Directorate for Mathematical and Physical Sciences (MPS) Advisory Committee
Meeting July 20-21, 2021 (all times EDT)
National Science Foundation
2415 Eisenhower Ave, Alexandria, VA
Room E2020

Summary Minutes

Tuesday, July 20, 2021

Advisory Committee Members in Attendance (All Virtual):

Dr. David Awschalom
Dr. Anna Balazs
Dr. Susanne Brenner
Dr. Tabbetha Dobbins
Dr. Miguel Garcia-Garibay
Dr. Lynne Hillenbrand
Dr. Catherine Hunt
Dr. Robert Kirshner
Dr. Cornelia Lang
Dr. Herbert Levine
Dr. Jennifer Lewis
Dr. Andrew Millis
Dr. Jill Pipher
Dr. William Tolman
Dr. Roldolfo Torres
Dr. Ed Thomas, Jr.

Call to order and official opening of meeting, FACA Briefing – Catherine Hunt, MPSAC Chair**,** Sean L. Jones, Assistant Director, MPS; Kathleen McCloud, Staff Associate, MPS

The meeting was opened at 12:00 pm by Dr. Catherine Hunt and began with a briefing from Dr. Kathleen McCloud on the policies of the Federal Advisory Committee Act regarding conflicts of interest for AC members, as well as a reminder that the meeting was open to the public and occurring under the guidelines of FACA. Dr. Catherine Hunt asked for introductions around the room. The minutes previous meeting, held in August 2020 and November 2020, were approved by a motion introduced by Dr. Hunt.

Update: MPS & Living World – Dr. Ka Yee Lee, Chair, University of Chicago

Dr. Ka Yee Lee, Chair, University of Chicago, provided an interim update/report on MPS and the Living World: "Building Strategic Collaborations Across MPS and Beyond".

I. Four (4) Subgroups inform Subcommittee Organization as a whole: Tools, Emerging Theories, Critical Applications/Problems and Human-Biotechnology Interface. These subgroups:
    a. Gather resources from NSF and other materials for the committee
    b. Gain outside information to inform subgroup's work
    c. Presentations by outside experts
    d. Community outreach
    e. Subgroup's findings inform Subcommittee's work

II. Future of Biotechnology Workshop: June 29-30, 2021. Workshops were Big Picture Talks and Panel, Tools for Biotechnology: Theory and Computation, Tools for Biotechnology: Imaging, Critical Applications and Problems in Biotechnology and Human-Biotechnology Interface

a. Tools: Imaging - furthering our understanding of the function and organization of metabolites, biomolecules and organelles within the cell, and the interplay and communication within tissue and organismal systems

Advancing Imaging Tools

- Small-molecule fluorophores: with improved photostability, switchable properties for super-resolution imaging, band incorporate fluorophores into biomolecules
- Protein fluorophores: engineering and screening to improve photo-physics, maturing time, and in-vivo stability
- Functional probes: improved biosensors that monitor cellular processes such as metal influx/efflux, electrochemical gradients, redox potentials, etc.
- Increased spatial and temporal resolution ➔ fluorophore designs and instrumentation
- Multiplexing: analyzing 10-100 biomolecules concurrently (DNA-barcoded antibodies)
- Correspondence between DNA/RNA sequencing and imaging: better integrate available single-cell sequencing tools with single-cell imaging
- Thick sample imaging ➔ instrumentation and sample preparation advances
- Data analysis: necessary for entire imaging pipeline
- Collaboration across disciplines: Chemistry, Physics, Computer Science, Mathematics, Materials Science, Biology

Data Acquisition and Image Reconstruction

- Data acquisition (electronics costs) and image reconstruction times (computing costs) need to be shorter than time scale of system changes
- Limitations prevent realization of RT remote sensing on macro, micro and nano scales
- Physics: Imaging tools are implementations of practical solutions to inverse problems. It is therefore critical that such inverse problems be defined with sound physics that efficiently define the problem without unnecessary physics content.
- Mathematics: Mathematical tools are needed to simplify the equations that underpin the inverse problem. Formulating inverse problems in ways that require fewer computation steps are badly needed.
- Computational Science: Novel equation solvers are needed to minimize time to solution.
- Novel methods for solving inverse problems needed to image multiple properties of biological system

