NSF-CREST Center for Cellular and Biomolecular Machines (CCBM)

All-Hands Meeting
March 20, 2017
Project Goals and Significance

• **Multidisciplinary:**
  Chemistry, physics, biology, and engineering fields—to study **how biological matter assembles to perform specific tasks**, in hopes of eventually being able to **engineer and develop innovations** (from designer cells and tissue to novel diagnostic and therapeutic devices)

• **Research Thrusts:**
  *Biomolecular Instruments*
  *Macromolecular Assemblies and Hybrid Devices*
  *Cellular and Multicellular Systems*

• **Significance:**
  Nobel Prize, 2016—molecular machines
  Multi-scale biomolecular and cellular assemblies
  Control over Biological Systems and Designs

• **Education and outreach:**
  A pipeline for highly qualified STEM workforce
  Produce high caliber, diverse trainees at all levels
  Spur growth in Central Valley
Novel Approaches and Challenges

**Novel Approaches:**

A. Interdisciplinary research and training across physics, chemistry and biology, hands on training modules
B. Entrepreneur/scholar program
C. Team-based student-led research

**Challenges and opportunities for a center on young campus with local UR demographics**

- Newest UC campus (2005)/first American research university of 21st century
- Extends URM student access to UC system
- Major base of advanced research, model of sustainable design-construction and stimulus to economic growth and diversification
- Horizon 2020 Project—$1.3 billion to duplicate campus size and number of faculty
- Aligned with Strategic Academic Focusing Initiative
Collaborations and Future Plans/Next Steps

- Strong internal and external partnerships/collaborations to enhance programming and efforts
- Recruitment of URM students from the Central Valley
- First NSF center on campus
- Maintaining NSF center presence on campus
- Grow into a Full Fledged Research Institute
- Influencing direction of university in growth stage
- Nucleate expertise, research facilities and funding opportunities in biophysics and bioengineering
Research Focus

Quantitative (Physical) Biology:
Integration of experiment, theory and computation into
general descriptions that rationalize experiments, distill
mechanisms, and make new testable predictions of
molecular and cellular biological phenomena

Synthetic Molecular-Cellular Biology (Biological
Engineering):
Transformation of quantitative knowledge into engineering
strategies for designing and building synthetic biological
components with novel functionalities and/or behaviors
Bringing together physical and engineering approaches to understand biological machines and design and develop new functional machines.

Research Challenge: Understand

We are interested in investigating hierarchical assemblies of molecular, cellular and multicellular structures seeking to:
1- understand how they perform remarkably robust functions in their highly noisy natural environments
2- exhibit emergent properties unanticipated from just the sum of the components (e.g. filament-motor assemblies involved in mitosis to slime molds and biofilm formation to morphogenesis)

Technological Goals: Exploit

1- Better fundamental understanding of multi-scale biological assemblies
2- Attain control of their functional dynamics potentially leading to therapeutic improvements in human health
3- Implement design principles for building bio-inspired materials and machines
Transformative advances in this area require contributions from many different fields:

**Biochemistry** to understand biomolecular recognition and signaling mechanisms

**Soft matter physics and materials science and engineering** to understand and characterize material properties

**Optical physics** for cutting edge imaging and manipulation

**Bioengineering** approaches for molecular, mechanical and manipulation

**Biology and chemical biology** to probe functional properties in vivo

**Theory and computation** to rationalize and test what is observed experimentally

No single department, unit or group can accomplish such an innately interdisciplinary task

**Why do we need a center to work in this area?**
It Makes Strategic Sense

UCM has the right mixture of expertise to achieve significant progress and national prominence in this area with faculty that shares a common vision for research and education.

CCBM leverages the uniquely interdisciplinary structure at UCM with few departmental boundaries, to join faculty from physics, bioengineering, materials science, quantitative biology, applied mathematics, chemistry and chemical biology forming a diverse, interdisciplinary research community.

UCM has a significantly large fraction of its faculty working at the interface of the physical and biological sciences and engineering (CCBM participants alone make up more than 12% of the total faculty at UCM).

