissemination.

PROSPER Education and Workforce Development

Education and Workforce Development is led by Rachel Navarro and Sarah Sletten (both UND) and co-led by Richard (Josh) Wayt (ND EPSCoR). Team members include: Austin Allard (TMCC), Aaron Bergstrom (UND), Mikhail Bobylev (MiSU), Van Doze (UND), Marcus Fries (DSU ***[Approved by NSF 8/27/21]***) Nicholas Galt (VCSU), Kerry Hartman (NHSC), Khang Hoang (NDSU ***[Approved by NSF 2/18/21]***), Mark Hoffmann (UND ***[Approved by NSF 5/16/22]***), Khwaja Hossain (MaSU), Kalpana Katti (NDSU), Mafany Ndiva Mongoh (SBC), Mike Parker (CCCC), Ryan Summers (UND), Hilde van Gijssel (VCSU), and Brent Voels (CCCC).

The team will facilitate a variety of activities that grow knowledge, motivate innovation, and develop talent in materials engineering, cell biology, and computational sciences with special emphasis on the inclusive excellence of underrepresented groups (e.g., women, and racial and ethnic minorities) along the education/career continuum. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 7).

Working in close conjunction with all ND-ACES participants, this initiative supports faculty professional development, student training, and K-12 student bioscience, engineering, and computational exposure. This group's efforts link to ND-ACES tracks 2, 4, and 5 (which are adopted as the Strategies for Education and Workforce Development) and integrate with the CCBSE goals.

Education and Workforce Development Element Goal 4.1: Strengthen North Dakota's bioscience/STEM ecosystem by building a diverse pool of competitive researchers, skilled workers, effective educators, and engaged students.

- **Education and Workforce Development Element Objective 4.1a:** Retain/advance CCBSE's early-career faculty and graduate students in bioscience/STEM careers and disciplines, particularly those from underrepresented groups (e.g., women, and racial and ethnic minorities).

- Supporting Activities:
    - Early Career Faculty (ECF) Mentoring Program.
    - Early Career Faculty Professional Development Activities.
    - Student Research Training Groups (RTG).
    - Graduate Student Cyber-infrastructure and STEM Teaching Assistantships (State Office).

- **Education and Workforce Development Element Objective 4.1b:** Engage/develop K-16 student interest in bioscience/STEM careers and disciplines, particularly those from underrepresented groups (e.g., women, and racial and ethnic minorities).
    - Supporting Activities:
    - Distributed Research Experience for Undergraduates (dREU).
    - Engagement of grade 6-12 students in Nature/Sunday Academy activities.
    - Training of rural and tribal K-12 teachers in the use of PROSPER bioscience lesson plans.
    - Pre-service STEM teachers will engage in rural/tribal student teaching experiences.

Table 7. Education and Workforce Development Element Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

BROADER IMPACTS/PROSPER GOAL: Education and Workforce Development Element						
Goal 4.1: Strengthen North Dakota's bioscience/STEM ecosystem by building a diverse pool of competitive researchers, skilled workers, effective educators, and engaged students • **Objective 4.1a: Retain/advance CCBSE's early career faculty and graduate students** • **Objective 4.1b: Engage/develop K-16 student interest in biosciences**						
Objective 4.1a	**Specific milestones**					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: Early Career Faculty Mentoring Program ***[Metric changes approved by NSF 3/9/21 and 5/10/22]***	Set baseline for Early Career Faculty professional/ technical skills, self-efficacy, persistence intentions, retention, sense of belonging and scholarly productivity. Hold monthly Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty. Gather information from ECF about their mentorship and professional development needs. Identify mentor training materials and/or programs	Two new faculty will be hired. Hold monthly Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty. PROSPER personnel (at least 2) will engage in training and/or independent study in mentorship best practices via the CIMER Project (https://cimerproject.org/) (Summer-Fall 2021). CIMER Project	Hold monthly Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty. CIMER Project Trained PROSPER personnel will then train 25% ND ACES CBBSE Faculty in mentorship best practices	Hold monthly Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty	Hold monthly Pillar meetings between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty	Lead: **R. Navarro,** S. Sletten

		Trained PROSPER personnel will then train 25% ND ACES CBBSE Faculty in mentorship best practices				
Activity 2: Early Career Faculty Professional Development Activities	Identify or develop in-person and Web-based ECF professional development activities	Continued	Continued	Continued	Continued	Lead: **R. Navarro,** S. Sletten
Activity 3: Student Research Training Groups (RTG)	Establish student mentor-mentee relationships and train students in research and technical scientific communication skills & set baselines for student professional/ technical skills, self-efficacy, persistence intentions, retention, sense of belonging, and scholarly productivity	Student mentor-mentee relationships will be revisited, creating new relationships for new students and revising ones that necessitate changes, and transitioning graduate students from mentee to mentor as appropriate	Continued	Continued	Continued	Lead: **S. Sletten**, R. Navarro

Activity 4a: Graduate Student Cyber-Infrastructure	Graduate students will receive CI training and support	Continue to provide CI support to graduate students and conduct a Cyberinfrastructure (CI) Needs Survey of the ND-ACES CCBSE pillar (Computational, Materials, and Cellular) senior personnel (CCBSE researchers) and their graduate students	Continue to provide CI support to graduate students and based on the results of the Y2 survey and input from the CCBSE Computational Approaches Pillar Leads, CCAST (NDSU's HPC center) and CRC (UND's HPC center) will: 1) each develop a new, or customize an existing, CI workshop, which will be offered a min of at least once per year and 2) provide CI training to CCBSE faculty researchers and graduate students	Continued	Continued	Lead: **A. Bergstrom, K. Hoang, J. Wayt** ***[Responsibility changes approved on 2/18/21, 8/27/21, 10/18/21, and 5/10/22]***
Activity 4b: STEM Teaching Assistantship		Doctoral and/or Masters students receive and complete teaching assistantships at TCUs/ PUIs/MCU	Continued	Continued	Continued	Lead: **J. Wayt,** A. Allard, M. Bobylev, M. Fries, N. Galt, K. Hartman, M. Hoffmann, K. Hossain, K. Katti, M. Parker, S. Sletten, H. van Gijssel, B. Voels ***[Responsibility changes approved on 8/27/21, 10/18/21, and***

						5/10/22]

Objective 4.1b	Specific milestones					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: Distributed Research Experience for Undergraduates (dREU)	Distributed REU students placed. IRB will be written	Continued	Continued	Continued	Continued	Leads: **J. Wayt,** S. Sletten ***[Responsibility changes approved by NSF on 10/18/21 and 5/10/22]***
Activity 2: Engage grade 6-12 students in Nature/Sunday Academy	Set baselines for Grade 6-12 students (i.e., Nature/Sunday Academy participants) beliefs and attitudes about, interests in, and intentions to pursue bioscience/STEM disciplines	Increased numbers over baseline	Increased numbers over prior year	Increased numbers over prior year	Increased numbers over prior year	Leads: **R. Navarro**, J. Wayt, R. Burns ***[Responsibility changes approved by NSF on 8/27/21 and 5/10/22]***
Activity 3: Training of Rural and tribal K-12 teachers in the use of PROSPER bioscience modules	Plan and start developing PROSPER bioscience modules	Module 1 implemented, Module 2 developed, and K-12 teachers trained	Module 1 refined, Module 2 implemented, and K-12 teacher training continued	Module 1 disseminated, Module 2 refined, and K-12 teacher training continued	Modules 1 and 2 disseminated and K-12 teacher training continued	Leads: **R. Summers**, J. Wayt ***[Responsibility changes approved by NSF on 10/18/21 and***

						5/10/22]
Activity 4: Pre-service STEM teachers will engage in rural/tribal student teaching experiences	Establish pilot program that places preservice student teachers in rural/ tribal schools in the Spring 2021	Expand program to all pre-service teacher candidates at ND-ACES affiliated RUs, PUIs, and MCU in Fall 2021. Place two preservice student teachers in rural/tribal schools in Fall 2021 and Spring 2022	Continued	Continued	Continued	Leads: **R. Summers,** J. Wayt ***[Responsibility changes approved by NSF on 10/18/21 and 5/10/22]***

Across this Element	**Milestone metrics for Education and Workforce Development Element**				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 4.1a ***[Metric changes approved by NSF on 3/9/21 and 5/10/22]***	Activity 1: ECFs retained. Set baselines. Monthly Pillar meetings held between CCBSE research leads and faculty as a means of providing mentoring and guidance to ECF faculty. Information gathered from ECF about their mentorship and professional development needs	Activity 1: ECFs retained. 1 new faculty member hired at NDSU and 1 new faculty member hired at UND. Meet/ exceed baselines. Monthly Pillar meetings held between CCBSE research leads and faculty. Minimum of two EWD Personnel trained and prepared to facilitator training for all ND-ACES CCBSE faculty in mentorship best practices (Summer- Fall 2021). Train 25% ND ACES CBBSE Faculty in mentorship best practices by June 30,	Activity 1: ECFs and new hires retained. Meet/ exceed baselines. Monthly Pillar meetings held between CCBSE research leads and faculty. Train an additional 25% of ND-ACES CCBSE Senior Faculty in mentorship best practices by June 30, 2023	Activity 1: ECFs and new hires retained. Meet/exceed baselines. Monthly Pillar meetings held between CCBSE research leads and faculty	Activity 1: ECFs and new hires retained. Meet/exceed baselines. Monthly Pillar meetings held between CCBSE research leads and faculty

		2022			
	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 2 PD activities); track engagement with PD activities with goal that at least 70% of ECF participate	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 3 PD activities); track engagement with PD activities with goal that at least 70% of ECF participate	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 3 PD activities); track engagement with PD activities with goal that at least 70% of ECF participate	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 3 PD activities); track engagement with PD activities with goal that at least 70% of ECF participate	Activity 2: Develop list of ECF professional development activities available and disseminated to ECFs (alternatively develop and implement 2 PD activities); track engagement with PD activities with goal that at least 70% of ECF participate
	Activity 3: 10 mentor/mentee pairs will be established; mentor/ mentee pairs will meet monthly; mentee individual development plan created; 50% of RTG students present work at one regional/national meeting; set baselines	Activity 3: 10 mentor/ mentee pairs will be maintained or established; mentor/ mentee pairs will meet monthly; mentee individual development plan created; 80% of students present work at one regional/national meeting; 75% of students publish (first author) paper prior to graduation; meet/ exceed baselines	Activity 3: 10 mentor/ mentee pairs will be maintained or established; mentor/ mentee pairs will meet monthly; transition from mentee to mentor for graduate students progressing; mentee individual development plan created; 80% of students present work at one regional/national meeting; 75% of students publish (first author) paper prior to graduation; meet/exceed baselines	Activity 3: 10 mentor/ mentee pairs will be maintained or established; mentor/ mentee pairs will meet monthly; transition from mentee to mentor for graduate students progressing; mentee individual development plan created; 80% of students present work at one regional/national meeting; 75% of students publish (first author) paper prior to graduation; meet/exceed baselines	Activity 3: 10 mentor/ mentee pairs will be maintained or established; mentor/ mentee pairs will meet monthly; transition from mentee to mentor for graduate students progressing; mentee individual development plan created; 80% of students present work at one regional/national meeting; 75% of students publish (first author) paper prior to graduation; meet/ exceed baselines
[Metric changes approved by NSF 8/27/21]	Activity 4a: 30% of the total participants are trained	Activity 4a: 80% response from CCBSE researchers and	Activity 4a: 2 (1 from CCAST and 1 from CRC) new or customized CI	Activity 4a: 2 (1 from CCAST and 1 from CRC) new or customized CI	Activity 4a: 2 (1 from CCAST and one from CRC) new or customized

		graduate students to the CI Needs Survey	workshops developed	workshops developed	CI workshops developed
			Both workshops offered at least once during Y3	Both workshops offered at least once during Y4	Both workshops offered at least once during Y5
			10% of CCBSE researchers and graduate students participate in the Y3 workshop or other CI training programs	10% of CCBSE researchers and graduate students participate in the Y4 workshop or other CI training programs	10% of CCBSE researchers and graduate students participate in the Y5 workshop or other CI training programs
	2 CI assistantships offered; 2 CI GRAs hired	2 CI GRAs hired	2 CI GRAs hired	2 CI GRAs hired	2 CI GRAs hired
[Metric changes approved by NSF 2/9/22]	Activity 4b: THIS PROGRAM HAS BEEN MOVED TO Y2 DUE TO COVID-19	Activity 4b: Explore virtual options for doctoral student assistants	Activity 4b: 1-2 GTAs hired	Activity 4b: 1-2 GTAs hired	Activity 4b: 1-2 GTAs hired
		Reallocate unused funding to additional TCU/PUI/MCU faculty time.	Incorporate virtual options into the program	Continued	Continued
	Activity 5: N/A	Activity 5: 95% of participants presenting	Activity 5: 95% of participants presenting	Activity 5: 95% of participants presenting	Activity 5: 95% of participants presenting
Objective 4.1b	Activity 1: 6 dREU students complete research, and present at the state conference and undergraduate research showcase	Activity 1: 12 dREU students complete research and present at the state conference and undergraduate research showcase	Activity 1: 12 dREU students complete research, and present at the state conference and undergraduate research showcase	Activity 1: 12 dREU students complete research, and present at the state conference and undergraduate research showcase	Activity 1: 6 dREU students complete research, and present at the state conference and undergraduate research showcase; 50% of dREU students matriculate to graduate/ professional school; 8 dREU students in graduate/ professional school

	Activity 2: Baselines set Activity 3: Module 1 developed Activity 4: 2 pre-service teachers trained and placed in Spring 2021 semester	Activity 2: Meet/exceed baselines Activity 3: Baselines number of teachers reached set via Module 1. Module 2 developed Activity 4: 2 pre-service teachers trained each semester (Fall/Spring); 2 pre-services teachers placed each semester	Activity 2: Meet/exceed prior year's numbers Activity 3: Meet/exceed prior year's training numbers via Lesson plan 1 and 2 Activity 4: 2 pre-service teachers trained each semester; 2 pre-services teachers placed each semester	Activity 2: Meet/exceed prior year's numbers Activity 3: Meet/exceed prior year's training numbers Activity 4: 2 pre-service teachers trained each semester; 2 pre-services teachers placed each semester	Activity 2: Met/exceed prior year's numbers Activity 3: 100 total teachers trained over 5-year period Activity 4: 2 pre-service teachers trained each semester; 2 pre-services teachers placed each semester

Across this Element	**Anticipated Outcomes of Education and Workforce Development Element**	
	Short-term (5 Years) (changes in knowledge or capacities)	**Long-term (10 Years) (changes in actions or conditions)**
Objective 4.1a	Establish diverse and sustainable bioscience/STEM education and professional pathways for early career and graduate students in ND-ACES, particularly those from underrepresented groups (e.g., women and racial ethnic minorities) and establish CI and college teaching opportunities for STEM graduate students.	Foster ongoing development of skilled and diverse bioscience/STEM workforce in the state of North Dakota through continued engagement and support of early career faculty and graduate students and expand use of cyberinfrastructure across the state through continued training of graduate students in this area.
Objective 4.1b	Establish diverse and sustainable bioscience/STEM education and professional pathways for K-16 students throughout the state of ND, particularly those from rural and tribal communities.	Foster ongoing development of skilled and diverse bioscience/STEM workforce through sustained engagement and support of K-16 students and K-12 teachers in North Dakota.

Overall Outcomes	Establish mentoring programs and professional development activities as a means of improving early career faculty and graduate students' professional/technical skills, self-efficacy, intentions to persist in the field, actual retention in the field, sense of belonging and scholarly productivity; establish research training experiences that bolster K-16 students' interests in bioscience/STEM with hopes of broadening their participation in bioscience/STEM education and career opportunities, particularly those from underrepresented groups; establish student teaching experience in rural and tribal communities that promotes bioscience/STEM activities and increases the number of qualified STEM teachers in these communities; establish professional development opportunities for rural and tribal K-12 teachers focused on increasing their proficiency in bioscience/STEM education.	Impact the state's economy and expand bioscience research and education to schools beyond the RUs

PROSPER Broadening Participation

Led by Van Doze (UND) and co-led by Raymond Burns (ND EPSCoR ***[Approved by NSF 1/14/22]***), this initiative includes all ND-ACES participants (particularly those within the Education and Workforce Development team) in supporting American Indians and other underserved groups along the bioscience's pathway. Team members include the TCU NATURE Coordinators: Austin Allard (TMCC) Kerry Hartman (NHSC), Mafany Ndiva Mongoh (SBC), Brent Voels (CCCC ***[Approved by NSF 8/27/21]***).

The team will increase the participation of underrepresented/underserved groups engaged in bioscience education and disciplines. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 8).

This group's efforts link to ND-ACES tracks 1, 2, 4, and 5 (which are adopted as the Strategies for Broadening Participation) and integrate with the CCBSE goals.

Broadening Participation Element Goal 5.1: Open pathways in North Dakota's bioscience sector for increased interest, access, and contribution by underrepresented/underserved groups.

- **Broadening Participation Element Objective 5.1:** Increase the participation of all groups engaged in bioscience education and careers.
    - Supporting Activities:
        - TCU bioscience students will conduct outreach in their local K-12 schools.
        - Support engagement in biosciences at the B.S. level (particularly for American Indian).
        - TCU bioscience faculty will be offered research techniques and equipment training.
        - NATURE TCU camps for middle and high school kids at the four partnering TCUs.
        - NATURE Sunday Academies for middle and high school kids at the four partnering TCUs.
        - NATURE Bridge Camp for graduating high school seniors at the four partnering TCUs.
        - NATURE University Summer Camp for participants from all of the four partnering TCUs.