Tools: Theory and Computation
Gaps

- Minimal cell: Ability to define the kinetics of individual pathways, and the interrelationships among pathways in the environment of the cell ➔ How perturbations of these pathways effect the function of a cell
- Structural prediction by relating the architecture of a genome with activity, and to simulate this relationship: Need for next-generation methods and data analysis platforms for analyzing circulating DNA and circulating
- DNA modifications
- • Designing artificial enzymes to catalyze unnatural reactions: What gives amino acids specific catalytic power in
- the context of a protein? Need for the application of principles from physics, especially, to simulate the
- relationships between physical phenomena which lead to control mechanisms, communication, and catalysis

Potential Outcomes

- Build synthetic, programmable macrophages to combat disease
- Map a protein/enzyme to predict the effectiveness of a drug
- Design a protein to manipulate its function and that could work better than the native one.
- Synthetic biology with a focus on cell-free biology for specific synthetic goals
- Development of a platform to easily design microbes for synthesis
- Tools to decipher genomic signatures of molecular adaptations to environmental variation
- Algorithms and new ideas to interpret vast datasets

Emerging Theories
Development and validation of emerging theories will be based on a variety of data streams

Medical Data

- In-body and on-body sensors, smart environments, loT tracking, consumption tracking, location tracking (exposure), external and internal imaging, voice analysis, motion analysis
- Huge information sources and highly dynamic

Monitoring the Biosphere

- Biologics: Species number, diversity, DNA sequences and changes in genetics, epigenetic profiles, gene expression, pathogen spread, migration, molecular profiles.
- Physical: temperature, rainfall, fires, water purity, atmospheric conditions, dynamic details of the molecular make up of water, air, soil across the globe.

Agricultural Health

- Constant monitoring of the agricultural environment and the physiology of the plants and animals involved at all levels from the molecular to the field. Big challenges in collection, storage, computation, integration & interpretation of data

Emerging Theories

New Theories and Computational Approaches

Mining of multidimensional data sources

- Dynamic and spatial data and analysis to identify motifs predictive of cellular or physiological outcomes
- Computational complexity cost-to identify the most important degrees of freedom
- Apply physics-based and information-theoretical approaches to constrain large or incomplete data sets
- Combine developed models in control theory with new physics-based theories (e.g., non-equilibrium statistical physics) to apply energetic bounds that constrain system interactions.

Nondestructive temporal and spatial measurement analysis cycles

- e.g., high-throughput optical data where possible
- Control theory may be less constrained, thus making it predictive with less information.

Efficient data collection and analysis cycles

- To extract information efficiently may be more useful than acquiring more data
- To optimize ML approaches with other principles that may enable predictability with less test data

Merger of first principles theory with data intensive analytical methods

- Assume that the complex interactions of cellular components are constrained by the laws of physics, we should apply these constraints to enable enhanced predictability

Recommendations

Emerging Theories, Theoretical and Computational Tools

- Integrating the design of large-scale data collection with analytical approaches
- Integrate Al and machine learning with fundamental theory
- Explore a greater diversity of biological models and data collection modalities
- Incorporate environmental context and multiscale connections
- Better understand complex microbial communities
- Develop theoretical descriptions of synthetic cells
- Advance the theory of complex molecular machines

Critical Problems & Applications

- Living diagnostics & therapeutics via reprogramming cells - cells as sensors; cells as drugs
- Engineering human organs for repair and replacement- must recapitulate form and function
- Discover and measure the unknown (cheaper/faster tools) - from enzymes to quantifying human diversity
- Multiple advances in convergent fields ae needed
- Needs: Understanding design rules, more circuit components, using transient cells
- Improve yield & quality of therapeutic cells via artificial antigen-presenting materials
- Encapsulating cells within engineered hydrogels to prolong persistence and function in vivo