At UCM, interdisciplinary collaborations can thrive in an academic structure without academic boundaries that fosters collaboration by proximity and sharing of space.
It is Key for the Future Development of UCM

UCM is still in its early developmental stages, the establishment of CCBM can have truly transformative impact

UCM has world-class faculty but the research infrastructure is still very much in its growth phase

NSF-CREST center will allow us to marshal resources and acquire critical infrastructure and technical support staff to

(i) actively recruit and retain diverse, stellar faculty in this broad area
(ii) attain critical mass, expertise and facilities to subsequently compete for STC, ERC or MRSEC type grants as a lead institution

CCBM dovetails with the UCM strategic academic focusing (SAF) pillars of excellence by perfectly aligning with the Adaptive and Functional Matter Pillar

Establishment of CCBM’s innovative, interdisciplinary training program and aggressive recruitment of STEM graduates will have a key impact on culminating the 2020 Project
Research Thrusts

**Biomolecular Machines**
Circadian Molecular Clocks  
Rheostatic Protein Biosensors  
(Munoz (co-director), Escobar, Colvin, LiWang)

**Macromolecular Assemblies and Hybrid Devices**
Designer Vesicles for Transport  
DNA Origami-Nanocomposites  
Graphene-based Biosensors  
(Gopinathan (co-director), Hirst, Xu, Ghosh, Ye, Tian, Tung, Chin, Gadre)

**Cellular and Multicellular Systems**
Differentiating Tissue  
Bacterial Community Motility  
(McCloskey, Gopinathan, Lu, Liu, BalaSubramanian, Gopinath)
Protein Folding at Atomic Resolution

Engineering Protein Analogical Nanosensors

Thrust 1: Biomolecular Machines

Protein Folding in Single Molecules

Folding Coupled to Binding

Engineering Controllable Macromolecular Assemblies

V. Munoz, A. Li Wang
Plasmon actuated cargo delivery

Gold quantum dot shells self-assembled by liquid crystal ordering

Plasmon heating releases cargo

Fluorescence

Versatility in encapsulation
Low power, fast, tunable release

S. Ghosh, L.S. Hirst
Thrust 3:
Cellular and Multicellular Assemblies

Development of spatially patterned cardiac tissue from stem cells

K. McCloskey, A. Gopinathan

Mathematical model
Affiliated Faculty and Leadership

Kara McCloskey
biological engineering
stem cell and tissue engineering for regenerative medicine applications

Victor Muñoz, co-director
biological engineering
protein folding, structure prediction and design, protein aggregation

Andy LiWang
chemistry and chemical biology
structural biology of circadian clock proteins and nucleic acids, NMR spectroscopy

Anand Bala Subramaniam
biological engineering
experimental biophysics, cellular reconstitution, experimental synthetic biology

Lin Tian
physics
theoretical quantum optics, quantum information processing and quantum simulation in condensed matter systems

Vincent Tung
materials science and engineering
nanotechnology for sensing and renewable energy

Jing Xu
physics
experimental biophysics, quantitative biology, single-molecule analysis of molecular motors

Tao Ye
chemistry and chemical biology
biomolecular science and engineering, nanotechnology

Wei-Chun Chin
biological engineering
polymer physics and engineering of cellular and environmental systems

Mike Colvin
chemistry and chemical biology
models of biological processes and molecular dynamics of disordered proteins

Ariel Escobar
biological engineering calcium in cardiac cellular signaling and techniques to study cardiac cells in vivo

Anand Gadre
stem cell instrumentation foundry nanotechnology, medical device development, sensor development, drug delivery

Sayantani Ghosh
physics
experimental condensed matter physics, magnetism, metamaterials, nanoscience and quantum systems

Ajay Gopinathan, co-director
physics
theoretical biophysics, biopolymers, transport and collective behavior

Arvind Gopinath
mechanical engineering
fluid dynamics, polymers and active soft matter – theory and simulations

Linda Hirst
physics
experimental soft matter physics and biophysics

Bin Liu
physics
bacterial motility in complex media and single-cell behavior in biological processes
Center Organization
Mission

1- Perform cutting edge interdisciplinary research on multi-scale biomolecular and cellular assemblies

2- Become a model for integrated research, education and outreach that develops a pipeline for a highly qualified STEM workforce and produces high caliber, diverse trainees at all levels