Table 8. Broadening Participation Element Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

PROSPER GOAL: Broadening Participation Element						
Goal 5.1: Open pathways in North Dakota's bioscience sector for increased interest, access, and contribution by underrepresented/underserved groups. • **Objective 5.1: Increase the participation of all groups engaged in bioscience education and careers**						
Objective 5.1	**Specific milestones**					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: TCU bioscience students will conduct outreach in their local K-12 schools via bioscience lesson plans ***[Metric changes approved by NSF 2/9/22]***	Establish a library of K-12 STEM Lesson plans from NATURE Sunday Academy STEM Modules -	Continued 6-12 grade STEM teachers identified for Y3 and TCU student involvement planned or post-associate assistantships	Continued Fall 2022 and Spring 2023 TCU students identified and introduced to 6-12 grade STEM teachers 6-12 grade STEM teachers track the number of TCU student/6-12 grade student interactions 6-12 grade STEM teachers provide feedback on TCU student involvement 6-12 grade STEM teachers identified for Y4 and TCU student involvement planned based on	Continued Fall 2023 and Spring 2024 TCU students identified and introduced to 6-12 grade STEM teachers Continued Continued Continued	Continued Fall 2024 and Spring 2025 TCU students identified and introduced to 6-12 grade STEM teachers Continued Continued Manuscript written and submitted that outlines process	Leads: **R. Burns, V. Doze** ***[Responsibility changes approved by NSF 1/14/22]***

			prior year's feedback			
Activity 2: Support engagement in biosciences at the B.S. level (particularly for AI) ***[Metric changes approved by NSF 2/9/22]***	Engagement in biosciences at the B.S. level.	Continued	Continued	Continued	Continued	Leads: **V. Doze, Ray Burns, TCU ND-ACES researchers and academic officers** ***[Responsibility changes approved by NSF 1/14/22 and 2/9/22]***
Activity 3: TCU bioscience faculty will be offered research techniques and equipment training	Enhanced interdisciplinary collaborations and increased retention and advancement of faculty	Continued	Continued	Continued	Continued	Leads: **R. Burns, V. Doze** ***[Responsibility change approved by NSF 1/14/22]***
Activity 4: TCU camps for middle and high school kids at the four partnering TCUs	TCU NATURE coordinators will conduct summer camps at the four partnering TCUs	Continued	Continued	Continued	Continued	Leads: **R. Burns, V. Doze, NATURE coordinators**
Activity 5: Sunday Academies for middle and high school kids at the four partnering TCUs	TCU NATURE coordinators will be site coordinators for Sunday Academy bioscience learning modules conducted at four TCUs	Continued	Continued	Continued	Continued	Leads: **R. Burns, V. Doze, NATURE Coordinators** ***[Responsibility changes***

						approved by NSF 1/14/22]
Activity 6: Bridge camps for graduating high school seniors at the four partnering TCUs	TCU NATURE coordinators will be site coordinators for bridge camps at the four partnering TCUs	Continued	Continued	Continued	Continued	Leads: **R. Burns, V. Doze, NATURE Coordinators** ***[Responsibility changes approved by NSF 1/14/22]***
Activity 7: University Summer Camp for participants from the four partnering TCUs	TCU NATURE coordinators will be site coordinators for University Summer Camp for participants from the four partnering TCUs	Continued	Continued	Continued	Continued	Leads: **R. Burns, V. Doze, NATURE Coordinators** ***[Responsibility changes approved by NSF 1/14/22]***

Across this Element	**Milestone metrics for Broadening Participation Element**				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 5.1	Activity 1: 5 ND-ACES related bioscience lesson plans 2 TCU students deliver the bioscience lessons to 40 students	Activity 1: 5 additional ND-ACES related STEM lesson plans 2 TCU students deliver STEM lessons to 60 students.	Activity 1: 5 additional ND-ACES related STEM lesson plans 2 TCU students deliver STEM lessons to 60 students.	Activity 1: 5 additional ND-ACES related STEM lesson plans 2 TCU students deliver STEM lessons to 60 students.	Activity 1: 25 ND-ACES related STEM lesson plans developed over 5 years 2 TCU students deliver STEM lessons to 280 students over 5 years

	3 NATURE students matriculating into STEM degrees (either AS or above)	4 NATURE students completing STEM degrees.	4 NATURE students completing STEM degrees	4 NATURE students completing STEM degrees	>10 NATURE students with STEM B.S and >5 NATURE students with STEM graduate/ professional degrees over 5 years
[Metric change approved by NSF 2/9/22]	Activity 2: Plan research assistantships for juniors and seniors.	Activity 2: 2-3 students will have received research assistantships as juniors and seniors or post-associate assistantships	Activity 2: 2-3additional students will have received research assistantships as juniors and seniors and 1 student will have completed their B.S. degree or post-associate assistantships	Activity 2: 2-3additional students will have received research assistantships as juniors and seniors or post-associate assistantships and 1 additional student will have completed their B.S. degree	Activity 2: 7-10 students will have received research assistantships as juniors and seniors or post-associate assistantships and 3 of those will have completed their B.S. degree over 5 years

[Metric change approved by NSF 2/9/22]	Activity 3: One TCU faculty will visit CCBSE collaborators and learn a research technique/learn a HPC technique/expand knowledge in a Pillar area	Activity 3:	Activity 3: One additional TCU faculty will visit CCBSE collaborators and learn a research technique/learn a HPC technique/expand knowledge in a Pillar area	Activity 3: One additional TCU faculty will visit CCBSE collaborators and learn a research technique/learn a HPC technique/expand knowledge in a Pillar area	Activity 3: Five collaborative projects using the new skills over 5 years
		Survey for TCU STEM faculty re: training preferences developed and distributed	Continued	Continued	
		Preferences prioritized	Continued	Continued	
		Collaborating institutions' faculty requested to provide training in selected areas	Continued	Continued	
		One training video produced and released to TCU faculty	Continued	Continued with two training videos produced and released	
	Activity 4 120 participants	Activity 4: 140 participants	Activity 4: 140 participants	Activity 4: 140 participants	Activity 4: 680 participants over 5 years
	Activity 5: 350 participants	Activity 5: 350 participants	Activity 5: 350 participants	Activity 5: 350 participants	Activity 5: 1,750 participants over 5 years
	Activity 6: 10 participants	Activity 6: 15 participants	Activity 6: 15 participants	Activity 6: 15 participants	Activity 6: 55 participants over 5 years

	Activity 7: 20 participants	Activity 7: 20 participants	Activity 7: 20 participants	Activity 7: 20 participants	Activity 7: A total of 100 participants over 5 years

Across this Element	Anticipated Outcomes of Broadening Participation Element	
	Short-term (5 Years) (changes in knowledge or capacities)	**Long-term (10 Years) (changes in actions or conditions)**
Goal 5.1	More diverse and sustainable bioscience/STEM education and professional development pathways.	Increased numbers of underserved/underrepresented groups in bioscience degree programs and careers. Increased bioscience research activity at the TCU/MU/PUIs.
Overall Outcomes	Increased institutional commitment to broadening participation at all participating institutions.	A culture of increased broadening participation at all participating institutions.

PROSPER Partnerships and Collaborations

Led by Kelly Rusch (NDSU) and co-led by John Mihelich (UND) and Jean Ostrom-Blonigen (ND EPSCoR), this initiative builds research infrastructure and strengthens ND's research competitiveness through industry partnerships and other collaborations. Team members include the CCBSE and Pillar leads.

The team will facilitate a variety of activities that assist CCBSE researchers in forming partnerships and collaborations (particularly with industry in ND and the wider region) and promote ND's research competitiveness, innovation, and bioscience pathway development. The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 9).

This group's efforts link to ND-ACES tracks 1, 3, and 4 (which are adopted as the Strategies for Partnerships and Collaborations) and integrate with CCBSE goals.

Partnerships and Collaborations Element Goal 6.1: Ensure sustained educational and economic impact beyond the project through partnerships and internships.

- **Partnerships and Collaborations Element Objective 6.1a:** Expand the intellectual reach of the CCBSE by building stronger collaborations with other academic institutions and federal labs.
    - Supporting Activities:
        - Determine and build upon the baseline for meaningful internal and external collaborations (as defined in Section 4.7 of the proposal, Tactic 1).
        - Support participant interactions with external collaborators with travel funding.
        - Support interactions with external collaborators through funded seed awards with CCBSE senior personnel.
- **Partnerships and Collaborations Element Objective 6.1b:** Create pathways for translating research results into commercially viable end products by expanding existing and forging new bioscience partnerships with business economic development entities, and developing intellectual property (IP) and commercialization.
    - Supporting Activities:
        - Determine and build upon the baseline for partnerships (as defined in 4.7 of the proposal, Tactic 2).
        - Support partnerships.
        - Identify ND companies using tools like the North American Industry Classification System (NAICS).
        - Use prospectus to identify partnership opportunities (e.g., funding, licensing a technology, and startup analysis).
        - Identify IP protocols at all 10 ND-ACES institutions.
        - Understand how tribal laws impact IP disclosures.
        - Identify commercialization protocols at all 10 participating institutions.
        - Identify workshops/conferences to attend and mentoring opportunities (SHARPhub, USPTO Denver, SBIR, etc.).
        - Based on other activities, determine potential funding possibilities with other SHARPhub EPSCoR states (e.g., KS, NE, OK, SD).

Table 9. Partnerships and Collaborations Element Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

PROSPER GOAL: Partnerships and Collaborations Element

Goal 6.1: Ensure sustained educational and economic impact beyond the project through partnerships and internships

- **Objective 6.1a: Expand the intellectual reach of the CCBSE by building stronger collaborations with other academic institutions and federal labs**
- **Objective 6.1b: Create pathways for translating research results into commercially viable end products**

Objective 6.1a	Specific milestones					
	Year 1	Year 2	Year 3	Year 4	Year 5	Responsible parties
Activity 1: Determine and build upon the baseline	Survey senior personnel to establish the baseline collaborations	Build/extend baseline collaborations	Continued	Continued	Continued	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen
Activity 2: Support participant interactions with external collaborators with travel funding ***[Metric changes approved by NSF 2/9/22]***			1-3 trips to external collaborators and 1-3 external collaborators coming to campuses	Continued with 2-6 total visits	Continued with 2-6 total visits	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen
Activity 3: Support interactions with external collaborators			Fund at least one seed award between CCBSE and an external collaborator	Continue to fund one seed award per year	Continued	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen

Objective 6.1b	Specific milestones					
	Year 1	Year 2	Year 3	Year 4	Year 5	Responsible parties
Activity 1: Determine and build upon the baseline for partnerships	Survey campus industry relations offices and participants to establish the baseline for partnerships	Build/extend from baseline partnerships	Build/extend from prior year's partnerships baseline	Continued	Continued	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen, identified subject matter experts at NDSU and UND
Activity 2: Support Partnerships	Plan for Y2 communication efforts and determine measures of engagement	Provide support for current and identify next year's communication efforts	Continued	Continued	Provide support for and identify ongoing communication sustainability efforts	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen, identified subject matter experts at NDSU and UND
Activity 3: Identify ND companies using tools like NAICS ***[Metric changes approved by NSF 2/9/22 and 5/10/22]***	N/A	Following the April 2022 EAB meeting, together with CCBSE and Pillar leads, begin to develop a CCBSE prospectus for cultivating partnerships and exploring potential funding possibilities (BioND, EDA, SHARPhub/I-Corp, Innovate ND, Main Street,	Finalize a CCBSE prospectus	Update CCBSE prospectus	Continued	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen; CCBSE leads, Pillar leads, and other identified subject matter experts at all 9 CCBSE institutions

		SBIR, STTR)				
Activity 4: Identify partnership opportunities		Begin to identify opportunities and determine whether actionable by CCBSE leads	Continue to identify opportunities and determine whether actionable by CCBSE leads	Continued	Continued	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen, identified subject matter experts at NDSU and UND
Activity 5: Identify IP protocols at all 10 institutions	Work with campuses to identify IP protocols	Continue to work with campuses to identify IP protocols and determine how joint IP will be handled	Make necessary changes protocol document and joint IP agreement as necessary	Continued	Continued	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen, identified subject matter experts at NDSU and UND
Activity 6: Understand how tribal laws impact IP disclosures	Work with TCU campuses located in ND to identify impacts	Continue to work with TCU campuses located in ND to identify impacts and determine whether to survey other AIHEC campuses	If determined in Y2, survey other AIHEC campuses	If determined in Y2, compile survey data from other AIHEC campuses	If determined in Y2, publish results from other AIHEC campuses	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen, identified subject matter experts at NDSU and UND
Activity 7: Identify commercialization protocols at all 10 participating institutions	Work with campuses to identify commercialization protocols and enroll participants in SHARPhub	Continue to encourage CCBSE participants to enroll or take part in SHARPhub/I-Corps activities,	Updated campus commercialization protocols, as necessary, continue to encourage CCBSE participants to enroll in I-Corps activities, and	Continued	Continued	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen; CCBSE leads, Pillar leads, and SHARPhub/I-

[Metric changes approved by NSF 2/9/22 and 5/10/22]		work with campuses to identify commercialization protocols and enroll participants in SHARPhub/I-Corps In Spring 2022, meet with the ND SHARPhub/I-Corps coordinator to determine next steps	assistance with IP disclosures			Corps coordinator; and other identified subject matter experts at all 9 CCBSE institutions

Activity 8: Identify workshops / conferences to attend and mentoring opportunities (SHARPhub/I-Corps, USPTO Denver, SBIR, etc.	Identify initial workshops related to typical processes (e.g., NDSU and UND IP offices, Holly Gabriel, Patent and Trademark Searching) for participants to discuss IP	Continue to identify workshops related to typical processes for participants to discuss IP	Continued	Continued and host 1 CCBSE workshop or conference	Continued	Possible partners (ND entities): Bismarck-Mandan Development Assoc., Campus Career Centers, Innovate ND, Jamestown/ Stutsman Development Corp., Minot Economic Development Corp., NDSU EDA Makerspace (Brian Kalk), NDSU Ozbun Entrepreneurship Center (Kodee Furst), NHSC Applied Engineering Center (Ann Vallie), UND Center for Innovation
Activity 9: Based on other activities, determine potential funding possibilities with other SHARPhub/I-Corps EPSCoR states	N/A	After Spring 2022 meeting with the SHARPhub/I-Corps coordinator and April 2022 EAB meeting, together with CCBSE and Pillar leads and the UND I-Corps coordinator /trainer to explore potential conversations	Begin conversations with other EPSCoR states with bioscience research agendas, including those that previously participated in SHARPhub	Based on conversations with other EPSCoR states, determine and engage in action Items	Engage in action items and determine sustainable potential of action items	Lead: **K. Rusch** Co-leads: J. Mihelich, J. Ostrom-Blonigen; CCBSE leads, Pillar leads, and I-Corps coordinator/ trainer; and other identified subject matter experts at NDSU

[Metric changes approved by NSF 2/9/22 and 5/10/22]	with other EPSCoR states participating in SHARPhub				and UND all 9 CCBSE institutions. Possible partners: EPSCoR offices

Across this Element	**Milestone metrics for Partnerships and Collaborations Element**				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 6.1a	Activity 1: Baseline established Activity 2: N/A Activity 3: N/A	Activity 1: 20% increase in meaningful collaborations over prior year Activity 2: Meeting the numbers outlined Activity 3: N/A	Activity 1: 20% increase in meaningful collaborations over prior year Activity 2: Meeting the numbers outlined Activity 3: Meeting the number outlined	Activity 1: 20% increase in meaningful collaborations over prior year Activity 2: Meeting the numbers outlined Activity 3: Meeting the number outlined	Activity 1: 20% increase in meaningful collaborations over prior period Activity 2: Meeting the numbers outlined Activity 3: Meeting the number outlined
Objective 6.1b	Activity 1: Baseline established using CDAs, MTAs, other efforts (grant applications, etc.)	Activity 1: Increase in partnership engagement or partner activities over baseline - measured by the provision of valuable resources (as defined in 4.7, Tactic 2)	Activity 1: Increase in partnership engagement or partner activities over the prior year - measured by the increased provision of valuable resources	Activity 1: Increase in partnerships or partner activities over prior year and continued evidence of provision of valuable resources	Activity 1: Increase in partnerships or partner activities over prior year and continued evidence of provision of valuable resources

	Activity 2: Identification of Y2 support efforts based on baseline data and determination of measures [# participants (if event), # of inquiries following communication effort, etc.]	Activity 2: Increased engagement by meeting of prior year's identified support efforts	Activity 2: Increased engagement by meeting of prior year's identified support efforts	Activity 2: Increased engagement by meeting of prior year's identified support efforts	Activity 2: Increased engagement by meeting of prior year's identified support efforts
	Activity 3: N/A	Activity 3: Completed prospectus	Activity 3: Prospectus updated	Activity 3: Prospectus updated	Activity 3: Prospectus updated
	Activity 4: N/A	Activity 4: Identify 3-5 opportunities, 1-3 of which are actionable	Activity 4: Identify 3-5 opportunities, 1-3 of which are actionable	Activity 4: Identify 3-5 opportunities, 1-3 of which are actionable	Activity 4: Identify 3-5 opportunities, 1-3 of which are actionable
	Activity 5: >50% protocols identified	Activity 5: 100% protocols identified; Collaborative decision made regarding the handling joint IP and updated protocol document	Activity 5: Up to date protocol document and joint IP agreement	Activity 5: Up to date protocol document and joint IP agreement	Activity 5: Up to date protocol document and joint IP agreement
	Activity 6: 50% identified	Activity 6: 100% identified	Activity 6: Survey developed and released	Activity 6: Survey results compiled	Activity 6: Results published
[Metric changes approved by NSF 2/9/22]	Activity 7: >50% protocols identified and 25% of participants enrolled in SHARPhub	Activity 7: 100% protocol identified	Activity 7: Updated protocol document, and 1 invention disclosure	Activity 7: Updated protocol document, 3+ invention disclosures,	Activity 7: Updated protocol document, 3+ invention disclosures, 2+

				and 2+ provisional patents	provisional patents, and 2+ patents
	Activity 8: 1+ workshop or conference attended by >40% CCBSE participants	Activity 8: 1+ workshop or conference attended by >60% CCBSE participants.	Activity 8: 1+ workshop or conference attended by >75% CCBSE participants	Activity 8: 1+ workshop or conference attended by 75%+ CCBSE participants and 1 CCBSE workshop or conference attended by 80% CCBSE participants	Activity 8: 1+ workshop or conference attended by 85%+ CCBSE participants and 1 CCBSE workshop or conference attended by 80% CCBSE participants
[Metric changes approved by NSF 2/9/22]	Activity 9: N/A	Activity 9: N/A	Activity 9: List of action items for other EPSCoR states	Activity 9: States continue to be engaged	Activity 9: 1-3 sustainable goals for at least 3 states

Across this Element	**Anticipated Outcomes of Partnerships and Collaborations Element**	
	Short-term (5 Years) (changes in knowledge or capacities)	**Long-term (10 Years) (changes in actions or conditions)**
Goal 6.1a	Existing external collaborations become more meaningful; as evidenced by increased conference, journal, and proposal co-authorship among project participants, and between project participants and external organizations; joint working papers; regularly established interactions that may lead to the submission of an article/proposal, increased use of facilities and equipment (i.e., increased use of CCAST and CRC by MCU/PUI/TCU researchers [and internal collaborators]; and increased use of Extreme Science and Engineering Discovery Environment [XSEDE] by all participating institutions [an external collaboration]). New external collaborations are built to produce meaningful outcomes/impacts.	Sustained, meaningful external collaborations with other academic institutions and federal labs.

Goal 6.1b	Existing partnerships make more provisions of valuable resources (student internships, collaborative research opportunities, insight into needs and future direction of ND and regional industry [Inc. stakeholder advisory groups], sharing/commercialization of IP). New partnerships are built with an expectation of the provision of resources.	Sustained partnerships that positively impact North Dakota's economy.
Overall Outcomes	Impact beyond the project with partnerships and internships expanded by 50%.	Foster the ongoing development of a skilled, diverse workforce; positively impact state economy; supply research outcomes for growing/new bioscience ventures and partners; and open new research avenues.

PROSPER Communication and Dissemination

This group's efforts link to ND-ACES tracks 1, 3, and 4 (which are adopted as the strategies for Partnerships and Collaborations) and integrate with CCBSE goals.

Led by Zoltan Majdik (NDSU ***[and Justin Walden, effective 6/30/22, approved by NSF on 5/16/22]***) and co-led by Cailin Shovkoplyas (ND EPSCoR), this ND-ACES- wide initiative keeps all stakeholders informed, supports the harmonious interactions of all ND- ACES groups, assists research and programmatic participants in disseminating their work to legislative, scientific, and citizen stakeholders, and develops materials for consumption by lay audiences. Team members include all senior personnel.

The team will increase awareness of the CCBSE's role in developing the state's bioscience ecosystem from education to economic diversification (Table 2). The goal of this Pillar is outlined below and in detail, by year, in the corresponding table of milestone activities and metrics (Table 10).

Communication and Dissemination Element Goal 7.1: Develop an elevated public understanding of the economic impact of growing North Dakota's bioscience sector through strategic research investments as a result of data-sharing, communication, and outreach.

- **Communication and Dissemination Element Objective 7.1a:** Provide clear communication between all participants.
    - Supporting Activities:
        - Facilitate communication across the different groups and Pillars that are part of the ND-ACES project through regular meetings.
        - Facilitate communication across the different groups and Pillars that are part of the ND-ACES project by providing updates.
        - Facilitate communication across the different groups and Pillars that are part of the ND-ACES project by providing internal communication training.

- **Communication and Dissemination Element Objective 7.1b:** Inform and educate stakeholders.
    - Supporting Activities:
        - Populate the website and social media with relevant public-facing content.
        - Assist team members from CCBSE and PROSPER with creating public-facing communication products.
        - Disseminate project milestones and talking points to stakeholders and decision makers in the state.

- **Communication and Dissemination Element Objective 7.1c:** Contribute to a scientifically informed citizenry.
    - Supporting Activities:
        - Offer workshop opportunities for faculty and graduate students to learn about topics and practices in science communication to increase science communication skills.
        - Include public engagement opportunities as part of the annual conference.

- Ensure that we have a diverse representation of science and scientists on our website to help engage all publics.
- Engage with local publics about the value and the benefits of the science.