Organ Engineering

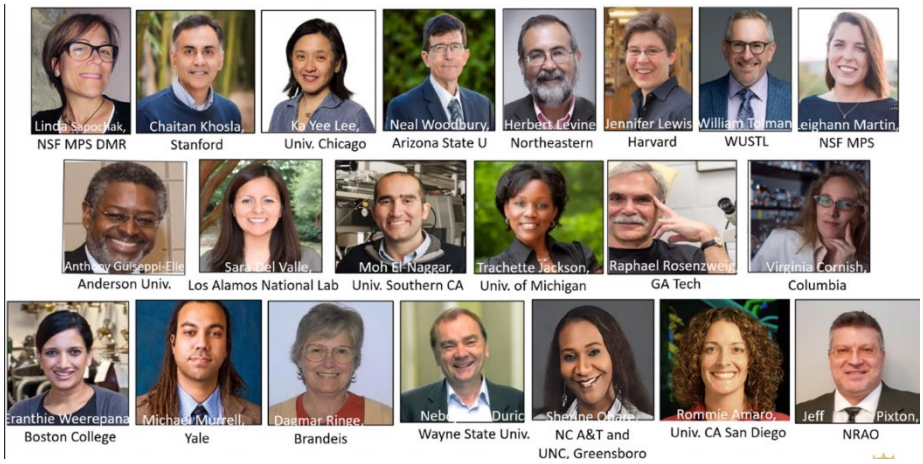
Engineering human organs at scale is a grand challenge - must recapitulate form and function

Critical needs:

- Human organ maps delineating each cell type and location in 3D/4D
- Synthesis of fully defined extracellular matrices that promote cell phenotype & function
- Scalable, reproducible, and low-cost production of patient-specific stem cells, organoids, and tissues with controlled cell populations, maturity, architecture & function
- In vivo readouts of real-time function of implanted tissues
- Enabled by programable synthesis, deep tissue imaging, machine learning

Recommendations

- Convergence research:
  - Promote collaborative work involving scientists from different disciplines around big problems
- Early integration and robust communications:
  - Promote integration of data science & theory/ML & mechanistic research
- Promote research that facilitates harnessing of heterogeneous data sources to address problems
- Promote non-model system research
- NSF should launch more interdisciplinary training/research centers ("Biotech MRSECs", "Biotech CCIs")
- Centers should be given some latitude in funding high-risk research
- From basic science to societal impact: Promote connections to industrial partners
- Training the next generation of biotechnologists
  - Diverse workforce
  - Cross-disciplinary training
  - Dual mentorship



Discussion

Question: Asked by the Committee Chair, Dr. Catherine Hunt

- How do we quantify, go beyond…the # of critical applications?

- AC Response: Dr. William Tolman responded
  - Interdisciplinary Training/Research Centers can help with the interdisciplinary problems/issues
  - NSF runs model well and can be successful
  - Loves recommendations
- AC Response: Dr. Herbert Levine responded
  - A lot of work to do
  - Emphasis on integration ➔ data might be useful or not ➔ community understands this ➔ just throwing in data is not the way ➔ the need to look broadly at problems & NSF has the advantage ➔ need to be some type of convergence ➔ problems are too big just for MPS going forward with whatever the best format
- MPS Answer/comment: Sean Jones
  - Phenomenal workshops ➔ PD/Managers participating across NSF ➔ discussions were great/outcome was wonderful ➔ will pass along the report

Planned to meet with the Director

Break

Meet with Director and COO

AC Chair, Dr. Catherine Hunt Welcomes Dr. Panchanathan, and Dr. Crim. Two new MPSAC members introduce themselves.

NSF Director Dr. Panchanathan makes introductory comments, thanks the new committee members for their service to NSF and notes the current positive situation with the President's budget recommendation and bipartisan support in Congress.