1. IB3 graduate training emphasis
2. 2 project scientists
3. Team based research Grad+UG
4. Training Modules
5. Entrepreneurship
6. High school outreach
7. CCBM fellowships
8. Summer research program/UG
9. Travel fellowships, supplies $$
Benefits of being a CCBM scholar

a. You will be eligible to become a CCBM fellow (a renewable semester by semester GSR equivalent fellowship). There will be 4 such fellowships in spring and this will increase in subsequent years. CCBM fellows will be selected from the pool of CCBM scholars based on their applications.
b. All CCBM scholars will be awarded up to $500 in supplies which can be used toward research related equipment/supplies/recharge in consultation with your PI.
c. You will benefit from our new IB3 (Interdisciplinary Biophysical sciences, Biomaterials, Biotechnology) graduate emphasis program. You can take our new specialized electives (from the UCSB BMSE program via videoconference) which are cross-listed as BEST, Physics and Chemistry grad courses (BEST/PHY/CCB 299).
d. You can take advantage of our 2-week hands-on training modules in Imaging/Spectroscopy, Nano-micro fabrication and/or Computational methods during the summer (starting in summer 2017).
e. You will be able to take part in all center activities that include career skills workshops, networking, outreach, etc. Details of activities will be available on our website - ccbm.ucmerced.edu
f. You will be able to host and meet with special CCBM seminar speakers
g. You will be eligible for CCBM travel fellowships

One of the conditions of being awarded a CCBM fellowship is that you take at least two of our specialized IB3 electives (these can count toward your own grad group elective requirements) and the summer training modules once during your graduate studies.
The IB3 graduate training emphasis
-Coursework

CCBM courses:
Fall 2016: Membrane and Protein Science
Fall 2017: Nucleic Acids and Proteins

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<tr>
<th>Graduate Group</th>
<th>BioEngineering and Material Science and Engineering</th>
<th>Chemistry and Chemical Biology</th>
<th>Physics</th>
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| Required Courses | BEST 240: Bimolecular Engineering  
BEST 214: Tissue Engineering and Design  
PHYS 204: Biophysics  
CHEM 216: Interfacial & Surface Chemistry | CHEM 212: Quantum Chemistry  
CHEM/PHYS 212: Statistical Mechanics  
CHEM 216: Interfacial & Surface Chemistry  
PHYS 204: Biophysics | PHYS 237: Quantum Mech. I  
PHYS 210: Electrodynamics  
PHYS 212: Statistical Mechanics  
PHYS 204: Biophysics |

| Elective Courses (Any 3 from list) | BMSE 2018: Chemistry & Structure of Nucleic Acids  
BMSE 201C: Biomembranes Structure & Function  
BMSE 276A: Biomolecular Materials I: Structure and Function  
BMSE 276B: Biomolecular Materials II | BMSE 201A: Protein Structure and Function  
BMSE 201B: Chemistry & Structure of Nucleic Acids  
BMSE 215: Biophysical Thermodynamics  
BMSE 293: Computational Methods Biochemistry & Molecular Biology | BMSE 215: Biophysical Thermodynamics  
BMSE 217: Electrostatics of Biopolymers  
BMSE 250: Bionanotechnology  
BMSE 271: Mechanical Force and Biomolecules |
1. A team based approach
2. Management, entrepreneurship, outreach

Team Research Approach

- CCBM graduate fellow + CREST undergrad scholar(s) + >2 PIs
- weekly team meetings
- monthly thrust meetings
The IB3 graduate training emphasis
-Hands-on Training Modules

3 modules
2 week duration each during summer

Computation and Modeling, Colvin, June 5-16, 2017
Imaging/Spectroscopy, Muñoz, June 19-30, 2017
Nano/Bio Fabrication, Gadre, July 31-Aug. 11, 2017
The workshop will cover training in basic spectroscopic-spectrometric methods to investigate biomolecules and optics based imaging methods (microscopy) to visualize macromolecular assemblies and living cells.

- 2 weeks (5 hours/day)
- Problem oriented labs using standard molecular systems
- Access to UCM Instrumentation
- Data acquisition and analysis software
- Hands on training:
  - 1 hour lecture
  - 2 hours on instrument
  - 2 hours data analysis
Spectroscopy and Imaging Workshop

Biomolecular Spectroscopy:

- Protein Expression
- Protein Purification by HPLC
- Circular Dichroism
- Fluorescence (quantum yield, lifetime, anisotropy, FRET)
- Nuclear Magnetic Resonance (NMR)
- Mass Spectrometry
Microscopy and Imaging:

- Fluorescence Imaging Modes in Live-Cell Microscopy
  - TIRFM
  - Laser Scanning Confocal
  - Widefield Fluorescence
  - Spinning Disk Confocal