Table 10. Communication and Dissemination Element Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

PROSPER GOAL: Communication and Dissemination Element						
Goal 7.1: Develop an elevated public understanding of the economic impact of growing ND's bioscience sector through strategic research investments as a result of data-sharing, communication, and outreach. • **Objective 7.1a: Provide clear communication between all participants** • **Objective 7.1b: Inform and educate stakeholders** • **Objective 7.1c: Contribute to a scientifically informed citizenry**						
Objective 7.1a	**Specific milestones**					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: Facilitate communication through regular meetings	Attending monthly CCBSE meetings, leadership meetings, and bi-monthly PROSPER meetings	Continued	Continued	Continued	Continued	Leads: **J. Walden, C. Shovkoplyas** ***[Responsibility change approved by NSF on 5/16/22]***
Activity 2: Facilitate communication across the by providing updates	Providing team updates (monthly newsletter/ web/social media), writing support for new funding	Continued	Continued	Continued	Continued	Leads: **J. Walden, C. Shovkoplyas** ***[Responsibility change approved by NSF on 5/16/22]***
Activity 3: Facilitate Communication by providing communication	Technical training in MS Teams provided for leadership on internal team communication. Annual evaluation of MS Teams based internal communication	Continued	Continued	Continued	Continued	Leads: **J. Walden, C. Shovkoplyas** ***[Responsibility change approved by NSF on 5/16/22]***

	practices					

Objective 7.1b	Specific milestones					
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Responsible parties**
Activity 1: Populate website and social media with relevant public-facing content	Measure dissemination website/social media/newsletter	Continued	Continued	Continued	Continued	Leads: **J. Walden, C. Shovkoplyas** ***[Responsibility change approved by NSF on 5/16/22]***
Activity 2: Assist team members from CCBSE and PROSPER with creating public-facing communication products	Offer individual consulting sessions for presentation preparation and PR/public dissemination strategies	Continued	Continued	Continued	Continued	Leads: **J. Walden, C. Shovkoplyas** ***[Responsibility change approved by NSF on 5/16/22]***
Activity 3: Disseminate project milestones and talking points to stakeholders and decision makers in the state	Press releases drafted for submission to regional/national news as well as NDUS PR offices. Talking points sent to key decision makers and legislators	Continued	Continued	Continued	Continued	Leads: **J. Walden, C. Shovkoplyas** ***[Responsibility change approved by NSF on 5/16/22]***

Objective 7.1c	Specific milestones					
	Year 1	Year 2	Year 3	Year 4	Year 5	Responsible parties
Activity 1: Offer workshop opportunities for faculty and graduate students	Plan ND EPSCoR-sponsored communicating science workshop to develop better skills in disseminating their work/public engagement	Host ND EPSCoR-sponsored communicating science workshops to develop better skills in disseminating their work/public engagement	Continued	Continued	Continued	Leads: **J. Walden, C. Shovkoplyas** ***[Responsibility change approved by NSF on 5/16/22]***
Activity 2: Include public engagement opportunities as part of the annual conference	ND EPSCoR will host an annual conference, provide skill-building resources to participants - *COVID-19 permitting	Continued	Continued	Continued	Continued	Leads: **J. Walden, C. Shovkoplyas** ***[Responsibility change approved by NSF on 5/16/22]***
Activity 3: Ensure that we have a diverse representation of science and scientists on website, to help engage all publics		Scoring by external evaluation firm's diversity rubric		Responsiveness to Y2 scoring		Leads: **J. Walden, C. Shovkoplyas** ***[Responsibility change approved by NSF on 5/16/22]***
Activity 4: Engage with local publics about the value and	Support science cafes - *COVID-19 permitting	Continued	Continued	Continued	Continued	Leads: **J. Walden, C. Shovkoplyas**

the benefits of the science					***[Responsibility change approved by NSF on 5/16/22]***

Across this Element	**Milestone metrics for Communication and Dissemination Element**				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Objective 7.1a	Activity 1: Meeting attendance Activity 2: At least monthly outreach to participants, stakeholders, and citizens Activity 3: Training offered at least quarterly	Activity 1: Meeting attendance Activity 2: At least monthly outreach to participants, stakeholders, and citizens Activity 3: Training offered at least quarterly	Activity 1: Meeting attendance Activity 2: At least monthly outreach to participants, stakeholders, and citizens Activity 3: Training offered at least quarterly	Activity 1: Meeting attendance Activity 2: At least monthly outreach to participants, stakeholders, and citizens Activity 3: Training offered at least quarterly	Activity 1: Meeting attendance Activity 2: At least monthly outreach to participants, stakeholders, and citizens Activity 3: Training offered at least quarterly
Objective 7.1b	Activity 1: Same metric framework for all: Baseline established of interaction (engagement rate) Activity 2: Needs research products; sessions begin in year two	Activity 1: ≥5% Increase in number of interactions per day divided by followers. Activity 2: 5 sessions per year completed	Activity 1: ≥5% Increase in number of interactions per day divided by followers. Activity 2: 5 sessions per year completed	Activity 1: Maintain engagement over the prior year. Maintain number of interactions per day divided by followers. Activity 2: 5 sessions per year completed.	Activity 1: Maintain engagement over the prior year. Maintain number of interactions per day divided by followers. Activity 2: 5 sessions per year completed.

	Activity 3: 2+ press releases	Activity 3: 4+ press releases; Updating stakeholders on project milestones (quarterly)	Activity 3: 4+ press releases; Updating stakeholders on project milestones (quarterly)	Activity 3: 4+ press releases; Updating stakeholders on project milestones (quarterly)	Activity 3: 20 press releases over the 5-year period. Updating stakeholders on project milestones (quarterly)
Objective 7.1c	Activity 1: 2 workshops planned annually. Workshops begin year 2 Activity 2: 2021 Annual conference with attendees from each of the participating campuses. Activity 4: Science cafes planned annually. Science cafes begin year 2	Activity 1: 40+% attendance by ND-ACES participants Activity 2: 2022 Annual conference with attendees from each of the participating campuses. Activity 3: Scoring by external evaluation firm's diversity rubric Activity 4: 1-2 science cafes supported	Activity 1: 55+% attendance by ND-ACES participants Activity 2: 2023 Annual conference with attendees from each of the participating campuses. Activity 4: 2 science cafes supported.	Activity 1: 75+% attendance by ND-ACES participants Activity 2: 2024 Annual conference with attendees from each of the participating campuses. Activity 3: Scoring by external evaluation firm's diversity rubric Activity 4: 2-3 science cafes supported	Activity 1: 90% of ND-ACES participants will have attended at least 1 workshop over the 5-year period Activity 2: 2025 Annual conference with attendees from each of the participating campuses. Activity 4: 2-3 science cafes supported

Across this Element	Anticipated Outcomes of Communication and Dissemination Element	
	Short-term (5 Years) **(changes in knowledge or capacities)**	**Long-term (10 Years)** **(changes in actions or conditions)**
Goal 7.1a	Facilitate communication and collaboration across the research Pillars and broader impacts elements.	Contribute to a shared understanding across disciplines.
Goal 7.2b	Increase the awareness of the research that expands ND's bioscience research, capacity, and expertise.	Foster the ongoing awareness of the research that expands ND's bioscience research, capacity, and expertise.
Goal 7.3c	Engage the public in scientific research.	Contribute to a more scientifically informed citizenry.
Overall Outcomes	Communication and dissemination efforts will increase awareness of the role of the CCBSE in developing the state's bioscience ecosystem from education to economic diversification.	Develop a robust understanding of the importance of the communication of science among all participants and contribute to a more scientifically informed citizenry.

PROSPER – Overall Summary

As previously stated, the goal of PROSPER is to broaden the impact of the CCBSE within the jurisdiction. This goal will be accomplished through the successful completion of the Education and Workforce Development, Broadening Participation, Partnerships and Collaborations, and Communication and Dissemination metrics outlined above in Tables 7, 8, 9, and 10. Additional CCBSE outcomes that will be obtained through the combined efforts of the PROSPER elements are outlined in Table 11.

Table 11. PROSPER Overall Timelines of Activities, Milestones, Metrics, and Anticipated Outcomes

PROSPER Broader Impacts: Overall					
Goal: Expand North Dakota's emerging biosciences capacity through a STEM-enabled, well-trained workforce and position ND-ACES as North Dakota's leading scientific and educational resource					
PROSPER Strategies	**Specific milestones**				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Expand ND's biosciences capacity through a STEM-enabled, well-trained workforce	Successful completion of Education and Workforce Development Element Y1 activities	Successful completion of Education and Workforce Development Element Y2 activities	Successful completion of Education and Workforce Development Element Y3 activities	Successful completion of Education and Workforce Development Element Y4 activities	Successful completion of Education and Workforce Development Element Y4 activities, metrics, and outcomes
Increase advanced scientific computing capabilities	Successful completion of Education and Workforce Development and Broadening Participation Element Y1 activities and metrics	Successful completion of Education and Workforce Development and Broadening Participation Element Y2 activities and metrics	Successful completion of Education and Workforce Development and Broadening Participation Element Y3 activities and metrics	Successful completion of Education and Workforce Development and Broadening Participation Element Y4 activities and metrics	Successful completion of Education and Workforce Development and Broadening Participation Element Y5 activities, metrics, and outcomes
Broaden the participation and number of STEM undergraduate and graduate students	Successful completion of Broadening Participation Element Y1 activities and metrics	Successful completion of Broadening Participation Element Y2 activities and metrics	Successful completion of Broadening Participation Element Y3 activities and metrics	Successful completion of Broadening Participation Element Y4 activities and metrics	Successful completion of Broadening Participation Element Y5 activities, metrics, and outcomes

Provide professional development to rural and tribal K-12 teachers and outreach to K-12 students	Successful completion of Education and Workforce Development and Broadening Participation Element Y1 activities and metrics	Successful completion of Education and Workforce Development and Broadening Participation Element Y2 activities and metrics	Successful completion of Education and Workforce Development and Broadening Participation Element Y3 activities and metrics	Successful completion of Education and Workforce Development and Broadening Participation Element Y4 activities and metrics	Successful completion of Education and Workforce Development and Broadening Participation Element Y5 activities, metrics, and outcomes
Solicit industry-focused activities that build or expand on existing partnerships	Successful completion of Partnerships and Collaborations Element Y1 activities and metrics	Successful completion of Partnerships and Collaborations Element Y2 activities and metrics	Successful completion of Partnerships and Collaborations Element Y3 activities and metrics	Successful completion of Partnerships and Collaborations Element Y4 activities and metrics	Successful completion of Partnerships and Collaborations Element Y5 activities, metrics, and outcomes
Create a suite of communication activities will engage, inform, and educate	Successful completion of Communication and Dissemination Element Y1 activities and metrics	Successful completion of Communication and Dissemination Element Y1 activities and metrics	Successful completion of Communication and Dissemination Element Y1 activities and metrics	Successful completion of Communication and Dissemination Element Y1 activities and metrics	Successful completion of Communication and Dissemination Element Y1 activities, metrics, and outcomes

Overall milestone metrics for PROSPER	
Meet annually with TCU presidents to report on the impacts of the collaboration efforts between CCBSE, PROSPER, and the TCUs. Report also on the numbers of American Indian students who are involved in ND-ACES programming	5
Meet annually with MCU and PUI presidents to report on the impacts of the collaboration efforts between CCBSE, PROSPER and those campuses. Report also on the numbers of their students who are taking advantage of the programming	20
Number of TCU visits (some of these visits will be virtual due to COVID-19)	20
Number of MCU and PUI visits (some of these visits will be virtual due to COVID-19)	20
Number of legislator visits	10

Number of annual conferences (some of these conferences will be virtual due to COVID-19)	5
Number of External Advisory Board meetings (some of these meetings will be virtual due to COVID-19)	10
Number of ND-ACES Management meetings (to be scheduled monthly)	60
Number of ND-ACES Leadership meetings (to be scheduled quarterly)	15
Number of ND-ACES All-Participant meetings (to be scheduled twice annually)	10
Number of CCBSE and PROSPER meetings (to be scheduled every other month)	25-30

Across PROSPER	**Anticipated Outcomes of PROSPER**	
	Short-term (5 Years) (changes in knowledge or capacities)	**Long-term (10 Years) (changes in actions or conditions)**
Meet PROSPER's Goal	Expand North Dakota's emerging biosciences capacity through a STEM-enabled and well-trained workforce. to broaden the impact of the CCBSE.	Effect sustainable engagement and position ND-ACES as North Dakota's leading scientific and educational resource.

ND-ACES – Overall Impacts

The jurisdictional impacts (listed in Table 12) of meeting the ND-ACES outcome metrics for CCBSE and PROSPER are to fulfill the mission of ND-ACES to contribute to cancer research in ways that have state, national, and international ramifications and underpin sustainable activities for a trained and diverse workforce and informed populace.

Table 12. Jurisdictional Impacts

Across ND-ACES Jurisdictional Impacts
North Dakota will become the Northern Plains leader in new and sustainable biosciences technology advances.
North Dakota will have a sustainable, competent, and diverse state biosciences and bio- technology workforce from A.A. through Ph.D.
North Dakota's bioscience industry will have grown into a major economic sector with new partners, growing businesses, and expanded workforce opportunity.

Risk Management Plan

During the Strengths, Weaknesses, Opportunities, and Threats (SWOT) Analysis Meetings (synchronous and asynchronous) and the Strategic Planning Meeting, senior personnel were asked to consider all potential risks to the ND-ACES project and associated consequences. This exercise also included the consideration of three NSF-facilitator driven scenarios related to COVD-19: 1) back to normal, 2) some hybrid between back to normal and continued restrictions, and 3) full restrictions (i.e., virtual). A description of the SWOT analysis meetings and strategic planning meeting schedules/overview are included in Appendix H.

Table 13 summarizes the deliberations around normal risks (those that ND-ACES would need to address independent of COVID-19). Risks specifically associated with COVID-19 are listed in Table 14.

Table 13. Normal Risk Mitigation Matrix

No.	Potential Risks	Consequences	Impact	Likelihood	Mitigation
1	Team is very large and diverse with many complex collaborative tasks to complete in a limited time-frame.	Delay in meeting ultimate project goals.	High	Medium	Redesign/adjust composition of project; project leadership to communicate frequently with project management about concerns impacting project success. All senior personnel have adopted our Collaboration Agreement (Appendix C).
2	Cyberinfrastructure resources are not equal on all campuses and in all communities.	Barrier to collaborative work.	Medium	High	Work with the TCUs, MCU, and PUIs to develop additional accessibility options and alternative lines of access whenever necessary.
3	Obstacles inevitable in our complex research plan that will require the team to be very adaptable.	Barrier to collaborative work.	Medium	Low	Quarterly review process will identify areas in need of attention/change. Mitigating strategies will be developed, in conjunction with our program officer, as necessary.
4	Interruptions in ND-ACES activities due to COVID-19.	Potential to halt all activities.	High	High	Multi-scenario mitigation plan developed and updated quarterly or as events change, in conjunction with our

					program officer, as necessary (Table 14).
5	Inability to recruit new faculty hires.	Reduced expansion into new areas of materials science. Inability to meet this programmatic condition.	High	Low	Revisit and revise the hiring plan (Appendix G), addressing whatever the cause for failure. If the failure is the inability (e.g., financial) to complete the hire, then the mitigation plan might be to turn to one of the other campuses to see if one of them can complete the hire or return to negotiation with our program officer if no hire is possible.
6	Decline or discontinuation of state support during the 2021, 2023, or 2025 legislative sessions.	Decline in the ND EPSCoR state cash commitment.	High	Low	Turn to the RUs to provide the required match.
7	A researcher becomes unable to contribute to project due to illness, overload, or departs university.	Unable to meet Metrics.	Medium	Medium	Shift work to another peer investigator, hire an additional investigator through a seed grant proposal; or initiate a new faculty search for a replacement, if needed and possible.

Table 14. COVID-19 Scenario Planning

Scenario	Implications	Impact	Likelihood	Mitigation
New normal	Project activities continue without accommodations.	Low	Medium	Conform to institutional safety protocols.
Some hybrid between back to normal and continued restrictions	Potential slowdown of research, outreach, and education occur in a hybrid model.	High	Medium to High	In-person research and outreach will conform to institutional safety protocols. Research - It may be necessary to limit the number of people allowed in lab spaces at one time, augmented cleaning protocols, increase work on virtual platforms, etc. Each activity and circumstance will

				be evaluated by co-leads on a case-by-case basis as required. Accommodations will seek consistency across campuses if possible; alternatively, work may be shifted from one campus to another if possible and necessary to keep the project on pace. Outreach – it may be necessary to develop online/virtual activities that students can do at home. Summer 2020 NATURE programs will be used as a template for the creation of virtual outreach activities.
Full restrictions (i.e., virtual)	Outreach in person is not possible; restricted access to facilities impedes research.	High	Medium	Research – activities may be postponed or modified to occur remotely; use of core services may be outsourced on a fee-for-service basis. Frequent communication with our program officer will occur. Outreach – online/virtual activities that students can do at home will be developed. Summer 2020 NATURE programs will be used as a template for the creation of virtual outreach activities.

Succession Plan

ND EPSCoR State Office is administered by NDSU in Fargo, ND under a memorandum of understanding with the ND University System. Kelly A. Rusch, Associate Department Chair and Professor, Civil and Environmental Engineering and Special Assistant to the President at NDSU, serves as the ND EPSCoR State Executive Director. Casey Ryan, a member of the North Dakota University System State Board of Higher Education, chairs the ND EPSCoR Steering Committee. ND ACES leadership staff are also located at both UND (Co-PI: John Mihelich, Interim Vice President for Research and Economic Development) and NDSU (Co-PI: Jean Ostrom-Blonigen, ND EPSCoR Project Administrator).

Management Structure: The ND EPSCoR State Office Executive Director (Rusch) and Co-PIs (Mihelich and Ostrom-Blonigen) will oversee the implementation of ND-ACES. They will work with the subawardee/campus PIs and the ND-ACES leads/co-leads to ensure timely execution of project components and delivery of outcomes and outputs. The ND EPSCoR State Office team coordinates project management, data gathering for reports, and global event planning. The leads/co-leads ensure that the strategic priorities of the cooperative agreement are met.

Succession Plan: The purpose of the Succession Plan (Table 15) is to ensure that the leadership and management of the program are in place for the duration of the project. The succession plan will be reviewed and updated annually.

Table 15. Succession Plan

Position	Strategies for Succession
PI/PD	The NDSU Provost will be responsible for the search for a new, permanent replacement. An internal search will be conducted. Finalists for the position will meet with representatives of the ND-ACES team and the ND EPSCoR State Steering Committee. Input from these groups will be provided to the NDSU Provost prior to final selection. Once a replacement has been identified, a formal "change of PI" request will be made to NSF. Once the change is approved by NSF, the replacement will shadow the PD/PI who is leaving for as long as possible prior to the PD/PI's departure date.
Co-PIs	Co-PIs will inform the PD/PI as soon as possible that they will be leaving his/her position. Replacement of the UND Co-PI will be by the UND president and/or Provost. Replacement of the NDSU Co-PI/PA (Project Administrator) will be identified by the PD/PI through an external/internal search. Once a replacement has been identified and accepts the position, a formal "change of Co-PI" request will be made to NSF. Once the change is approved by NSF, the replacement will shadow the Co-PI who is leaving for as long as possible prior to the Co-PI's departure date.
CCBSE Leads	Each RU has designated a lead. Thus, the other assumes the full CCBSE leadership role during any planned or unplanned absences of the other campus CCBSE Lead. In the event that the absence is greater than one month (but less than five months), a second interim campus lead will be named by the PD/PI in consultation with the Co-PIs and the remaining CCBSE Lead. If a CCBSE Lead leaves his/her institution, a new campus Lead will be selected either from the pool of Pillar Leads or through an internal campus search.
CCBSE Pillar and PROSPER Section/Element Leads	Each CCBSE Pillar has designated a lead from each RU. Thus, the other assumes the full Pillar leadership role during any planned or unplanned absences of the other campus Pillar Lead. In the event that the absence is greater than one month, a second interim Pillar lead will also be named by the PD/PI in consultation with the Co-PIs and the other Pillar leads. If a Pillar Lead leaves his/her institution, a new Pillar Lead will be selected either from the faculty pool within the Pillar or through an internal campus search.
Benchmark/Activity Leads	Succession planning is not an issue as most benchmarks/activities have two individuals named for backup and collaboration between the campuses; however, in the event that the individuals named are from different campuses, the project research cluster members will assist with collaboration efforts. In the instances where just one benchmark/activity lead is named, the component lead for that portion of the project will name an interim benchmark/activity lead.