Dr. Hunt notes that the MPS AC has a lot to say about the new NSF Directorate for Technology, Innovation, and Partnerships (TIP). Members echo the excitement and concerns about how it will integrate old and new ways for the community to interact with NSF.

Dr. Panchanathan emphasizes that the impact of TIP must be nationwide. NSF will also partner with other agencies for the creation of opportunity to help talent stay in every region of the country.

Q: AC member, Dr. Edward Thomas, asks how the TIP directorate will interact with the established NSF EPSCoR program.

A: Dr. Panchanathan sees TIP as energizing and leveraging what is already happening in the directorates. TIP is also 'icing on the cake' in the sense that opportunity will spread and be available everywhere.

A: AC Member Dr. William Tolman comments that interdisciplinary coordination is done well through centers.
A: Dr. Panchanathan states that centers are the focal points for fostering collaboration and sustainable progress.
A: AC member Dr. Andrew Mills wants there to be future discussion on TIP. The MPSAC would like to be helpful in making TIP a success and understand how TIP will interact with MPS and other directorates.
A: AC Member Dr. David Awschalom says it will be interesting to see how NSF will leverage the success that other agencies have already had in TIP.
A: Dr. Panchanathan summarizes his interaction with other agency heads in TIP. He has already established communication with other agency heads on this topic. He is a huge fan of interagency partnerships.

Dr. Hunt thanks the Director and emphasizes that the MPSAC wants to work with him to preserve basic research.

Discussion of ERE and Award Subcommittee

MPS AD gave a presentation on MPS working with special programs within the Office of Integrative Activities (OIA). He noted that all 3 programs (AC ERE, CEOSE and Alan T. Waterman) are coordinated in OIA.

The AC ERE would provide advice and recommends support of NSF ERE portfolio with interdisciplinary approaches. Deliberations are similar how the MPS AC runs.
MPS AD asked what would our AC like to do regarding this new AC ERE?

- **W. Tolman** volunteered to join the new AC ERE.

MPS AD - Alan T. Waterman award has a nomination period that open and closes in September and allows 3 awardees early. Awardees are by disciplines and the nominees need to be diverse. We are thinking of getting the word out on these recommended changes. One of the suggestions were to form a subcommittee.

- Add a Liaison to the AC for ERE
- Add a Liaison to CEOSE (the timing of these is important). Whoever volunteers would be considered a part of the 2022 cohort. You must be an AC member to volunteer to serve.
    - **T. Dobbins** volunteered to serve on AC CEOSE.

C. Hunt mentioned NSF wants to diversify the research fellows award. They had a webinar of what a good nomination package looks like. It was recorded and had a Q&A. C. Hunt was going to ask them how they did the canvassing of this reaching out to Department Chairs. When folks serve as Dept. Chairs where do they look for nominating people for their awards?

- **AC answer:** Often its ad hoc, some agencies have central help. J. Pipher noted they are trying to launch this at her agency.

- **A. Millis** – It's almost never the case, it must come from the departments. Ask the department. Almost all departments have a process of getting people nominated. The intellectual gut must come from the departments. You must go to the department to solicit, tap people for award nominations. They use a canvas committee to sharply separate.
- **W. Tolman** -The number of people is small, and the nominations is small.
- **E. Thomas** – The provost office, VRE offices flow down nominations.
- **J. Pipher**– Professional Society has a national award committee and looks at national awards and tries to gather names and contact people to generate nominations. Melody Wood received the Waterman award. It can be a successful way to generate nominations.

C. Hunt mentioned, A canvassing committee from this AC is needed. Should it be 5 people? How does canvassing work? Are there AC members willing to volunteer on the **canvassing committee**?