Single-Molecule Confocal Fluorescence Microscopy

Total Internal Reflection Fluorescence Microscopy

Fluorescence Lifetime Imaging Microscopy
NanoBio Fabrication Workshop

- This workshop will be housed in the Stem Cell Instrumentation Foundry (SCIF).
- 2 weeks (4 hrs/day),
- Hands on training in Class 1000 and Class 100 Cleanrooms for graduate students
  - Micro/nanofabrication processing
  - Bacterial/cell/tissue culture techniques.
  - Instrumentation - related to photolithography, microfluidics, electrospinning, and cell culture experiments.
  - Equipment specific training
  - Virtual demonstrations to introduce the concepts of nanotechnology and cell/tissue culture work.
Goal: Basic proficiency with a range of scientific computing tools through exposure to hands-on examples

Format: Two weeks@6 hr per day in Linux computer lab

Part 1: Scientific computing “toolkit”
- Linux/BASH: Job control and data management
- R: Data analysis and statistical modeling
- Python: OO scientific simulations & data manipulation
- C: High speed simulations

Part 2: Molecular simulations
- Basic principles of classical MD
- Transport properties and EOS for Argon
- Mixtures: NaCl, PE in H₂O or C₆H₁₂, Micelles
- DNA and proteins: Effects of structural mutations
Molecular dynamics demonstrating increasing more complex simulations

Labs taught using Gromacs & associated tools

T dependence of salt dissolution

Polymers in good and bad solvents

Simple micelle thermo-stability

DNA Structural effects of single mismatches

Thermo-destabilizing mutations in proteins
• Research with CREST faculty
• Introduction to graduate school and GRE preparation: CREST mentor led workshop to be held once per semester
• Enhanced student learning and community building: Academic help on understanding specific math and science concepts through STEM resource center
• Summer Internships:
  A. NSF MRSEC REU @UCSB: biophysical sciences, biomaterials and biotechnology
  B. California Institute for Quantitative Biosciences (QB3): wide-range of entrepreneurial activities
  C. Molecular Foundry (Lawrence Berkeley National Lab, LBNL): Science Undergraduate Laboratory Internship program
Undergraduate Research Fellowship Overview/C-SIP

- 9 week undergraduate research fellowship at the University of California, Merced
- June 4-August 5, 2017
- Research experience in biophysics, biochemistry & bioengineering
- Experimental learning & hands-on training on cutting edge research instrumentation
- Research & academic guidance and mentoring from CCBM faculty & graduate students

Create a STEM pipeline for our graduate programs and beyond
• $3000 stipend
• Free room and board provided on UC Merced campus
• $500 in expenses for off-campus participants
• Training expenses covered
• Rich professional development
• Faculty, graduate student, and peer networking
• Social activities
• Collaborations with the other university units, including UROC and STEM Resource Center
Undergraduate Research Fellowship Overview/C-SIP

- Special CCBM sessions, lectures, and meetings
- Undergraduate Research Opportunities Center (UROC) cohort
- Orientation, social events, Summer Research Symposium (presentation and poster)
- Trainings, including safety training
- Bootcamps (Matlab, Wetlab, more)
- Workshops
Workshop Topics:
1. Getting the Most Out of Your Research Experience
2. Graduate School Panel
3. CV Review
4. Graduate School Admissions
5. Abstract Review
6. Predoctoral Fellowships
7. Communicating and Presenting Your Research
8. Career Planning

Other Sessions:
- GRE preparation panel discussions
- Lab group meetings
- Training for oral presentation
- Poster presentation at a Summer Research Symposium
Application Deadline: February 28, 2017
--Applications may be considered after this date if space permits
--It is best to apply early, as we will begin to review applications before the application deadline (semi-rolling applications).

Prepare application materials:
1. Resume/CV
2. Unofficial transcript(s)
3. 300 word statement of research interests including thrust area preference (http://ccbm.ucmerced.edu/research.html)
4. Contact information of one reference

Eligibility:
• Full time undergraduate students with at least two semesters of college experience (GPA 3.0 or above)
• U.S. citizen, U.S. national, or permanent residency required to participate (due to NSF funding)

Please note:
• CSU and Merced College students strongly encouraged to apply
• Students from underrepresented minority groups, women, and students with disabilities strongly encouraged to apply

Email application as a combined PDF:
Carrie Kouadio, CCBM Executive Director ckouadio@ucmerced.edu
Undergraduate recruitment

Strong culture of undergrad research, 2000+ S&E majors
- Faculty participation in SWE, ACS, APS… student chapters
- Freshman seminar series
- Tables at UC Merced Preview Day, CCBM open day