Appendix A – ND-ACES Personnel, Teams, External Advisory Board, and ND EPSCoR State Steering Committee

ND-ACES Personnel and Roles			
PI/PD and Co-PIs (meets every two weeks)			
Last Name	**First Name**	**ND-ACES Role**	**Institution**
Rusch	Kelly	PI/PD Lead: Partnerships & Collaborations	NDSU/ND EPSCoR
Mihelich	John	Co-PI Co-Lead: Partnerships & Collaborations	UND
Ostrom-Blonigen	Jean	Co-PI/PA Co-Lead: Partnerships & Collaborations Co-Lead: Education and Workforce Development ***[Approved by NSF 10/18/21]***	NDSU/ND EPSCoR

Senior Personnel			
Last Name	**First Name**	**ND-ACES Role**	**Institution**
~~Alemadi~~ [Left the project 10/16/21]	~~Shireen~~	~~Co-lead: EWD~~	~~NDSU~~
Allard	Austin	Materials Researcher NATURE Coordinator	TMCC
Bergstrom	Aaron	UND Cyberinfrastructure	UND
Bobylev	Mikhail	Materials Researcher	MiSU
Burns ***[Approved by NSF 1/14/22]***	Raymond	Co-Lead: Broadening Participation	NDSU
Cakir ***[Approved by NSF 5/16/22]***	Deniz	UND Lead: Computational	UND
Combs	Colin	Cellular Researcher	UND
~~Dahlen~~ [Left the project 6/2021]	~~Chris~~	~~NATURE Coordinator~~	~~CCCC~~
~~Delhommelle~~ [Leaving the project 5/15/22]	~~Jerome~~	~~Computational Researcher~~	~~UND~~
Dhasarathy	Archana	UND Lead: Cellular	UND
Doze	Van	Lead: Broadening Participation	UND
Du	Guodong	Materials Researcher, Cellular Team Liaison	UND
Fries ***[Approved by NSF 8/27/21]***	Marcus	Computational Researcher	DSU
Galt	Nicholas (Nick)	Cellular Researcher	VCSU
Haage	Amanda	Cellular Researcher	UND
~~Hanson~~ [Left the project 8/27/21]	~~Scott~~	~~Co-Lead: Broadening Participation~~	~~NDSU~~

Hartman	Kerry	Cellular Researcher NATURE Coordinator	NHSC
Hoang ***[Approved by NSF 2/18/21]***	Khang	NDSU Cyberinfrastructure	NDSU
Hoffmann ***[Approved by NSF 7/28/21 and 5/16/22]***	Mark	CCBSE co-Lead and Computational Researcher	UND
Hossain	Khwaja	Materials Researcher	MaSU
Katti	Dinesh	NDSU Lead: Computational	NDSU
Katti	Kalpana	CCBSE co-lead and Materials / Cellular Researcher	NDSU
Kilina	Svetlana	Computational Researcher	NDSU
Kim	Jiha	Cellular Researcher	NDSU
Liu	Lu	Computational Researcher	NDSU
Le	Trung	Computational Researcher	NDSU
Loh ***[Approved by NSF 5/10/22]***	Yen Lee	Computational Researcher	UND
[Leaving the project 6/30/22]			
Mallik	Sanku	NDSU Lead: Materials	NDSU
Navarro	Rachel	Lead: EWD	UND
Ndiva Mongoh	Mafany	NATURE Coordinator	SBC
Parker	Mike	Materials Researcher	CCCC
Quadir	Mohiuddin (Mohi)	Materials Researcher	NDSU
Sletten	Sarah	Lead: EWD	UND
Summers	Ryan	EWD Researcher	UND
Shovkoplyas	Cailin	Co-lead: Communication	NDSU
~~Skow~~ [Left the project 2/9/21]	~~Dane~~	~~NDSU Cyberinfrastructure~~	~~NDSU~~
~~Steffan~~ [Left the project 8/5/21]	~~Joshua~~	~~Cellular Researcher~~	~~DSU~~
Voels	Brent	Materials Researcher NATURE Coordinator	CCCC
Van Gijssel	Hilde	Cellular Researcher	VCSU
Walden ***[Approved by NSF 5/16/22]***	Justin	Lead: Communication	NDSU
Wayt	Richard (Josh)	Co-lead: EWD	NDSU/ND EPSCoR
Wilkinson	John	NDSU Lead: Cellular	NDSU
Xia	Wenjie	Computational Researcher, Materials Team Liaison	NDSU
~~Yu~~ [Passed away in June 2021]	~~Tao~~	~~UND Lead: Computational~~	~~UND~~
Zhao	Julia	UND Lead: Materials	UND

Management Team (meets monthly)			
Last Name	**First Name**	**ND-ACES Role**	**Institution**
Rusch	Kelly	PI/PD Lead: Partnerships & Collaborations	NDSU/ND EPSCoR
Mihelich	John	Co-PI Co-Lead Partnerships & Collaborations	UND
Ostrom-Blonigen	Jean	Co-PI/PA Co-Lead: Partnerships & Collaborations	NDSU/ND EPSCoR
Katti	Kalpana	CCBSE NDSU Lead	NDSU
Hoffmann ***[Approved by NSF 8/27/22 and 5/16/22]***	Mark	CCBSE UND Lead	UND
Navarro	Rachel	Lead: EWD	UND
Sletten	Sarah	Lead: EWD	UND
Dhasarathy ***[Approved by NSF 8/27/21]***	Archana	UND Lead: Cellular Systems Pillar	UND
Burns ***[Approved by NSF 1/14/22]***	Ray	Co-Lead: Broadening Participation	NDSU/ND EPSCoR
Doze	Van	Lead: Broadening Participation	UND
Cakir ***[Approved by NSF 5/16/22]***	Deniz	UND Lead: Computational Approaches Pillar	UND
Katti ***[Approved by NSF 8/27/21]***	Dinesh	NDSU Lead: Computational Approaches Pillar	NDSU
Walden ***[Approved by NSF 5/16/22]***	Justin	Lead: Communication and Dissemination	NDSU
Mallik ***[Approved by NSF 8/27/21]***	Sanku	NDSU Lead: Materials Design Pillar	NDSU
Shovkoplyas	Cailin	Co-lead: Communication and Dissemination	NDSU/ND EPSCoR
Wayt	Richard (Josh)	Co-lead: EWD	NDSU/ND EPSCoR
Wilkinson ***[Approved by NSF 8/27/21]***	John	NDSU Lead: Cellular Systems Pillar	NDSU
Zhao ***[Approved by NSF 8/27/21]***	Julia	UND Lead: Materials Design Pillar	UND

Leadership Team (meets quarterly) ***[NSF Approved combining with Management Team 8/27/21]***

Other ND-ACES Teams	
All Participant Teams	Meets twice annually
CCBSE Research Team	Meets monthly
CCBSE Research Pillar Operational Teams	Each Pillar team meets monthly

PROSPER Team	Meets every other month

ND-ACES External Advisory Board			
Name	**Title**	**Institution/Company**	**Location**
Marc D. Basson, M.D., Ph.D., M.B.A., F.A.C.S.	Senior Associate Dean for Medicine and Research Professor of Surgery, Pathology, and Biomedical Sciences	UND School of Medicine & Health Sciences	Grand Forks, ND
Rajendra K. Bordia, Ph.D. [added in May 2022]	George J. Bishop, III Professor of Ceramic and Materials Engineering, Department of Materials Science and Engineering, College of Engineering, Computing and Applied Sciences	Clemson University	Clemson, SC
James Brown, Ph.D.	President of Research Grade Nucleic Acids	Aldevron	Fargo, ND
Annalies Corbin, Ph.D.	President & CEO	The Past Foundation	Columbus, OH
~~Tejal Desai, Ph.D.~~ [resigned 2/7/22]	~~Deborah Cowan Professor, Department of Bioengineering and Therapeutic Sciences~~	~~University of California~~	~~San Francisco, CA~~
~~Larry Henry~~ [resigned 3/10/22]	~~Retired Teacher~~		~~Belcourt, ND~~
Lucy Fredericks [added in May 2022]	Director, Indian/Multicultural Education	Department of Public Instruction	Bismarck, ND
VICE CHAIR: Sinan Keten, Ph.D.	Associate Professor of Civil & Environmental Engineering, Associate Professor of Mechanical Engineering, and Director of Graduate Studies in Mechanical Engineering	Northwestern University	Evanston, IL
David Pearce, Ph.D.	President of Innovation and Research	Sanford Research	Sioux Falls, SD
CHAIR: Candan Tamerler, Ph.D.	Associate Dean of Research, School of Engineering Wesley G. Cramer Professor, Department of Mechanical Engineering	The University of Kansas	Lawrence, KS
Daniel M. Tuvin, MD FACS	Surgical Oncologist	Sanford Health	Fargo, ND

ND EPSCoR State Steering Committee			
Name	**Title**	**Institution/Company**	**Location**
CHAIR: ~~Casey Ryan, MD~~ [replaced 5/12/21] John Warford, DDS	~~Vice Chair~~ Member	NDUS State Board of Higher Education	~~Grand Forks~~ Bismarck
VICE CHAIR and TCU	President	Nueta Hidatsa	New Town

Representative: Twyla Baker, Ph.D.		Sahnish College	
DPI Representative: Steve Snow	Assistant Director	ND Dept. of Public Instruction (DPI)	Bismarck
Industry Representative: Megan Gelinske [filled vacant position 5/12/21]	Independent Consultant	Bio Tech	Fargo
Legislative Representative: Vacant	State Senator		
Legislative Representative; Corey Mock	State Representative	District 18	Grand Forks
Legislative Representative; Merrill Piepkorn	State Senator	District 44	Fargo
Legislative Representative; Vicky Steiner [filled vacant position 5/12/21]	State Representative	District 37	Dickinson
PUI/MCU Representative: Andre DeLorme, Ph.D.	Professor and Chair, Science Department	Valley City State University	Valley City
RU Research Representative: Chris Nelson, Ph.D.	Associate Dean and Associate Professor, Graduate School	University of North Dakota	Grand Forks
RU Research Representative: Colleen M. Fitzgerald, Ph.D.	Vice President, Research and Creative Activity	North Dakota State University	Fargo
RU Research Park Representative: Brian Kalk, Ph.D.	Executive Director	North Dakota State University	Fargo
RU Research Park Representative: Amy Whitney, Ed.D.	Director, Center for Innovation	University of North Dakota	Grand Forks

Appendix B – 2020 Strategic Planning Process and Timeline

Date	Activity
5/27	Collaboration Plan CCBSE Subgroup Session
5/28	Collaboration Plan PROSPER Subgroup Session
6/15	EPSCoR RII Track-1 Strategic Planning Webinar with NSF, PI, Co-PIs, CCBSE Leads, and ND EPSCoR Communication Manager
6/18	Full Collaboration Plan Session
6/29	Initial Strategic Planning Meeting Preparatory Meeting with NSF Facilitator, PI, Co-PIs, and ND EPSCoR Communication Manager
6/30	Researcher Preparatory Meeting with NSF Facilitator and ND-ACES Leadership Team
7/14	All-Hands Introductory Meeting and SWOT Analysis Synchronous Meeting
7/29-7/31	Strategic Planning Meeting with NSF Program Officer, NSF Facilitator, and External Evaluator (The Mark, USA)
8/14	Initial Drafts of CCBSE Pillar and PROSPER Element Implementation Sections Due from Leadership Team to ND EPSCoR
8/21	Initial Draft of Full Strategic Plan due back to Leadership Team and External Evaluators
9/1	Initial Full of Strategic Plan due from Leadership Team to ND EPSCoR
9/14	Final Draft of Full Strategic Plan due back to Leadership Team and External Evaluators
9/21	Final Full Strategic Plan due from Leadership Team to ND EPSCoR for final editing and formatting
10/1	Strategic Plan due to NSF

Appendix C – Collaboration Plan

ND-ACES National Science Foundation (NSF) EPSCoR Track-1 Collaboration Agreement

Rationale for Team Approach and Configuration

North Dakota-New Discoveries in the Advanced Interface of Computation, Engineering, and Science (ND-ACES) team members have expertise that spans multiple disciplines and arenas across organizational and geographic boundaries and integrate a diversity of approaches and methodologies. To maximize our success, we respect each member's unique contributions and appreciate that everyone's expertise adds value to our collective efforts.

Collaboration Readiness

The complex nature of our effort necessitates that we operate under a culture of collaboration and shared respect for the achievement of the goals. Trust is critical to our success; we strive to make certain that all voices are heard, our processes are transparent, and members' contributions are appreciated and respected. The team recognizes and appreciates the diversity of its members. Our different personalities, work styles, and experiences influence how we engage in team-based work. We recognize the importance and strength that these differences bring to our team and continue to identify strategies for appreciating and managing such differences.

ND-ACES is a diverse collection of 10 academic institutions across the state that includes four Tribal Colleges/Universities (TCUs), three Primarily Undergraduate Institutions (PUIs), one Master's College/University (MCU), and two Research Universities (RUs) [see Figure 1]. All of the institutions have previous experience in EPSCoR management and administration and look to each other to bring existing partnerships that help the overall project achieve its overarching goals. We recognize the importance of these partnerships and strive to develop a shared understanding of the different roles and levels of faculty time commitment across the different institutions. For example, faculty at the TCUs, PUIs, and MCU work closely with undergraduates while teaching a full load of classes. Faculty at the RUs are focused on research productivity and teach fewer classes. We recognize and value that, while these differences are our strengths, they also need to be managed.

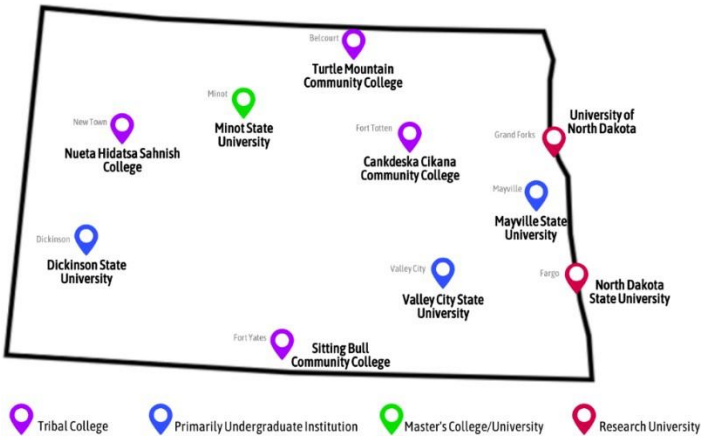


Figure 1. Map of North Dakota ACES NSF EPSCoR partner institutions of higher education.

Technological Readiness

Due to the distributed nature of the team, it is important that all members realize sufficient connectivity and access to technology to carry out research. ND-ACES will generate and steward valuable data as an asset of the project and will work to expand the Data Management Plan to address the full lifecycle of our data, from discovery to long-term archive. Project leadership strives to balance the timely public dissemination of the data with appropriate

protection of research intellectual property rights and will develop a clear and detailed plan to guide data management decisions.

Technological connectivity includes access to both video and audio resources for communication needs and remote computational resources and equipment. We understand the challenge of the “digital divide” between the TCUs, PUIs, MCU, and RUs and the variability of bandwidth across the state and specific platforms. Connectivity to High-Performance Computing (HPC) platforms for all members of the project, including those who are not located at RUs, is critical to the success of the project. Due to the importance of research literature, all participants will have access to the tools they need to secure scientific papers via affiliate accounts at the RUs. Moreover, since maintaining a sufficient funding level may prove challenging, we adopt a flexible approach to decision-making that allows for changes in methods, equipment, and software to benefit the project. Technological upgrades, including hardware and software, and the maintenance of key instruments are understood as important to team effectiveness.

Team Functioning

Effective team functioning is critically important for our success. Mutual respect, shared understanding, thoughtful communication, and the pursuit of excellence through unified goals will serve as our guiding principles. We value the development of a strong and communicative team with a shared understanding of project goals and respect for teammates who represent all project elements. Participants are expected to recognize, participate in, and promote key activities and approaches as defined below:

- Team training for all personnel that emphasizes communication, collaboration, cultural sensitivity, conflict prevention, and conflict resolution;
- Detailed discussions about the expectations of participants and their respective roles in accomplishing ND-ACES goals;
- Topical seminar series highlighting progress in the science projects, educational components, and outreach objectives of ND-ACES that avoid discipline-specific jargon so that they are comprehensible to an audience of diverse backgrounds;
- Discussions and preparation of guiding principles for materials and data sharing, publication authorship (appendix A), proposal development, and invention disclosures;
- Agreement on common software tools for ND-ACES-wide use for uniformity of illustrations and drawings (Lucidchart, Biorender, Illustrator, etc.); and,
- Implementation of Microsoft Teams as the uniform software platform for collaborations, meetings, and seminars to mitigate COVID-19-related effects and provide ease of access for all ND-ACES members.

Responsibilities of each team member include completing deliverables promptly, responding to requests for information from other members and leadership, and collaborating with other members to accomplish the project's goals.

Communication and Coordination

Internal communication and coordination: Our internal communication framework allows team members to develop “ambient awareness,” which occurs outside formal meetings and required team gatherings. We may develop and employ tools such as annual team network maps, surveys on team functioning, and data flow visualizations to gather information and reflect on team development and internal communication pathways. Conscious efforts such as group listening exercises and collaboration training will be employed in conjunction with team meetings and provide the opportunity to bring together ideas, identify tensions before they become conflicts, and develop a deeper understanding of the different institutional, geographic, and disciplinary cultures of our team participants. Team members agree to actively develop their deep listening skills by, for instance, participating in regular team meetings and asking relevant

questions, suspending their own beliefs before team dialogue, and acknowledging other's perspectives.

External communication: As a team, we share the responsibility for disseminating research results, engaging the public in research events, and communicating the overall impact of ND-ACES and the enhancement of ND's research ecosystem.

Leadership, management, and administration

The Leadership Team (PI, co-PIs, and CCBSE, Pillar, and PROSER Leads) is responsible for carrying out the project's mission and goals, reporting results, managing resources, supporting evaluation, serving on hiring committees, overseeing compliance approvals, and communicating with extended team members, collaborators, and partners. Our leaders are responsible for developing a shared understanding of the project among the full project team, including students and stakeholders.

The Strategic Plan serves as a clear rubric for the achievement of program goals, which will be monitored on an ongoing basis. The Leadership Team is responsible for communicating commitments and tracking the progress of all members as defined by the ND-ACES handbook and ongoing communication in mandatory meetings. Recognizing that NSF approves changes in direction and personnel that are required for the timely progress of project elements, the Management Team (PI, co-PIs, and CCBSE Leads) will actively work to prevent and minimize bureaucracy and related burdens on team members. We strive for transparency of management decisions and communication with grace and respect. We facilitate conversations to bring about a deeper understanding of cultural differences among the various institutions represented to develop a common understanding and respect for the benefits and challenges of doing team research.

Our project intentionally engages faculty from many institutions. Microsoft Teams, email, phone calls, regularly scheduled mandatory meetings, and a yearly conference are used to engage team members. All members of the Management team and those members of the Leadership team with CCBSE/PROSPER participants will travel to partner institutions during the first two years of the project. Thereafter, the PI/Co-PIs will travel to all participating institutions once or twice each year to engage in dialogue with participants and campus leaders, ensure that work continues to evolve in a collaborative and supportive manner, and address any emerging concerns across the project.

Conflict prevention and management

Conflict arises in many ways. Inter-personal conflicts between individuals, scientific conflicts centered around data ownership and manuscript authorship (appendix A), and allocation of resources are all potential sources of conflict. Our goal is to encourage healthy debate within and across teams while understanding and supporting demographic, cultural, and disciplinary diversity. Strategies to avoiding conflict include clear communication between not just teams and individuals but between the diverse set of institutions that constitute the overall program.

Communication will involve setting clear expectations, avoiding unrealistic deliverables, and encouraging thoughtful debate. Formal means of communication about the project include the ND-ACES Handbook, which sets expectations and offers solutions and or suggestions for each facet of the program, the authorship plan (appendix A), and the data management plan.

Avoidance of conflict is not always possible, and therefore we adopt a basic plan for resolution if conflicts arise. If possible, the conflict will be identified early and resolved collaboratively with active engagement by all parties. Open lines of communication, first to the Pillar/ PROSPER Leads, and then to the CCBSE Leads will support the resolution of conflict within the team.

Wherever applicable, mediation plans that are specific to both intra-institutional and inter-institutional conflicts will be observed. The final resolution of conflicts that cannot be resolved at a closer level will be determined by the members of the PI/co-PIs.

Training

We understand the importance of training. To ensure the timely completion of required training, the Management Team will track and provide clarification on training requirements. We understand that the participation of multiple institutions within the project is critical to our success, and we are respectful and understanding of differences due to access, support, time, and varying levels of resources at each campus. Our participants embrace a variety of worldviews and ways of knowing, and this diversity in thought will be expected, respected, and valued by all participants. Due to the complexity of this project and diversity of participants, we offer multiple mechanisms to access and participate in both required and optional meetings and strive to support multiple ways of learning and connecting to relevant material.

Quality improvement activities

Our team commits to spending time to reflect on progress, both in terms of the research goals and team functioning. Systematic reflection on team performance will be realized through time set aside to discuss and reflect at leadership meetings as well as pre-briefing and debriefing of more extensive activities such as annual statewide project meetings. The results will be summarized, and, to improve the quality of our collaboration, the Leadership Team will promptly address potential challenges.