- **AC Answer:** E. Thomas, S. Brenner, D. Awschalom, A. Millis and W. Tolman volunteered to serve on it.
- **A. Millis** If NSF wants to convey the message to a diverse group of applicants, it may be appropriate to have NSF create a committee. If it has a status, that is better.
- **MPS AD:** We will take it to the committee, be careful about the perception of COIs. Be careful of how its named. We are not a nominating committee but a canvassing committee.
- **L. Hillenbrand**: You could have the same people nominated for the same awards. **Get fresh ideas**.

AC Member – It should be a separate look at this. MSRI of Berkeley Human Resource Advisory Committee. Make sure no one is overlooked so that applicants will not get lost in the process.

- **C. Hunt** – Explained the difference between the committees. The canvassing committee will contact people to encourage them to apply. The selection committee must get the packages for two separate committees.

Break

Agency Priorities and Budget Update - Caitlyn Fife

Topics discussed were as follows: **Budget Process, Current Year Update 2021**, **Budget Year, Update 2022**, **What's Next FY 2023**

Budget Planning Timeline run to September 30, 2021. NSF submitted a detailed request in May. Since FY2022 will be a transition year, it is later than normal. It is working its way through Congress. The house has released their appropriation and we are waiting for Senate Action. We are well practiced in starting the new FY. A call for budget request is the Monday after Labor Day. Sending over our first proposal for FY2023. Interactions with science board able to update our advisory meetings with the status updates. Due to bipartisan support, NSF received an increase from the last 10 years. Next is the fall, where NSF will be watching the news and preparing the FY23 budget. Engage with the administration in the fall. It will be published around February 2022. There will be an Infrastructure package and NSF anticipates the OMB

OSTP and R&D Budget. Priorities memo will be released later this summer and will be more detailed than what we've seen before.

Q&A:

Q: T. Dobbins -In some of the earlier slides you had a list of what types of measures NSF is taking to the impacted groups.

> **A**: **MPS AD-** Those that are closest to the community about how to deploy them. Pos docs there has been a significant amount to increase in this area and Career. We are investing more in Pos Docs i.e., new ASCEND program. There is an increased opportunity for demographics. Looking at our platform for minority. There are interesting awards coming out that have not been in our portfolio before. There has been an increase of new PIs that we hope will be with us for a long time.

Q: R. Kirshner – He shares the optimism, but on the other hand the big picture funding for science broadly puts as a fraction of the discretionary budget as the economy is going down. We are not properly getting the message out regarding the additional funds. Goals for society. Yes, good but there's more work to do. FY2022 for MREFC is no bigger than the line in 2021. Why is the agency backing away in this area?

> **A**: **C. Fife** - NSF does not have new facilities that are coming on-line. That's not a 1–2-month process and then be able to include in the budget. Remember the budget is a public document. We are still assessing the long- term impact of Covid. Out of the construction phase and moving into operations it could bring impact in the out years. This is the discretionary part of the budget. Including the infrastructure packet as they presented the discretionary request. The 10.2 billion is not the extent into what NSF could make. This is a large project to get going before you know what the cost will be.
> **MPS AD** - Ramping down on some projects is a normal thing we see with MRFC.

Q: C. Lang – Amplify support ARA funding AC weighed in on similar recommendation. Re: TIP – the increase in budget request is a new emerging area but there is not enough money associated with you.

> **A**: **C. Fife** -TIP directorate 860M with 364M for existing programs moving into this new organization structure. Increase for NSF is 1.2 billion about 500M was increased for TIP and related programs. Each of the things that are moving appropriations authorizing legislations House and Senate they don't have specific numbers for TIP because it speaks to the high regard that we would be in collaboration to include in the partnership across the Foundation. Once we get that ultimate direction from Congress then we can work for what is the right size for the new directorate.

C. Hunt – will send out an e-mail to AC members for writing assignments. We are proud of the progress we are making as an AC and a directorate. Not actually utilizing the strengths and talents that you bring to the agency. Appreciates the work you do behind the scenes and engaging with the community.

Closing remarks and adjourning for the day

C. Hunts thanks AC members and states how very appreciative she is for their help.
Meeting Adjourned. 5:00PM