Graduate Recruitment

- CREST scholars
- CSU participants in CSIP program
- Other REU programs on campus
- participation in CSUPERB annual symposium
- publicizing at SACNAS, ABRCMS…
E-scholars

• Management undergraduate majors
• Training to secure investment for STEM-centered start-up businesses
• UCM Office of Business Development (OBD) will provide mentoring
• Graduate students will:
  a) serve as STEM mentors for the Management undergraduates, assisting and guiding them in selecting research projects for further development and helping them learn and understand the scientific principles behind them, and
  b) will learn the basics of business development and market research via their interactions with the E-scholars
• Enhance science curriculum in local high schools - develop educational modules
• Summer training workshop for HS teachers and 1-2 HS students
• Semester long module presentation in schools by CCBM fellows and faculty
• Research opportunities for high school students
• College application prep for high school students
**Timeline**

**Spring 16** -
CREST Fellowship and Scholarship nomination calls; Coordination for delivery of Fall courses for IB3 emphasis with UCSB BMSE. Research begins on all thrusts. Searches for the two project scientists begin.

**Summer 16** –
First visit of external advisory board. Selected CREST Fellows and Scholar teams enroll in thrusts. Project scientists are interviewed and hired.

**Fall 16** –
IB3 coursework begins. Annual recruitment drives (SACNAS, ABRCMS, CSUPERB (Jan), CSUs). Purchase and set-up of core facility instrumentation (LCMS and Bioreactor).

**Spring 17** -
Hiring of Executive Director, Program Manager; Prep for Annual Summer programs - STEP, E-Scholars, and C-SIP. Coordination with MRL-UCSB, LBNL and QB3. Prep for summer training modules

**Summer 17** -
Summer training modules (6 week bootcamp). STEP, E-scholar prep, C-SIP kickoff.

**Fall 17** -
First annual symposium/open day. Annual visits of External Advisory Board and evaluator to overlap with symposium. CCBM Grad fellows continue with E-scholar teams/STEP program. CCBM co-sponsored seminars begin. Purchase and set-up of first set of HPC nodes (next set in F19).

**Spring 18** - *At this point all elements of the center and activities have been implemented and will proceed as per plan.*
Internal and External Evaluation

**Internal - SATAL**
- pre-post course evaluations, administer surveys

**External Evaluation**
- develop evaluation instruments; design surveys
- review findings from surveys, interviews, website analytics, program records...
- monthly phone meetings, annual site visit, annual report

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<tr>
<th>Activity</th>
<th>Sample Evaluation Questions</th>
<th>Possible Indicators (Outputs and Outcomes)</th>
<th>Data, Evaluation Methods</th>
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<tbody>
<tr>
<td>Graduate and Undergraduate Education and Training</td>
<td>Are students receiving high quality quantitative research training across disciplines that emphasize working in multi-disciplinary environments?</td>
<td>Short-term: # of URM students participating</td>
<td>Pre-post course assessments (SATAL)</td>
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<td>Is the program building a pipeline to the graduate program, especially for underrepresented students?</td>
<td>Long-term: # of project-related collaborations, # of project-related publications, # of students placed in industry and academia, # of undergraduate students applying to graduate school in STEM</td>
<td>Mentor assessment of participant progress (CREST Program)</td>
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<td>Are the E-Scholars and STEP programs enhancing students’ educational experiences?</td>
<td>E-scholars report they have knowledge to secure investment for STEM-centered start-ups and engage in start-ups; STEP participants report enhanced engagement with educational outreach</td>
<td>Annual surveys of faculty and students, Interviews/Focus groups (External Evaluator)</td>
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<td>Are PhD graduates securing employment in academia or industry?</td>
<td>Students report the program activities:</td>
<td>Program records (Student Demographics, # of Collaborations, # of Publications, Course Grades, etc.)</td>
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<td>* increased their interest in STEM fields and STEM careers including graduate school in a STEM field (including at UC Merced)</td>
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Center Requirements

Reporting:
NSF Annual Report due March 31 each year

Visits to Washington, D.C./NSF:
Reverse Site Visits
Annual CREST Meetings (March)
Other Opportunities

- Outreach events (April 11)
- External Advisory Board Meeting (August 21)
- Open House (September)
- Thrust Meetings
- News for website and announcements
Questions?

Center Website
http://ccbm.ucmerced.edu

General Inquiries:
Carrie Kouadio
CCBM Executive Director
ckouadio@ucmerced.edu