Budget/resource allocation

Under our cooperative agreement, funding is authorized on a year-to-year basis. To ensure the successful implementation of all activities, no participant is guaranteed funding beyond the current project year. Thus, each year following the submission of the Annual Report [May 1], the CCBSE leads will meet with the research Pillar leads and the individual Pillar participants and review progress to determine budget changes necessary for ongoing project success, take advantage of emerging and innovative research, and produce optimal research results. The PI/PD has final approval on recommended changes to the budget and resource allocation. *[NOTE: Due to COVID-19, a mid-year budget review will occur.]*

Simultaneously, following the submission of each Annual Report on May 1, the PROSPER leads will meet with each of their section participants to determine what budget and IRB changes are necessary for the upcoming year to better meet the PROSPER Strategic Plan metrics, to respond to evolving changes in outreach activity protocols, and to produce optimal results for the activity participants. Once fully developed, recommended changes in budget and resource allocation will be presented to the PI/PD for final approval. *[NOTE: Due to COVID-19, a mid-year budget review will occur until otherwise noted.]*

Links to the documents that our team has adopted

- *Link to the diagram of organizational structure*
- *Link to ND-ACES Strategic Plan*
- *Link to ND-ACES Participant Handbook*

Appendix

- *Authorship Plan*

Appendix A: Authorship Plan

Our team agrees that as collaborative activities, the authorship and dissemination of research or outreach processes, products, events, or results stemming from most ND-ACES efforts will be a joint decision among all involved participants.

Therefore, as soon as possible our team agrees to write, adopt, and incorporate into the Collaboration Plan, a publishing model similar to the one promoted by the National Center for Ecological Analysis and Synthesis (NCEAS), which includes the following guiding principles:

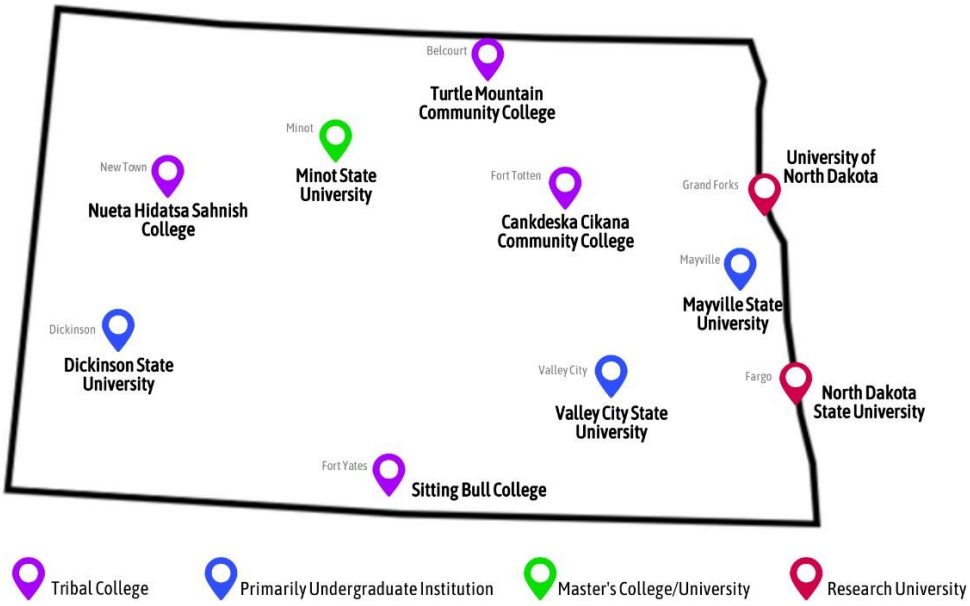
- Authors and co-authors communicate early and often about roles and responsibilities;
- Papers often have many co-authors, due to the collaborative nature of the research;
- Working group members are proactive about their interest in participating in manuscripts, and lead authors are open to the involvement of others;
- Authorship is inclusive (including students), but avoids honorary authorships.

Appendix D – Glossary of Acronyms

CCCC	Cankdeska Cikana Community College, Fort Totten, ND
CCBSE	Center for Cellular Biointerfaces in Science and Engineering
CI	Cyberinfrastructure
DoE	Department of Energy
DSU	Dickinson State University, Dickinson, ND
HPC	High-Performance Computing
MaSU	Mayville State University, Mayville, ND
MiSU	Minot State University, Minot, ND
NATURE	Nurturing American Tribal Undergraduate Research and Education
ND-ACES	New Discoveries in the Advanced Interface of Computation, Engineering, and Science
NDSU	North Dakota State University, Fargo, ND
NHSC	Nueta Hidatsa Sahnish College (formerly Fort Berthold Community College), New Town, ND
PROSPER	PROmoting Sustainable Partnerships in Education and Research
PUIs	Primary Undergraduate Institutions
REU	Research Experience for Undergraduates
RII	Research Infrastructure Improvement
SA	Sunday Academy
SBC	Sitting Bull College, Fort Yates, ND
TCUs	Tribal Colleges and Universities
TMCC	Turtle Mountain Community College, Belcourt, ND
UND	University of North Dakota, Grand Forks, ND
VSCU	Valley City State University, Valley City, ND

Appendix E – Location of Participating Institutions

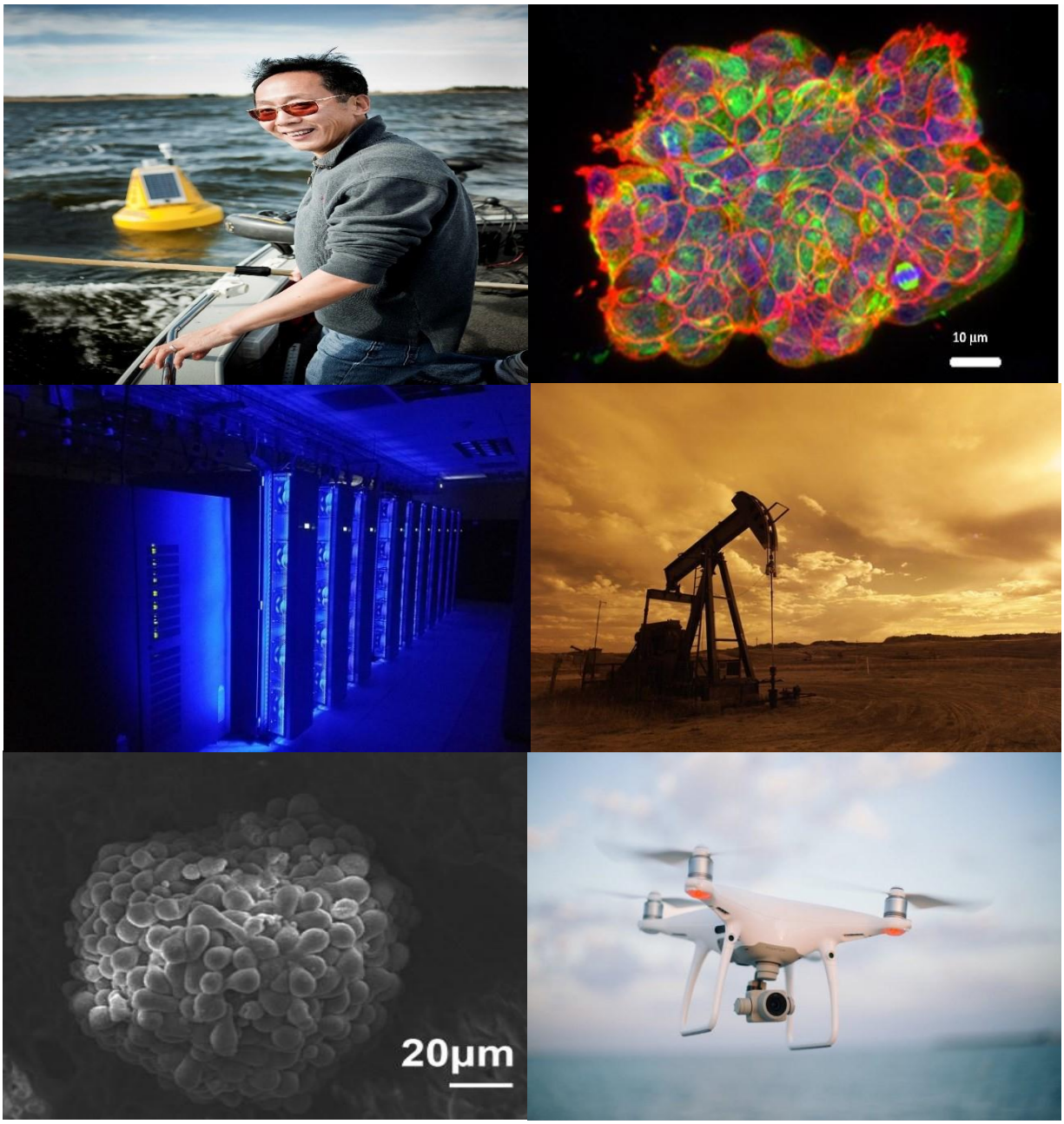
ND-ACES integrates research, education, and human resources with workforce development initiatives to strengthen the state's overall research competitiveness. The collective impact includes active involvement in research, outreach, education, and broadening participation activities by faculty, students (undergraduate and graduate), and staff throughout the state. There are ten participating institutions, including two research universities (RU), one master's college/university (MCU), three primarily undergraduate institutions (PUI), and four tribal colleges/universities (TCU).



Appendix F – North Dakota Science and Technology Plan and Letter of Reaffirmation

NORTH DAKOTA

SCIENCE AND TECHNOLOGY PLAN



Effective: July 1, 2018

Comments and credits for photos on cover page

Top left:	Dr. X. Zhang from the UND Center for Regional Climate Studies – collecting data from the weather station located in Devils Lake (reproduced with the permission of Dr. X. Zhang (UND)).
Top right:	Confocal microscopy image of prostate tumoroid created on bone-mimetic scaffold (reproduced with permission from Dr. K. Katti (NDSU)).
Middle left:	Bank of servers in the Center for Computationally-assisted Science and Technology (reproduced with permission from D. Skow (NDSU)).
Middle right:	Stock photo representing North Dakota's vibrant energy industry.
Bottom left:	In vitro creation of prostate cancer metastasis - prostate cancer tumor on bone site (reproduced with permission from Dr. K. Katti (NDSU)).
Bottom right:	Stock image representing North Dakota's growing UAV industry.

INTRODUCTION

North Dakota continues to expand its science and technology economy and ranks in the top quartile for net formation of high science, engineering and technology businesses as a percentage of all business establishments (1). The transformation of the state's two research universities – North Dakota State University [NDSU] and University of North Dakota [UND] – into Carnegie recognized research entities over the past twenty years has been a major contributor to and driver of this growth. The research expenditures for the two institutions grew from $56 million to almost $227 million (1997 to 2016) (2), providing a platform for growth in Science, Technology, Engineering and Mathematics (STEM) talent development, new scientific discovery and innovation and translation into new economic sectors.

The state's economy will always be tied to the agriculture and energy sectors. However, continual relevancy and competitiveness within commodity-based sectors will require execution of cutting-edge scientific discovery, increased development of the STEM pipeline and development of advanced technologies and secondary products to expand economic opportunities.

The growth of biosciences research and increasing opportunities related to unmanned aircraft systems (UAS) and software engineering, in the Red River Valley, combined with statewide business development, provide the state tremendous opportunity to grow the future economy in a well-balanced and diversified fashion. Economic development in these areas will need to rely on strong research and development capabilities of the state's institutions of higher education.

The North Dakota Economic Development Strategic Plan 2010-2020 (created by the North Dakota Economic Development Foundation and implemented by the Department of Commerce) focuses on five target industries (Figure 1) and five strategies (Table 1) to broaden the state's economic base, create new wealth and generate quality jobs for the state's citizens (3). North Dakota was designated by the FAA as an unmanned aerial system test site on December 30, 2013. After this designation, unmanned systems was added as an additional target industry. The Department of Commerce is focusing on biotechnology and bioenergy as developing areas, which hold promise for economic diversification (4).

Figure 1. North Dakota Department of Commerce target industries. Credited to the North Dakota Department of Commerce.

The foci and strategies of the previous 2012 edition of the North Dakota Science and Technology
Plan remains salient to the current North Dakota Economic Development Strategic Plan and the updated plan under development by the North Dakota Economic Development Foundation.

Table 1. North Dakota Department of Commerce essential strategies [these three of the five are relevant to this S&T Plan].

1. Continue investing in university-based research and development conducted with the private sector that engages North Dakota in emerging industries such as life sciences and advanced technology.

2. Embrace entrepreneurism and foster a culture of entrepreneurship where innovative, tech-savvy companies can thrive.

3. Continue investing in statewide talent strategies that address education, training recruitment and retention to provide a steady supply of skilled workers needed to fuel ling-term business growth.

The 2018 Science and Technology Plan updates the 2012 Plan where needed and introduces new foci and directions of the North Dakota University System. The 2012 Science and Technology Plan proposed seven strategies to position the state for continued growth of its science and technology enterprise:

- Focus research and development in areas that are already strengths in the state so that North Dakota can continue to increase its competitive advantage.
- Support and expand the infrastructure for research, particularly at the two research universities.
- Support technology transfer and, where appropriate, commercialization of inventions and innovations developed by universities.
- Foster partnerships between the private sector and research universities.
- Find ways to produce, hire, and retain more high school-level STEM teachers (a shortage occupation in the state), especially for small rural schools.
- Increase state investment in research at the institutions in the North Dakota University System.
- Create ways to increase awareness of the S&T capacity of the state, and to use it to develop regulatory policy based on sound science.

These strategies have been supported over the past six years by the continuation and expansion of existing initiatives and implementation of new activities (this is not an exhaustive list):

EPSCoR-funded Center for Regional Climate Studies
https://und-crcs.org/

EPSCoR-funded Center for Sustainable Material Science
https://csms-ndsu.org/

North Dakota STEM Network
http://www.ndstem.org/

Valley Prosperity Partnership
http://www.valleyprosperitypartnership.com/

Envision 2030

https://ndus.edu/media-and-publications/resource-library/#852-state-board-of-higher-education-reports-p1

Research ND
https://www.commerce.nd.gov/research/

Northern Plains Unmanned Systems Test Site
http://www.npuasts.com/

BioND [Bioscience Association of ND]
http://www.ndbio.com//

NDSU-UND Joint Biomedical Engineering Graduate Degree Program
https://bulletin.ndsu.edu/programs-study/graduate/biomedical-engineering/

https://engineering.und.edu/bme/

Additionally, the North Dakota University System has implemented a Digital Initiative Task Force to ensure networking and advanced scientific computing infrastructure keeps pace with the research needs of the system; particularly NDSU and UND. North Dakota already enjoys a robust broadband connectivity across all public schools/universities and state]. Governor Doug Burgum (on March 22, 2018) announced a 100-gigabyte upgrade to the state network, which will place North Dakota as a leader in connectivity.

Investment in these strategies and targeted sectors, along with a strong STEM job growth (5), positions North Dakota for substantial scientific advancement over the next 6-10 years.

North Dakota is one of 26 Established Program to Stimulate Competitive Research (EPSCoR) eligible (FY18) states designated by the National Science foundation (NSF); the EPSCoR program is directed at those jurisdictions that have historically received lesser amounts of NSF Research and Development (R&D) funding. It is designed to create sustainable improvements in a state's research infrastructure and R&D capacity, with the goal of increasing the state's national R&D competitiveness. North Dakota has been funded almost continuously by NSF EPSCoR since 1985 and has enjoyed strong support in the form of matching funds appropriated by the state.

The 2018 Science and Technology Plan was developed with one eye focused on the state's historic strengths [agriculture and energy] and the other eye looking towards a future, diversified economy.

The foundation of the S&T Plan is designed to accomplish the following objectives:

- expand higher education investments in areas of emerging strength that are focused on diversifying North Dakota's economy;
- provide flexibility for scientific advancement and development in any one of the currently defined North Dakota Department of Commerce targeted industries; and,

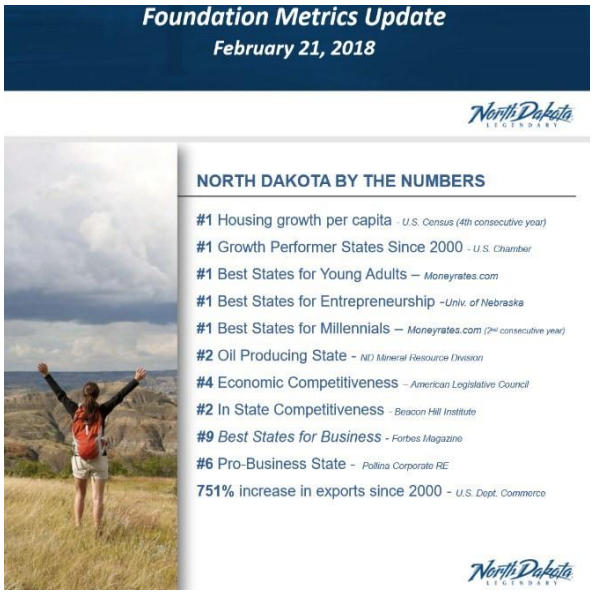


Figure 2. A snapshot of the business and innovation and entrepreneur climate in North Dakota. Chart credited to the North Department of Commerce; North Dakota Economic Development Foundation.

- develop initiatives that expand advanced scientific computing and visualization capacity that is foundational to innovation across the targeted industries.

NORTH DAKOTA'S SCIENCE AND TECHNOLOGY ECONOMY

North Dakota's economy has enjoyed robust growth during the past decade. In 2007, the state's gross domestic product was $28.9 billion and grew to $59.5 billion by 2014 (current dollars) (6). However, in 2016 ($53.3) and 2017 ($55.5), the GDP dropped, in part due to the State's reliance on a bi-commodity economy. Overall, however, North Dakota enjoys a very positive profile with respect to the business climate and innovation and entrepreneur activity (Figure 2).

The U.S. Chamber of Commerce's 2015 Enterprising States report ranks North Dakota as the nation's No. 1 in economic performance and talent pipeline and No. 6 in business climate (5).

Science and Technology Employment

In 2018, STEM jobs will represent 4% of all jobs in the state, and 60% of those jobs will require a B.S. or advanced degree (7). While the number of STEM jobs only numbered 19,820 in 2017 (8), the diversification of North Dakota's economy beyond traditional agriculture and oil and gas will require an expansion of the STEM talent pipeline to fill future jobs not yet conceived.

As of April 2018, North Dakota's unemployment rate was 2.6 percent (9). Total nonfarm employment has decreased by 1.8 percent in the previous 12 months. In the Mining and Logging sector, which included the state's oil and gas industry, employment increased 15.0 percent since May 2017. Manufacturing increased 3.3 percent, while information decreased by 1.9 percent.

Job Service North Dakota reported that in April 2018, there were 14,738 online job openings listed in the state (10). Of these jobs, 25.1% require at least a B.S. degree. Within the computer and mathematical occupation code, the state has observed an increase of 7.3 percent increase in openings over the past few years. Education, training, and libraries observed an increase in openings of 19.4 percent, while architecture and engineering has seen an increase of 72.7 percent.

The U.S. Chamber of Commerce 2015 Enterprising States report ranked North Dakota No. 1 for its talent pipeline (#1 in higher-ed degree output, #1 in STEM job growth, #2 in college affordability, #3 in educational attainment, and #5 in high-tech growth) (5). According to the U.S. Census Bureau, 28.2% of North Dakotans over the age of 25 have at least a B.S. degree (11).

Research Funding at the State's Two Research Universities

The Enterprising States report also ranked North Dakota No. 13 in State R&D Investment and #16 in Academic R&D Intensity (5) (Table 2). Academic R&D intensity is calculated as academic R&D funding as a percentage of Gross State Product. It should be noted, however, that in absolute terms, North Dakota ranks very low nationally (due to its small population): 40th in academic R&D and 46th in total R&D performance in 2015, according to the National Science Foundation (2).

Table 2. North Dakota rankings from the U.S. Chamber of Commerce Foundation Enterprising States Report - 2015.

U.S. Rank	Metric
1	Long-term job growth; gross state product growth; productivity growth; per capita income growth; legal environment; **higher-ed degree output**; labor force utilization; **STEM job growth**
2	Short-term job growth; road quality; state fiscal condition; college affordability
3	Adjusted median family income; **Kaufmann Entrepreneurism Index**; **educational attainment**
5	**High-tech job growth**
7	**New startup rate**
10	U.S. Business Policy Index
13	**State R&D investment**
14	Small business lending
16	**Academic R&D intensity**; cost of living
19	Bridge quality
20	**Broadband speed availability**
22	Higher-ed efficiency
24	Business tax climate

When looking at the results for the state's two primary research universities, the impact of the research dollars can be clearly seen. In FY2000, external grants and contracts at UND totaled $41.6 million, and by FY2006, had increased to $82.9 million. External funding hit an all-time high of $127.9 million in FY2010, and then fell to $98.6 million in FY2011, after the end of federal "earmarks." UND's ability to reach this goal as quickly as it did was undoubtedly aided by earmarks, which peaked at $39.9 million in FY2010. That these earmarks helped to build research capacity and competitiveness can be inferred from FY2012 grants and contracts that totaled $87million. UND's research and development expenditures for FY2016 were $70M as reported for the NSF Higher Education Research and Development survey (2).

NDSU experienced similar increases in external funding, including federal appropriations, achieving $112 million in external dollars for FY2011. Research spending at NDSU has consistently been above $100 million annually since

2004. For FY2016, NDSU's research expenditures were $156M as reported for the NSF HERD survey (2).

NDSU and UND are both classified by the Carnegie Classification as Doctoral Universities – Higher Research Activity. The challenge for the future will be for North Dakota's two research universities to remain competitive for what is predicted to be an increasingly smaller pot of federal research funds.

Both universities have developed strategic plans centered on grand challenges that are intended to focus research in areas of strength and emergence. NDSU's three grand challenges focus on food systems and security; healthy populations and vital communities; and, sustainable energy, environment and societal infrastructure. UND developed five grand challenges that promote energy security and environmental sustainability; address health challenges through basic, clinical and transitional discovery; help rural communities solve their unique health and social problems; drive the world-changing developments of UAS and do so in a way that reflects UND's values; and, effectively, efficiently, and ethically produce, manage, and securely use information in the age of big data.

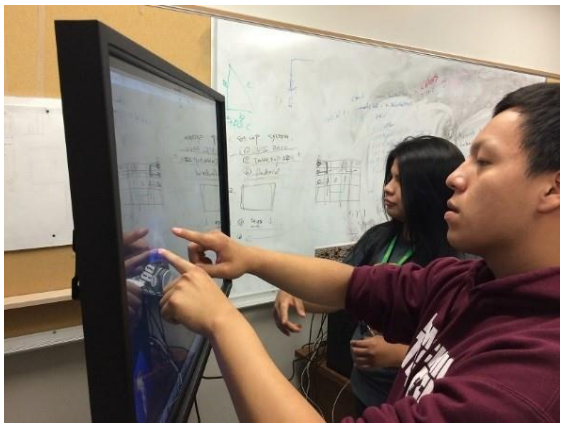


Figure 3. Students participating in the North Dakota Summer Nurturing American Tribal Undergraduate Research and Education (NATURE) Camp (2017). Photo received from the ND EPSCoR Office (photo release permitted by the students).

STEM Education in North Dakota

The U.S. Department of Education lists significant teacher shortages for math and science in North Dakota for 2016-2017 and 2017-2018 (12). According to Job Services North Dakota, the state produced 39 bachelor's-level math teachers in 2016, and 32 science and computer teachers (13).

To some degree this may reflect the number of rural schools in North Dakota that do not have large enough enrollments to hire separate teachers for each area of science. However, the paucity of students seeking degrees in chemistry and physics teaching seems to indicate that the state is not producing enough high school teachers with solid backgrounds in chemistry and physics.

Despite this, the state produced 664 engineers, 220 computer science and mathematics graduates, 78 physical scientists, and 281 biological scientists at the B.S. level (13).

Advanced degrees were awarded in biological sciences-61, engineering-164, computer science and mathematics-64, and 35 in the physical sciences. ND EPSCoR's NATURE (Nurturing American Tribal Undergraduate Research and Education; Figure 3) program works to engage American Indian students in STEM research as a means to increase interest in a STEM career.

NORTH DAKOTA'S TARGETED INDUSTRY SECTORS – STEM RESEARCH PRIORITIES

North Dakota's important science and technology sectors include agriculture, energy, biotechnology, unmanned systems, and advanced scientific computing and data analytics. These sectors align with North Dakota Department of Commerce's targeted industrial sectors in its 2010-2020 Strategic Plan (see figure 1). They also align with the targeted research areas outlined by the Valley Prosperity Partnership for building research and development capacity in the Red River Valley (a partnership of approximately 20 very significant businesses in the Valley/state), including (material science, unmanned systems, advanced manufacturing, energy and natural resources, healthcare and medical services, and agriculture and food safety) (14).

Agriculture - The historical foundation of North Dakota's economy has always been, and will continue to be, agriculture. In 2016, the state led the nation in the production of beans [all dry edible, pinto and navy], peas, canola, flaxseed, honey, oil sunflowers, durum and spring wheat, and all sunflowers (15). As of 2017, 39.1 million acres of land were in agricultural production across 29,900 farms (15). North Dakota ranks 11th in the nation in the total value of agricultural products sold, a tribute to both the quality of the products and to the extensive value-added innovations.

However, global commodity prices have impacted crop agriculture from 2012-2017. The average net farm income bottomed out in 2015 at $28,600; the lowest in two decades (15).

While agriculture will always be the backbone of the North Dakota economy, the "way agriculture is envisioned and implemented" will need to continually evolve to offset the global boom-and-bust cycles. In 1987, the number of persons living in cities and non-rural areas overtook those living in rural areas in the state. Today, 76 percent of North Dakota's population lives in incorporated cities (16). At the same time, the number of farms has decreased from 35,289 (1987) to 30,961 (2012) and the size of farms has increased from 1,143 to 1,268 acres (15).

Agriculture has significantly benefitted from modern methods of crop and livestock genetics, breeding, nutrition, soil management and fertility, pest management, and remote sensing data for enhanced crop management. The majority of these advances stem from research within the North Dakota University System. As just one example, since 2017, the NDSU Research Foundation has entered into 106 non-exclusive and 17 exclusive plant variety licenses since 2017 (Jolynne Tschetter, personal communication, March 2018), illustrating the multiple benefits of university-private partnerships.

The state has also seen an expansion of agricultural electronics companies, which provide technical solutions to agriculture's growing complexities. As examples - Phoenix International, an anchor tenant in the NDSU Research and Technology Park (RTP), was created to develop rugged agricultural electronic systems for agricultural application. In 1999, they were bought out by John Deere, which remains an anchor tenant in the NDSU RTP, and is the world headquarters for John Deere's agricultural electronics division. John Deere fully transitioned to a distinct brand – John Deere Electronic Solutions [and away from Phoenix International] in 2014. One of the original founders of Phoenix International created a new agricultural advanced electronics company, Appareo in 2003, which also is an anchor tenant in the NDSU RTP and employs over 193 full-time people.

The two research and education centers (Figures 4 and 5) funded by the current NSF EPSCoR RII cooperative agreement (EPSCoR OIA Award #1355466) are both tied to the state's agriculture prominence: Center for Regional Climate Studies (CRCS) and Center for Sustainable Materials Science (CSMS).

Figure 4. Student researchers collect samples as part of the Center for Regional Climate Studies. Photo received from ND EPSCoR (photo release permission provided by the researchers.

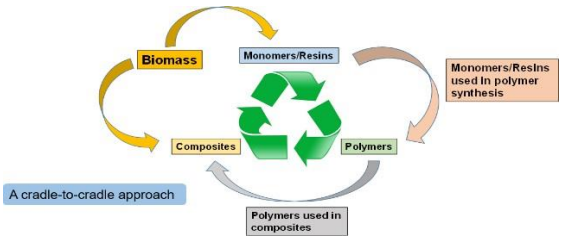


Figure 5. The Center for Sustainable Material Science focuses on the use of agricultural feedstocks for the development of novel monomers, polymers, and composites.

Energy – North Dakota has vast energy resources and currently ranks 6th in the country in total energy production (17). North Dakota established the EMPOWERED ND Commission in 2007 to develop a comprehensive energy policy to ensure the state proactively and efficiently manages its resources. In 2009, the legislature made EMPOWERED ND a permanent policy body (Century Code Chapter 17-07). The current comprehensive policy spans 2010-2025, with a stated goal of doubling the energy production from all sources by 2025 (the baseline is 2007) (18).

The state has the largest lignite deposits in the world. The first commercial mine opened in Morton County in 1873. By 2015, the lignite industry accounted for $3.4B of the state's economy and directly employed 3,942 persons. It is currently the 5th largest industry in the state, behind agriculture, oil and gas, tourism and manufacturing (19). Since 1988, lignite mines have produced approximately 30 million tons per year, most of which is used to make electricity for the region. In 2014, production stood at 28.7 million tons (20). The state currently has seven power plants, two poly-generation plants and six mines. While research takes place at many institutions within the state, the Energy and Environment Research Center at UND is a

world leader in low rank coals and provides applied technical solutions to the industry [https://lignite.com/mines-plants/research-facilities/energy-and-environmental-research-center/].

North Dakota has found itself significantly impacted by an oil boom because of the Bakken and Three Forks formations, which has positioned the state as the second largest oil producer in the country behind only Texas. On June 17, 2014, the state surpassed 1 million barrels per day in the Bakken shale formation within the Williston Basin. The Bakken/Three Forks formation is the largest known oil field in the world, covering a land area the size of West Virginia (21). It wasn't until the mid-2000s when advanced technologies for horizontal drilling and hydraulic fracturing were applied to the formation that the Bakken became an economic play. In five short years, North Dakota went from fourth in the nation to the second leading oil producer, accounting for 12% of U.S. production.

This recent positioning follows decades of booms and busts. The first wells were drilled in western North Dakota in 1910, but did not yield much oil due to primitive techniques and tools. The first major discovery of oil took place on the Clarence Iverson farm near Williston, North Dakota in 1951 by Amerada Petroleum (22). The discovery of oil in the Clarence Iverson No. 1 well began the state's first oil boom.

Since those early days, additional oil-boom/bust cycles have come and gone. Not until the concept of horizontal drilling in miles-deep oil shale deposits became technically feasible did the recent oil boom develop. The crude oil proved reserves have increased from 0.42 billion barrels in 2005 to 5.27 billion barrels at the end of 2016 (23). At the same time, the shale gas reserves have risen from 1 trillion cubic feet to 8.61 trillion cubic feet. In 2015, the industry supported 72,350 direct and indirect jobs and had an economic impact of $30.2 billion (24). At its peak in May 2014, the industry had 189 active drilling rigs. Following global price declines, the number of active rigs decreased to a low of 25 in May 2016 (25). However, increased technological efficiency measures have resulted in a rebound in active drilling rigs, which currently stands at 61 (25). While this number is less than 50% of the peak, the efficiency measures taken by industry at North Dakota's 14,000+ wells has kept daily production at or above 1 million barrels.

While North Dakota's lignite and oil industries enjoy the highest public profile and most legislative support, the state is also 5th in the nation for electricity generated by wind power (26). In 2017, wind energy generated 2,996 MW of electricity or 26.87% of the electric grid mix in the state and 3.36% of the nation's total wind energy (27).

Although several bills were introduced during the 2017 legislative session to reduce/eliminate tax credits for wind energy projects, the session closed without the passage of these bills. Because of North Dakota's wind resources, which average wind speeds from 10-13 miles per hour, investments in this industry are expected to grow over time.

In recent years, additional renewable energy sources have gained a foothold in the state. Ethanol production ranks in the top ten in the nation (26). North Dakota's only biodiesel production facility has a capacity of 85 million gallons per year.

An important component of the state's energy portfolio is found on the tribal lands located within the state borders. North Dakota's American Indian population stands at 42,000 and is the largest demographic behind white, Caucasian at 5.5% (11). While constituting only 2% of the state's land, tribal lands contributed to approximately 20% of the oil production in early 2017 (17). The majority of this production is concentrated on the Fort Berthold Indian Reservation, which is home to the Mandan, Hidatsa, and Arikara Nations [three affiliated tribes]. The Standing Rock Sioux Reservation is ranked in the top five nations in the country for its wind-generated electricity capacity (26). The Spirit Lake Reservation created the Fort Totten school as the first one in the nation [on tribal lands] to be a net zero energy school (28).

Biotechnology and Biomanufacturing – North Dakota's largest advanced manufacturing sector is biomanufacturing, while its largest biotechnology foci are found in the biomedical, life sciences, and agricultural sciences. These areas represent an evolving maturation of thought and strategy to diversity North Dakota's economy. The biotechnology sector is an emerging, but highly important sector to the state.

The biotechnology sector can be characterized by a growth in agricultural technologies and the biosciences (i.e., biomedical, bioengineering, biomechanics, etc.). Several factors point to bioscience and biotechnology's promise for future growth.

First, the state has always been an exporter of raw agricultural products, but only recently has North Dakota advanced its research with agricultural biotechnology. In 2014, the National Corn Growers Association selected Fargo, ND as the home for the National Agricultural Genotyping Center; a collaboration of the corn group and Las Alamos National Laboratory in New Mexico. The overarching goal of the facility is to develop on-site tests for corn diseases and diseases in other crops and for food-borne illnesses.

Academic R&D strength has developed in the use of raw agricultural residues for the creation of sustainable materials. These efforts have resulted in numerous discoveries, technology transfer activities, and start-up companies.

Second, as North Dakota's urban population began to exceed its rural population in the mid-1980s, the gap has continued and is currently the largest in the state's history. As of the 2014 population estimate, 76% of North Dakota residents resided in an urban area, with 80% of the growth since 2010 accounted for in nine cities (29). The rural to urban shift has also invited new perspectives on where limited research resources should be directed.

Third, North Dakota has enjoyed one of the lowest unemployment rates in the country (April 2018 – 2.6%) over the past 10 years (9). Unfortunately, the state struggled (and continues to) with a lack of talent pool for permanent positions. Numerous efforts were initiated to attract people to the state during the 2014-2017 time period. The

Department of Commerce's "It's a Good Life" Campaign sought to attract young people by exploiting the state's growing entrepreneurial ecosystem and technology-based urban centers, with a focus on high-technology opportunities.

Fourth, the median age of North Dakotans is 35, which makes it the fifth youngest state (11). As the population becomes more urban and younger, new industrial sectors are needed to support continued economic growth and attract a talent base that more aligned with an urban existence. A 2017 Business Insider article listed North Dakota as the 2nd ranked state for the influx of young people; lagging only Colorado (30).

Fifth, the incidences of chronic diseases (cancer, Alzheimer's, cardiovascular, and diabetes) have increased within North Dakota's population over the past decade (31). Historically, North Dakota focused its healthy population efforts on rural health initiatives and telepharmacy practices to reach the vast rural areas of the state. Subsequently, building technological R&D capacity (public and private sector) at the forefront of new discoveries and cures to address growing health concerns was not a priority. However, with the research developments in higher education, combined with emerging and established medical research companies now moving into or expanding in the state, there has been a shift in emphases. The thought process has changed, and the overall climate now favors an expansion into biotechnology endeavors as an emerging industrial sector that could help mitigate the boom-and-bust commodity economy and position North Dakota as a regional hub (and in particular, the Red River Valley) in the upper great plains.

North Dakota's bioscience/biomedical sector is small but emerging and holds tremendous potential. The Red River Valley Corridor, alone, is home to both research universities, numerous bioscience-related start-up companies, a brand-new Sanford Health hospital in Fargo (the largest center in the state and region, and the state's only level-1 trauma center), three clinical trial research facilities, several biomanufacturers and a growing presence of a Sanford Health R&D footprint.

In addition, NDSU and UND have, over the past several years, built critical mass and capacity in areas of materials, biosciences focused on disease and health, and advanced scientific computing. The two institutions implemented a joint graduate biomedical engineering program in 2017 and a joint graduate public health program in 2014. Both institutions include healthy populations in their respective grand challenge strategies. This growing collective higher education and private sector ecosystem has the potential to reshape North Dakota's economy in the future.

UAS – The North Dakota Department of Commerce added unmanned aerial systems to its list of targeted industries in recognition of the vast infrastructure in place to support growth and market share. North Dakota is home to the Minot and Grand Forks air bases, several National Guard installations, the second ranked aviation program in the country (John D. Odegard School of Aerospace Sciences), vast open-air space, multiple independent aviation-related businesses, and a favorable business climate.

The State of North Dakota was awarded one of the six FAA UAS test sites on December 30, 2013. Unlike the other five test sites, North Dakota's site is a statewide entity governed by the Northern Plains Unmanned Systems Authority [http://www.npuasts.com/]. The test site, administered by the University of North Dakota, has been working with the FAA to integrate UASs into the navigable airspace.

North Dakota has led the nation in many UAS efforts including the first daisy chain operation, first night flights, first to fly a large UAV for research purposes, and first to receive approval for flights in all parts of the country. In addition to the activities of the test site, North Dakota has created the Grand Skies UAV Business Park on the Grand Forks Air Base; the first in the nation. Tenants of the Park work in cooperation with the Northern Plains Test Site and have access to the air base's 12,351-foot runway via a cooperative agreement between the air base and Grand Skies.

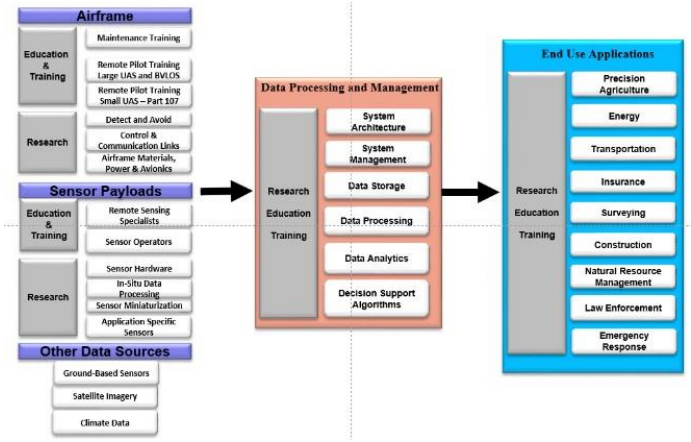


Figure 6. North Dakota is a leader in the country in unmanned aerial systems, and has a focus on building the data supply chain for the industry.

Research and education activities across the state have substantially grown since 2013.

Lake Region Technical College has developed a UAV-based precision agriculture course as well and a "learn to fly" course. UND and NDSU have both developed robust research and education programs focused on institutional strengths. UND has developed the Research Institute for Autonomous Systems [RIAS], with a vision of being a global leader in unmanned and autonomous systems research, application, and policy development. UND's historic strength in aviation positions the university to be a leader in training and systems logistics. NDSU has developed a strong research platform in the use of UAS in precision agriculture and has a proposed degree program in precision agriculture. Both universities have a focus on the data supply chain across the numerous UAS application sectors (Figure 6).

The global UAV market is expected to grow from $20.7B to $52.3B from 2018 to 2025 or a 14.51% compounded annual growth rate (32). North Dakota is the leading state in UAV research and testing and has been labeled the Silicon Valley of drone innovation by Silicon Valley and Technology [https://www.voanews.com/a/north-dakota-silicon-valley-drones/4172079.html]. Since 2005, the State has invested more than $38M in UAV research, testing, and application.

While precision agriculture still holds tremendous promise, the adoption of UAS in other sectors including energy, mining, military, and retail expands opportunities for sector growth in North Dakota. Collectively, NDSU and UND have partnered with several industrial sector entities since 2013 on research focused on precision agriculture, new

sensor development, utility line inspections, beyond line of sight operations and communications, wind turbine blade inspection, and data analytics. Over $5M of this research has been financed via the Research-ND funding vehicle.

Connectivity and advanced scientific computing – The Statewide Technology Access for Government and Education network (STAGEnet) is the sole centralized network that serves all state, city, and county governments, K12 educational entities, and all higher education campuses in the North Dakota University System (NDUS). The network was formally created in 1999 and is legislatively mandated to provide voice, video, and data services. STAGEnet provides wide area network (WAN) services which include routing real world Internet Protocol (IP) address blocks directly to the campuses. STAGEnet also serves as a backbone for campus to campus connectivity, allowing NDUS to centralize services such as Domain Name System (DNS)/Dynamic Host Configuration Protocol (DHCP) as well as voice, and to utilize the centralized video services.

North Dakota's advanced scientific computing infrastructure is evolving to keep pace with the growing computational needs of academic researchers and to provide critical infrastructure to the entire North Dakota University System and the Tribal Colleges. In addition, NDSU and UND are increasingly first choice partners to provide needed scientific computing and infrastructure for the rest of the state.

NDSU's Center for Computationally Assisted Science and Technology (CCAST) was established in 2003 and is a fully functioning core research center in support of the institution's land-grant mission. CCAST provides approximately 150 TFLOPS of computational power, 1 Petabyte (10^{12} bytes) of online storage, and 1 Petabyte of offline storage all connected with fast network fabric. CCAST has a permanent staff of 3.5 FTE, a student internship program with 12 students, and 2 FTE openings for user support staff (effective FY18).

Computational Chemistry, Digital Agriculture, and Engineering are the current major users of CCAST resources.

UND's Computational Research Center (CRC) was established in 2005. CRC will provide, when current upgrades are complete, approximately 170 TFLOPS of computational power, 0.7 Petabyte (10^{12} bytes) of online storage, and 1 Petabyte of offline storage all connected with fast network fabric. CRC has a permanent staff of 1 FTE, a student internship program with 1 student and contracted staff (2 FTE) from NDUS.

UND is a partner of the Midwest Big Data Hub. Digital Agriculture, Ecology and Computer Science are major users of the CRC facility.

NORTH DAKOTA ESTABLISHED PROGRAM TO STIMULATE COMPETITIVE RESEARCH (EPSCoR)

The Science and Technology Plan is a requirement of the NSF EPSCoR Research Infrastructure and Improvement cooperative agreement. The purpose of the plan is to

align North Dakota's science and technology goals and activities with those priorities of the federal government.

While the current and past EPSCoR funding has been pivotal in advancing the research capacity and competitiveness of the two research universities, the education, workforce development and diversity efforts have reached across the state to six of the eleven North Dakota University System institutions and the five Tribal Colleges.

The cumulative impact of EPSCoR has been substantial. Since 1986, ND has received >$63M in state funds that has been leveraged to garner >$350M in other external funding.

SCIENCE AND TECHNOLOGY PLAN

The North Dakota 2018 Science and Technology Plan details objectives, strategies, and actions for scientific discovery, education, workforce development, diversity and communications that will help drive decisions on new directions for the state's higher education institutions. The Plan also provides a framework for statewide discussions on STEM advancements that result in a more dynamic and innovative economy.

This Plan consists of five strategies that align with efforts by the North Dakota Department of Commerce, Valley Prosperity Partnership, Department of Public Instruction, and NDUS.

- Focus research and development in areas that are already strengths and those that are emerging as strengths so that North Dakota can continue to increase its competitive advantage;
- Support and expand the infrastructure in key R&D areas;
- Foster partnerships between the private sector, communities, educational sector, start-up entities, and research universities. Support technology transfer and, where appropriate, commercialization of inventions and innovations;
- Produce and retain STEM graduates who are technically-skilled and business-wise;
- Create ways to increase awareness of the S&T and innovation ecosystem within the state as a means to drive economic diversification.

Strategy 1: Focus research and development in areas that are already strengths and those that are emerging as strengths so that North Dakota can continue to increase its competitive advantage

A. Advocate for continued and increased state investments in North Dakota's targeted industrial sectors of importance.
   1. Technology
      i. Working with the Department of Commerce, develop a future-looking definition of "technology" as it applies to diversification of the economy;
      ii. Support an expanded advanced scientific computing and visualization foundation that not only serves all of higher education, but educational and industry needs of the entire state;

iii. Support efforts to nurture and develop the fledgling biotechnologies sector in the state. This includes agricultural-based biotechnology as well as bioscience/biomedical (including materials science) efforts;
iv. Support efforts to nurture and expand the emerging information technology and software engineering sectors;
v. Enlarge understanding of the emerging biotechnology sector and how higher education, communities, private businesses, and the Department of Commerce can converge to expand efforts in this area;
vi. Support the development of a "biosciences/biomedical" research corridor in the Red River Valley;
vii. Expand support across ND for materials science R&D, working with the Department of Commerce and other partners to develop applications within all of the important industrial sectors.

2. Unmanned Aerial Systems
   i. Work with the Department of Commerce to better understand the long-term R&D advantage of the state.
   ii. Foster better partnerships between private sector entities and higher education that result in a sustainable growth of the industry outside of the current service industry;
   iii. Support efforts to develop infrastructure [physical and human] to deal with the data supply chain as a result of the growth of the UAV industry;
   iv. Create an R&D ecosystem for both the use of UAVs and research on UAVs that positions North Dakota at the forefront of unmanned systems;
   v. Improve understanding throughout ND of unmanned systems beyond "aerial".
3. Value-added agriculture
   i. Continue to develop a deeper understanding of the market potential of post-harvested, value-added activities/processing;
   ii. Support further development of, and partners for, sustainable materials derived from agricultural products and wastes;
   iii. Working with the NDSU Agricultural Experiment Station, expand the use and understanding of genomics and bioinformatics as a means to develop new crop varieties that maintain North Dakota as a national leader;
   iv. Expand the understanding of regional climate shifts, and its impacts on growers' choice of crops, to continue North Dakota's agricultural leadership role;
   v. Gain a deeper understanding of agricultural crops that are compatible with the state's growing conditions and which can expand opportunities beyond food and fiber;
4. Energy
   i. Continue to gain a deeper research understanding of the oil shale resources of western North Dakota;
   ii. Support further development of enhanced efficiencies and environmentally sound methods of oil recovery;
   iii. Work with higher education, including UND's Energy and Environmental Research Center and NDSU's College of Engineering, to promote further R&D on oil-related issues such as carbon sequestration platforms, enhanced engineering efficiencies, and other improvement processes;
5. Advanced Scientific Computing and Visualization
   i. Expand the computing and networking infrastructure at NDSU and UND to meet the growing needs of researchers across the state;
   ii. Develop appropriate infrastructure at UND and NDSU for proper storage and management of data;

iii. Develop and support programs to train faculty and students in data science and management R&D across NDUS and the Tribal Colleges;
iv. Create training programs to develop a North Dakota high performance computing (HPC) workforce;
v. Engage NDUS, Department of Commerce, city economic development corporations, and state and local governments to expand usage of advanced scientific services [HPC, data analytics, informatics] beyond the two research universities.

B. Provide continued support for the grand challenge research at NDSU and UND.

Strategy 2: Support and expand the infrastructure in key R&D Areas

A. Make current technology infrastructure and equipment available throughout NDUS, Tribal Colleges, community-based entities, and businesses to expand use throughout the state and enhance collaborations.
   1. Expand efforts via the Digital Initiative Task Force to ensure all institutions in NDUS, the Tribal Colleges and public schools have access to networking and advanced scientific infrastructure;
   2. Extend the NDSU faculty expertise and equipment database model to all institutions within NDUS to promote the assets of North Dakota Higher Education to other statewide entities and private businesses.

B. Provide continued support for important infrastructure that expands R&D efforts and diversifies the economy, including but not limited to NDSU's CCAST, UND's CRC, STAGENet, Northern Tier, NDSU and UND's Institutional Core Facilities, NDUS' STEM-based Colleges, etc.
   1. Maintain and expand NDSU and UND's core advanced scientific computing capabilities;
   2. Hire and retain high quality STEM faculty throughout NDUS and the Tribal Colleges;
   3. Hire faculty in areas critical to UND and NDSU's grand challenges and the state's targeted sectors;
   4. Support the primarily undergraduate institutions, community and technical colleges, and the tribal colleges in the development of workforce programs that align with the R&D efforts;
   5. Recognize the importance of maintaining the networking capabilities (Northern Tier) through a committed NDUS and state effort.
   6. Hire, train, and retain highly qualified technical staff to support the technical services of NDSU's CCAST and UND's CRC;
   7. Hire, train, and retain highly qualified technical staff to support the advanced R&D efforts of faculty in targeted areas.

Strategy 3: Foster partnerships between the private sector, communities, educational sector, start-up entities, and research universities. Support technology transfer, and where appropriate, commercialization of inventions and innovations.

A. Promote better synergies between NDSU and UND and the private sector.
   1. Collaborate with the Valley Prosperity Partnership in providing information on development opportunities based on advanced scientific research at NDSU and UND;

2. Work with the Department of Commerce to expand public funding (i.e., Venture Grant) for early-stage, research-intensive business development and commercialization;
3. Develop better collaboration between NDSU and UND on technology transfer practices to create a more streamlined approach for companies;
4. Develop a more defined strategy for SBIR/STTR and venture capital for early- to mid-stage scientific research.
   i. Provide workshops for faculty and small businesses on grant-writing.
   ii. Provide small businesses with added resources to take research to market.
5. Create synergy between the research universities and state entities to support a cohesive path from scientific discovery to commercialization with emphasis on the following partners:
   i. Department of Commerce
   ii. Valley Prosperity Partnership
   iii. NDSU Research and Technology Park
   iv. UND Center for Innovation
   v. Idea Center - Bismarck
   vi. North Dakota Chamber of Commerce
   vii. Greater Fargo-Moorhead Economic Development Corporation
   viii. Greater Grand Forks Economic Development Corporation
   ix. Community-based Chambers of Commerce

Strategy 4: Produce and retain STEM graduates who are technically-skilled and business-wise

A. Continue to develop STEM awareness and engagement at the primarily undergraduate institutions (PUIs) and Tribal Colleges (TCs).
   1. Maintain an updated broader impacts white paper for the TCs and PUIs that outlines the needs of each institution in fulfilling their missions of STEM awareness.
   2. Continue to work with the TCs and PUIs on pipeline programs that facilitate streamlined student transfer processes to UND and NDSU for either B.S. degree completion [for students with A.S. degrees] and/or advanced studies.
   3. Expand EPSCoR's distributed research experience for undergraduates (dREU) program to allow for a larger student enrollment per year.
B. Prepare highly-skilled, globally-minded Bachelor level graduates with advanced knowledge of computational and data sciences and cybersecurity issues.
   1. Expand EPSCoR's cyberinfrastructure (CI) internship program on the NDSU and UND campuses;
   2. Develop an EPSCoR CI Intern program for the PUI/TCs;
   3. Continue to grow the cybersecurity certificate program administered by NDSU, in collaboration with Minot State University and UND.
C. Support advanced (Masters and Ph.D.) graduates with strong integrative skills that translate into R&D environments within the public and private sectors.
D. Continue to sustain current interdisciplinary graduate programs in biomedical engineering, cellular biology, and materials and nanotechnology.
E. Continue to expand the NDSU's Innovation Challenge program to encourage student entrepreneurism.

F. Develop A to Z programming to help student and faculty interested in creating start-up companies.
G. Work with the Department of Public Instruction, Community and Technical Colleges, Primarily Undergraduate Institutions, and private businesses to create scalable career pathways in biosciences/biomedical technology, energy, agriculture, computational and data sciences, and UAVs.
H. Build a stronger partnership between ND EPSCoR and the Department of Public Instruction and the North Dakota STEM Network.

Strategy 5: Create ways to increase awareness of the S&T and innovation ecosystem within the state as a means to drive economic diversification

A. Develop a clear and concise communication and marketing strategy for use with state, community, educational, and private entities.
B. Work with the Departments of Commerce and Public Instruction to collate and disseminate data about the impacts of STEM in an innovation- and knowledge-economy.
C. Provide frequent updates to state legislators, Governor's office and community-based economic development corporations on the progress of the innovation-economy.

ND EPSCoR will prepare an annual report detailing progress on efforts in this plan and how they cross-link with the NSF EPSCoR RII Cooperative Agreement activities, which will be provided to the North Dakota EPSCoR State Steering Committee.

Feedback from these reports will be used to refine and/or update the S&T Plan when necessary.

References Cited

1. **National Science Board.** *Science and Engineering Indicators 2018 . NSB-2018-1.* Alexandria, VA: National Science Foundation, 2018.

2. **National Science Foundation.** *Higher Education Research and Development Survey Fiscal Year 2016.* [Online] November 30, 2017. https://ncsesdata.nsf.gov/herd/2016/.

3. **North Dakota Department of Commerce.** *North Dakota Economic Development Strategic Plan 2010-2020.* Prepared by Covenant Consulting Group, 2010. Strategic Plan.

4. **North Dakota Department of Commerce - About Us.** [Online] [Cited: March 4, 2018.] https://www.commerce.nd.gov/about/.

5. **U.S Chamber of Commerce Foundation.** *States Innovate - North Dakota.* [Online] 2015. https://www.uschamberfoundation.org/enterprisingstates/#ND.

6. **U.S. Department of Commerce.** *Gross Domestic Product by State (millions of current dollars).* U.S. Bureau of Economic Analysis. [Online] [Cited: February 15, 2018.] https://www.bea.gov/itable/.

7. **Carnevale, Anthony P., Smith, Nicole and Melton, Michelle.** ***S****TEM State-Level Analysis.* Washington, D.C.: Georgetown University, Center on Education and the Workforce, 2011.

8. **U.S. Department of Labor.** *Occupational Employment Statistics.* Bureau of Labor Statistics. [Online] 2018. https://www.bls.gov/oes/#data.

9. **U.S. Department of Labor.** *Economy at a Glance.* Bureau of Labor Statistics. [Online] 2018. https://www.bls.gov/eag/eag.nd.htm.

10. **North Dakota Job Service.** *April 2018 Online Job Openings Report.* [Online] 2018. [Cited: May 1, 2018.] https://www.ndworkforceintelligence.com/gsipub/index.asp?docid=529.

11. **U.S. Census Bureau.** *Population Estimates, July 1, 2017 - North Dakota.* [Online] https://www.census.gov/quickfacts/fact/table/ND,US/PST045217.

12. **Cross, Freddie.** *Teacher Shortage Areas Nationwide Listing 1990–1991 through 2017–2018.* Washington, D.C. : Education, U.S. Department of; Education, Office of Postsecondary, 2017.

13. **North Dakota Job Service.** *Education Profile.* [Online] February 2018. https://www.ndworkforceintelligence.com/gsipub/index.asp?docid=565.

14. **Valley Prosperity Partnership Research Working Group.** *Expand Research Capacity & Relevancy in the Red River Valley. Report* 2016.

15. **Jantzi, Darin; Hegameister, Kara; Kuprich, Brenda.** *North Dakota Agricultural Statistics 2017.* USDA National Agricultural Statistics Service, Northern Plains Region, North Dakota Field Office. Fargo : North Dakota State University, North Dakota Department of Agriculture, United States Department of Agriculture, 2017.

16. **Cicha, Joe.** *Growing ND by the Numbers.* North Dakota Department of Commerce, 2015.

17. **U.S. Energy Information Administration.** North Dakota State Profile and Energy Statistics. [Online] 2018. [Cited: March 20, 2018.] https://www.eia.gov/state/?sid=ND.

18. **Empowered ND Commission.** *EMPOWERED North Dakota - Comprehensive State Energy Policy 2010-2025.* North Dakota Department of Commerce, 2010.

19. **Lignite Energy Council -** *Economic Impact.* [Online] 2018. [Cited: March 20, 2018.] https://lignite.com/what-is-lignite/economic-impact/.

20. **Lignite Energy Council -** *Production of Lignite.* [Online] [Cited: May 1, 2018.] https://lignite.com/what-is-lignite/production-of-lignite/.

21. **Energy of North Dakota - About the Resource.** [Online] [Cited: April 4, 2018.] https://energyofnorthdakota.com/home-menu/how-oil-is-produced/about-the-resource/.

22. **Bluemke, John P.** *The 50th Anniversary of the Discovery of Oil in North Dakota.* North Dakota Geological Survey Miscellaneous Series No. 89, 2001.

23. **U.S. Energy Information Administration.** *Crude Oil Proved Reserves, Reserve Changes and Production.* [Online] 2018. [Cited: April 4, 2018.] https://www.eia.gov/dnav/pet/PET_CRD_PRES_A_EPC0_R01_MMBBL_A.htm.

24. **Bangsund, D.A.; Hodur, N.M.** P*etroleum Industry's Economic Contribution to North Dakota in 2015.* Agribusiness and Applied Economics Report No. 766 , 2017.

25. **North Dakota Department of Mineral Resources.** *Current Active Drilling Rig Count.* [Online] [Cited: May 24, 2018.] https://www.dmr.nd.gov/oilgas/riglist.asp.

26. **U.S. Energy Information Administration.** *North Dakota State Energy Profile.* [Online] February 15, 2018. [Cited: April 4, 2108.] https://www.eia.gov/state/print.php?sid=ND.

27. **WINDExchange.** *Wind Energy in North Dakota.* [Online] Department of Energy, Office of Energy Efficiency and Renewable Energy, 2017. [Cited: April 4, 2018.] https://windexchange.energy.gov/states/nd.

28. **DSGW Architects.** *Fort Totten Builds First Zero Energy School on Tribal Land.* [Online] December 13, 2017. [Cited: April 4, 2018.] https://trimtab.living-future.org/blog/fort-totten-builds-first-zero-energy-school-on-tribal-land/.

29. **North Dakota Census Office.** *Growing ND by the Numbers.* [Online] North Department of Commerce, September 2015.

30. **Loudenback, Tanza.** The 15 US states where young people are moving in, jobs are plentiful, and business is booming. [Online] March 13, 2017. http://www.businessinsider.com/the-15-us-states-with-the-strongest-economies-2017-3.

31. **Dalrymple, Jack, Dwelle, Terry and Fremming, Krista.** *The Burden of Chronic Disease in North Dakota. A Status Report for 2016.* s.l. : North Dakota Department of Health, Cooperative Agreement Number DP4825-04-1, 2016.

32. **Research and Markets.** *Unmanned Aerial Vehicle Market by Application, Class, System, UAV Type, Mode of Operation, Range, Point of Sale, MTOW And Region - Global Forecast to 2025.* February 2018. p. 266. Report ID: 4402200.

NORTH DAKOTA
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June 10, 2019

Kelly A. Rusch, Ph.D., P.E., BCEE
Executive Director, ND EPSCoR
P.O. Box 6050 – Dept. 4200
Fargo, ND 58108

Dear Kelly,

On behalf of the North Dakota EPSCoR State Steering Committee [NDESSC], I am delighted to write this letter re-affirming the committee's endorsement of the Science and Technology Plan [Plan] released in July 2018. The research and education activities outlined in the ND-ACES RII Track-1 proposal align with the goals and strategies of the Plan and represent a collaborative effort to diversify the state's economy by serving as a catalyst for capacity building in the fledgling biotechnology arena.

As you are aware, the NDESSC embarked on a concentrated review and discussion of the Plan over the course of the past six months. As a result of this review, NDESSC articulated its top four priorities, which include:

1. Capitalize on the strong alignment of NDSU and UND priorities with state research areas by recognizing and nurturing symbiotic research and educational strengths not only in the PUIs and TCs, but in the state commitment to K-12.

2. Continue to expand the networking that ND EPSCoR supports, with special attention given to broadly communicating the impacts that science and engineering have had on ND.

3. Foster the understanding that research and educational quality are inextricably linked.

4. Connect research advances in basic and applied science and engineering to opportunities for commercial successes and especially those that have broad impacts on the state.

Recent expansions of several private sector biopharmaceutical/biomedical entities, commitment of the state's two research universities to research areas in the biosciences/health fields, and continued and growing collaborations with the primary undergraduate institutions, tribal colleges, and master's college/university fit well within these priorities. The overall expansion of efforts by ND EPSCoR, and the RII Track-1 in particular, is critical for the continued growth of STEM strength in the state.

Respectfully,

Casey Ryan

Casey Ryan, MD
Member, State Board of Higher Education
Chair, EPSCoR State Steering Committee

Appendix G – Programmatic Terms and Conditions - Hiring Plan

NSF Jurisdiction Specific Terms and Conditions: *Hiring of Faculty and other Key Personnel*: *The PI is responsible for ensuring that participating institutions follow through recruiting and securing all proposed hires of faculty and other key personnel as established by the original project proposal, any award conditions, or the approved RII Track-1 Strategic Plan. Any changes require prior NSF EPSCoR approval. The annual or final report must report on the status of faculty (and other key personnel) hires.*

Background

Both RUs have research foci in health (biosciences/biomedical) and infrastructure (data analytics/societal infrastructure).

- NDSU's commitment to health-related bioscience includes the recent hiring of seven faculty in biomedical engineering-sensors and 3D printing; materials/ mechanobiology; computational biology; cancer biology; polymer science; and; computational chemistry (the last two were hired under the 2014-2021 NSF Track-1 [INSPIRE-ND]). NDSU has also invested in the Center for Computationally Assisted Science and Technology (CCAST), increasing its footprint, procuring additional equipment, and recruiting a research facilitator (FY18).
- UND has also committed to hiring in the biosciences/biomedical arena, with plans to hire up to six research-intensive computational faculty with expertise in data analytics, machine learning (ML), artificial intelligence (AI), and deep learning. UND's School of Medicine has invested in the growth of cellular expertise through three recent hires in cancer cell biology and the establishment of a clinical and translational research center (IDeA; Dakota Cancer Collaborative on Translational Activity, which also includes NDSU). UND has also hired faculty in integrative systems biology and computational materials chemistry and recently expanded its Computational Research Center (CRC).

To fill the gap identified in state investments to meet the vision of becoming the Northern Plain's leading scientific and educational driver in new and sustainable biosciences technology advances, ND-ACES incorporates the recruitment and hiring of two materials faculty, one at NDSU and one at UND.

Recruiting and Hiring Plan

NDSU and UND will conduct national searches for the two tenure-track faculty members. It is anticipated that each hire will be at the assistant professor level.

NDSU: The new faculty hire (depending on the background of the selected candidate) may fit within one of several colleges: Engineering; Science and Mathematics; or Agriculture, Food Systems, and Natural Resources. Thus, a cross-disciplinary search committee will be selected to include faculty from each of these colleges and CCBSE researchers. The position will be advertised nationally and internationally, on the NDSU web page, within targeted scientific societies, and through directed emails and letters to chairs and faculty in the targeted research groups and others as well as relevant listservs.

The committee will filter applications to select a top tier list of candidates (approximately 10-12) for phone/video conference interviews. Three or four candidates will be selected as finalists for on-campus (or virtual) interviews. These interviews will take place over two days. The candidates will meet with college/department faculty, students (undergraduate and graduate), the chairs of the departments in which the faculty may fit, and deans of the three colleges. In addition, each candidate will present a public research seminar as well as teach a class lecture

pertinent to the materials area (the class will be determined by the search committee). NDSU has made a significant effort to recruit a diverse faculty including members from underrepresented and underserved groups.

The NDSU faculty search will begin in fall 2021. It was originally planned to have the new faculty member in place in year two. However, COVID-19 (and the financial implications) shifted this search to the fall of year two. The intent is for the new faculty to join the team at the beginning of year three.

UND: The new faculty hire will be recruited to join the Department of Chemistry in the College of Arts & Sciences. The position in materials science will contribute to the broad area of synthetic-biological chemistry applications and focus on the development of soft-tissue-like material. The new position will strongly complement the department's existing expertise in synthesis and modeling such systems and biomedical applications. This ties in directly to the department's emphasis on biomaterials for transformational health related applications.

The faculty search will follow standard practices for hiring tenure-track faculty at UND and practice within the Department of Chemistry. Since one goal is for the position to collaborate with faculty from the Department of Biomedical Sciences in the School of Medicine & Health Sciences, the search committee will include at least one member from that department. Per UND practice, the position will be widely advertised, posted on the UND website, and distributed through relevant listservs and professional groups. UND has made concerted efforts to recruit strong and diverse candidate pools and will do so in this process. The committee will review applicants and select a small group of candidates to progress through a phone/virtual interview and further narrow the group to candidates invited for an in-person or virtual campus visit. The intent is to commence the search in year one and have the new faculty member in place at the beginning of year two.

UND hired Binglin Sui, Assistant Professor, Chemistry. His contract begins August 1, 2021.

Mentoring Plan

New faculty members at all participating institutions and other faculty members wishing to participate, will be mentored by CCBSE personnel and by faculty within his or her department or college. Each new faculty member will receive an orientation to the CCBSE or PROSPER research programs, their goals, and expected outcomes from the CCBSE or appropriate PROSPER Leads; be included in the regular team meetings; and; meet with other team members to identify collaborations as a means to integrate them into CCBSE's or PROSPER's efforts. Each faculty hire will develop an academic strategic plan that is aligned to successful CCBSE research and their programmatic research agenda.

Monthly mentoring sessions throughout each academic year will include topics such as grant writing, graduate student and postdoctoral recruitment, establishing collaborations, etc. will be available to these faculty. In addition to formal mentoring, senior faculty colleagues will aid each other in reviewing proposals and manuscripts and providing advice on issues of science and research. Each mentored faculty member will be expected to prepare a plan for their research, including goals, milestones, and collaborations with other CCBSE or PROSPER team members.

Appendix H – SWOT Analysis

During the SWOT Analysis Meetings which occurred synchronously on July 14, 2020, asynchronously throughout the month of July, and then during the Strategic Planning Meeting, senior personnel were asked to consider all potential risks to the project and associated consequences. This includes the consideration of three NSF-facilitator driven scenarios related to COVD-19: 1) back to normal, 2) some hybrid between back to normal and continued restrictions, and 3) full restrictions (i.e., completely virtual).

ND-ACES SWOT Analysis

- Strengths Identified
  - Strong team with diverse and relevant expertise, an established track record of collaborative efforts, and confidence in and belief of the importance of the project
  - Access to expert technical resources
  - Solid research plan building on expertise and resources of team
  - Access to competent student pool
  - Increased opportunities for student participants
  - Team science approach to ensure the involvement of all Pillars
  - Institutions involved in project have good reputation in community/among stakeholders
  - All institutions have administrative buy-in
  - Centralized, experienced state EPSCoR office that handles a majority of the logistics
  - Cash match from the State of ND
  - One unified center will help to direct resources and guide sustainability efforts

- Weaknesses Identified
  - Team is very large and diverse with many complex collaborative tasks to complete in a limited timeframe – **see Risk Mitigation Plan #1**
  - Inability to maintain consistent research ties to TCU, MCU, & PUI faculty due to their full-time teaching schedules, travel distances, and weather
  - Technical resources are not equal on all campuses – **see Risk Mitigation Plan #2**
  - Obstacles inevitable in our complex research plan that will require the team to be very adaptable – **see Risk Mitigation Plan #3**
  - Few opportunities to expand diversity activities beyond American Indians and women
  - Inability to get time from RU industry engagement, intellectual property, research partners, and innovation center personnel
  - Social media accounts have low audience engagement/content
  - Limited experience among senior personnel in working under a cooperative agreement
  - With such diverse intuitions, communication regarding administrative deadlines can be complex

- Opportunities Identified
  - Discovery of new ways to conduct research and outreach due to COVID-19
  - Potential of ND-ACES to build research capacity, expand workforce, and stimulate industry growth in ND
  - Enhanced student and early career faculty opportunities
  - Potential to address today's research questions in this area

    - Increased focus on the importance of ND STEM's pathway
    - Members of ND-ACES external advisory board are national level experts well versed in this arena who are poised to assist the team in their ultimate goal of sustainability
    - New research subject matter to North Dakota; not commodity-based research, so chance to be received favorably by state's stakeholders

- Threats Identified
    - Interruptions in ND-ACES activities due to COVID-19 – **see Risk Mitigation Plan #4**
    - Inability to recruit new faculty hires – **see Risk Mitigation Plan #5**
    - Decline or discontinuation of state support during the 2021, 2023, or 2025 legislative sessions – **see Risk Mitigation Plan #6**
    - A researcher becomes unable to contribute to project due to illness or departs University – **see Risk Mitigation Plan #7**
    - Inability to recruit qualified students
    - Flooding shuts down campuses
    - New collaborative external proposals not funded
    - Cyberinfrastructure challenges limit distance options – **See Risk Mitigation Plan #2**
    - Limited local collaborative interest from individuals and public and private entities
    - Financial implications that may result due to COVID-19
    - New research subject matter to North Dakota; not commodity-based research, so chance to be received unfavorably by state's stakeholders

COVID-19 Impacts from Asynchronous SWOT meeting: Identified Threats

- **Threat 1**
    - The uncertainty COVID-19 creates. Normally I know what the semester looks like and how much time things take but right now nothing is sure and I do not know what is going to happen in the fall which makes incorporating research more complicated. Will I have time to properly supervise the students in their research?
    - Faculty are still working on reopening plans for the fall
    - Right now, it is uncertain how much research we can do in the fall semester.
    - Balance between teaching and research duties. Current reopening plans require more time for teaching preparation and execution.
    - Time and class schedules will be the biggest challenge and will affect how flexible faculty can be.
        - Addressing Threat 1: The senior personnel have gained experience with online academic, research, and outreach activities during the 2020 spring/summer, which will serve the project team well as we implement ND-ACES.
- **Threat 2**
    - Research slowed in late spring but has returned to a level approaching normal through the summer. Graduate students are coordinating with each other so that their time in the lab overlaps as little as possible. With no teaching activities to worry about this scheduling approach has been manageable. Lack of clarity about makes short term planning for when the summer ends a challenge.
    - The time each student can work in the lab is somewhat limited as we try to minimize overlaps between students.
    - Potential to completely stop this research - cannot be done remotely at all.

- Potential slowdown of research due to the limited time of students and access to the core facilities.
- Can we do experiments, period. If we close the university like we did in March experiments cannot be performed.
- Access to buildings and materials in case we get another stay in place order. If the institution is closed can we keep the cell cultures going?
- If TCU campuses and/or K-12 schools are closed because of the virus, will we be able to do outreach online?
- Teaching can be flexible online - cell culture cannot,
    - Addressing Threat 2: Until a dependable treatment or vaccine is available, we can prevent uncertainty. For example, the university may have to implement a stay at home order that may move into spring making research impossible. That will affect the 5-year plan. Thus, a quarterly review should be implemented with decisions based on all the available data; including scenarios for when students cannot be on campus. **See Risk Mitigation Plan #4.**
        - Some experiments currently planned to use core services may be outsourced on a fee-for-service basis
        - What are the alternatives to performing experiments and creating valuable experiences?
        - Need to acknowledge that progress on these projects may have to halt completely

- **Threat 3**
    - COVID-19 and the visa issues are restricting access to new graduate students for those of us that don't have one to take on this project yet. Many graduate students will not be here to start in the fall.
        - Addressing Threat 3: A quarterly review should be implemented with decisions based on all the available data; including scenarios for when students cannot be on campus. **See Risk Mitigation Plan #4.**
- **Threat 4**
    - The state of childcare or K-12 schools will directly impact the work some are able to do.
        - Addressing Threat 4: Senior personnel will work with their Pillar/ PROSPER leads as needed.
- **Threat 5**
    - What is the protocol if the students involved get COVID-19 or if they need to quarantine because a classmate/roommate/friend is infected?
        - Addressing Threat 5: A quarterly review should be implemented with decisions based on all the available data; including scenarios for when students cannot be on campus. **See Risk Mitigation Plan #4.**
            - Use additional PPE such as masks and face shields and develop a cleaning protocol of lab spaces. Research can continue as planned except for access to core facilities. Create a protocol for social distancing with students
            - Use PPE and social distancing during outreach activities.
            - Determine PPE need, and stock in advance knowing shipping and timing limits, Limit the number of people allowed in lab spaces at one time, increase cleaning protocol, increase work on virtual platforms as able, increase times lab spaces/tools are open and available for use

- Determine PPE needs, keep a close eye on the situation and pre plan for the worst-case scenario to make sure everyone has enough supplies. Make sure to order now, rather than waiting until no supplies are available. Implement everything mentioned in B and C - but also determine safety of continuing research in lab space

- **Threat 6**
  - If TCU campuses are closed for September and October, should we postpone NATURE Sunday Academies and hope that campuses will be open starting in November or should we offer the September and October Sunday Academies online?
    - Addressing Threat 6: TCU campuses are closed and NATURE Sunday Academies have been postponed. ND EPSCoR's Tribal Colleges/Universities and NATURE Manager and the Sunday Academy Co-Coordinators are working with the TCU NATURE Coordinators to bring this program entirely online. ND EPSCoR and the TCU NATURE Coordinators did this for the 2020 TCU Summer Camps, 2020 Bridge Camp, and 2020 University Summer Camp. Participants in those camps gave the online activities good reviews
- **Threat 7**
  - Consider alternative suppliers if reagent acquisition becomes a challenge.
    - Addressing Threat 7: Decision of each participant
- **Threat 8**
  - Given COVID-19 and the complications it brings, is it too early to ask for a supplement to achieve our original goals and seize the opportunities presented? For example, we will have to allow for the fact that we will not be able to gather people (easily) in large groups and will need to find ways to enable people to participate from their homes or local safe spots.
    - Addressing Threat 8: Quarterly budget reviews will address operational changes in the event that budget line items cannot be used. **See Risk Mitigation Plan #4.**

SWOT category	Identified Asset to Leverage	Area of Impact	Action to Leverage Asset	Responsible Parties	Timeline
Strength	Team Science approach	All	The development and continued reflection on and improvement of the collaboration plan	All participants	Immediate implementation, on-going revising
Strength	Strong team with diverse and relevant expertise, an established track record of collaborative efforts, and	All	Participate a networking baseline at the beginning of the project to engage in continuous improvement of	All participants	Immediate baseline gathered, ongoing continuous improvement process, networking

	confidence in and belief of the importance of the project		collaboration across institution and specialty		survey given annually
Strength	Access to expert technical resources	All	Networking with Computational Research Center for UND and CCAST at NDSU	Computational Approaches Pillar	Networking is on-going
Strength	Solid research plan building on expertise and resources of team	CCBSE	Research Pillars will meet and collaborate monthly, research Pillar have assigned liaisons	Materials Design, Cellular Systems, Computational Approaches Pillars	Research meetings occur monthly
Strength	Access to competent student pool	All	Active recruitment and retention efforts	EWD, All participants	Mentoring, recruitment, and retention efforts are an on-going effort
Strength	Increased opportunities for student participants	All	Active recruitment and retention efforts	Broadening Participation, All participants	Implementation efforts are on-going
Strength	Institutions involved in project have good reputation in community/ among stakeholders	All	Connect to established networks, engage in cross-institution communication and public relations strategies	Communication and Dissemination	Develop baseline
Strength	All institutions have administrative buy-in	All	All institutions engage in ongoing collaboration	All participants	On-going, all participant institutions responsive to situational change
Strength	Centralized, experienced state EPSCoR office that handles a majority of the logistics	All	Retention of existing staff, workflow prioritization of ND-ACES participant logistics	ND EPSCoR State Office	On-going
Strength	Cash match from the State of ND	All	Leverage existing relationships with legislators and prioritize	ND EPSCoR State Office	On-going efforts, focused efforts leading up to legislative sessions

			legislative outreach		
Strength	One unified center will help to direct resources and guide sustainability efforts	All	All researchers meet monthly to discuss resources, collaborate, and address sustainability efforts	CCBSE	Monthly CCBSE research team meetings
Opportunity	Discovery of new ways to conduct research and outreach due to COVID-19	All	Contingency planning, tolerance of ambiguity, and responsiveness	All participants	On-going, all participants are responsive to situational ambiguity
Opportunity	Potential of ND-ACES to build research capacity, expand workforce, and stimulate industry growth in ND	All	Bi-monthly PROSPER meetings and monthly research team meetings	All participants	Regularly collaborate across specializations on ND-ACES
Opportunity	Enhanced student and early career faculty opportunities	CCBSE	Student recruitment to interdisciplinary graduate programs, graduate students collaborate with PUIs and Tribal Colleges and Universities	Education and Workforce Development	on-going
Opportunity	Potential to address today's research questions in this area	CCBSE	Collaboration between researchers leading to new avenues of scientific exploration and discovery, new partnerships with outside organizations	CCBSE, Partnerships and Collaborations	on-going
Opportunity	New research subject matter to North Dakota; not commodity-based research, so chance to be received favorably by state's stakeholders	All	Connect with stakeholders regularly to assess engagement	K. Rusch, J. Ostrom-Blonigen, J. Mihelich	On-going

Opportunity	Increased focus on the importance of ND STEM's pathway	PROSPER	Regular outreach to K-16 stakeholders	PROSPER participants, all	On-going
Opportunity	Members of ND-ACES external advisory board are national level experts well versed in this arena who are poised to assist the team in their ultimate goal of sustainability	All	Frequent collaboration with ND-ACES external advisory board members	K. Rusch, J. Ostrom-Blonigen, J. Mihelich	embedded in project
Weakness	Multi-location project separated by large physical distances can make informal interaction difficult	Communication and Dissemination	Adoption of a unified communication and collaboration platform for ND-ACES	J. Walden, C. Shovkoplyas	Immediate implementation, on-going technical support
Weakness	Team is very large and diverse with many complex collaborative tasks to complete in a limited timeframe	All	Administrative use of a unified communication and collaboration platform	J. Walden, C. Shovkoplyas	Immediate implementation, on-going technical support
Weakness	Inability to maintain consistent research ties to TCU, MCU & PUI faculty due to their full-time teaching schedules, travel distances, and weather	TCU/PUI/MCU	Collaboration agreement and adoption of a unified communication and collaboration platform	J. Walden, C. Shovkoplyas; all participants	Immediate implementation, on-going technical support, on-going revisions
Weakness	Technical resources may not be equal on all campuses	All	On-going awareness of funding opportunities to support endeavor	A. Bergstrom,- ~~D. Skow~~ *[Left the project 2/9/21], K. Hoang* ***[Approved by NSF 2/18/21]***	On-going
Weakness	Obstacles inevitable in our complex research plan that will require the team to be very adaptable	CCBSE, research Pillars	Monthly research team meetings	K. Katti, M. Hoffmann	Immediate implementation of monthly research team collaboration meetings

Weakness	Few opportunities to expand diversity activities beyond American Indians and women	PROSPER	More research opportunities for TCU faculty, TCUs need SPOs	PROSPER; all participants	Once baseline is defined
Weakness	Inability to get time from RU industry engagement, intellectual property, research partners and innovation center personnel	Partnerships and Collaborations	Determine cause and develop action plan, for example, if interns cannot be placed due to COVID-19, determine whether interns are able to be placed with other partners	K. Rusch, J. Ostrom-Blonigen, J. Mihelich	Once baseline is defined
Weakness	Social media accounts have low audience engagement/ content	Communication and Dissemination	Focus on social media platforms that are most important to our organization and most relevant to the public we serve to effectively manage online communities	J. Walden, C. Shovkoplyas; all participants	Once baseline is defined, audit annually
Weakness	Limited experience among senior personnel in working under a cooperative agreement	All	Improve productivity by providing administrative implementation support	All participants	On-going
Weakness	With such diverse intuitions, communication regarding administrative deadlines can be complex	Communication and Dissemination	Adoption of a unified communication and collaboration platform for ND-ACES	J. Walden, C. Shovkoplyas; all participants	Immediate implementation, on-going technical support
Threat	Interruptions in ND-ACES activities due to COVID-19	All	Develop, implement and regularly updated multi-scenario mitigation plans	All participants	Develop multi-scenario mitigation plan immediately and update continuously
Threat	Financial implications that may result due to COVID-19	All	Be aware of funding opportunities to support endeavors	Administration	On-going

Threat	Inability to recruit new faculty hires	CCBSE, Research Pillars	Increase recruitment and retention efforts, develop new virtual approaches	All participants	Develop multi-scenario mitigation plan immediately and update continuously
Threat	Decline or discontinuation of state support during the 2021, 2023 or 2025 legislative sessions	All	Leverage existing relationships with legislators and prioritize legislative outreach	K. Rusch, J. Ostrom-Blonigen, J. Mihelich	On-going
Threat	A researcher becomes unable to contribute to project due to illness or departs university	CCBSE, Research Pillars	Development of clear succession and recruitment plans	All participants	Immediate plan development, on-going revision as necessary
Threat	Inability to recruit qualified students	CCBSE, Research Pillars	Develop, implement and regularly updated multi-scenario mitigation plans	All participants	Immediate plan development, on-going revision as necessary
Threat	Spring river flooding shuts down campuses	All	Develop, implement and regularly updated multi-scenario mitigation plans	All participants and their institutions	On-going plan development and revision
Threat	New collaborative external proposals not funded	All	On-going awareness of funding opportunities to support endeavor	All participants	On-going
Threat	Inability to keep data secure	All	Work with technical experts on the project within Computational Research Center for UND and CCAST at NDSU	All participants	On-going
Threat	Limited local collaborative interest from individuals and public and private entities	Communication and Dissemination	Plan coordinated communication and public relations campaigns	J. Walden, C. Shovkoplyas	On-going
Threat	Cyber-infrastructure challenges limit	All	Work with technical experts on the	A. Bergstrom, ~~D. Skow~~ *[Left the project*	On-going

	distance learning options		project within Computational Research Center for UND and CCAST at NDSU	*2/9/21], K. Hoang* ***[Approved by NSF 2/18/21]***	
Threat	New research subject matter to North Dakota; not commodity-based research, so chance to be received unfavorably by state's stakeholders	All	Leverage existing relationships with stakeholders and prioritize outreach	K. Rusch, J. Ostrom-Blonigen, J. Mihelich	On-going