U.S. Department of Health & Human Services

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Proposed Merger of Two Study Sections in the Biological Chemistry and Macromolecular Biophysics Integrated Review Group (BCMB IRG)

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BCMB IRG Study Sections

•**Biochemistry and Biophysics of Membranes [BBM] -** Membranes, membrane proteins, lipids

•**Macromolecular Structure and Function A [MSFA] -** Metalloproteins, metal ion homeostasis, misfolding/amyloids

•**Macromolecular Structure and Function B [MSFB] -** Protein folding, protein dynamics, RNA, nucleic acid-protein complexes

•**Macromolecular Structure and Function C [MSFC] -** Macromolecular complexes, motor proteins, nucleic acid-protein complexes

•**Macromolecular Structure and Function D [MSFD] -** Computational Biophysics

•**Macromolecular Structure and Function E [MSFE] -** Mechanistic enzymology, enzyme inhibitors, biosynthesis

•**Synthetic and Biological Chemistry A [SBCA]**
•**Synthetic and Biological Chemistry B [SBCB]**
•**Fellowships in Chemistry, Biochemistry and Biophysics [F04]**

BCMB Overview

•**Biochemistry and Biophysics of Membranes [BBM] -** Membranes, membrane proteins, lipids

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Historical Perspective

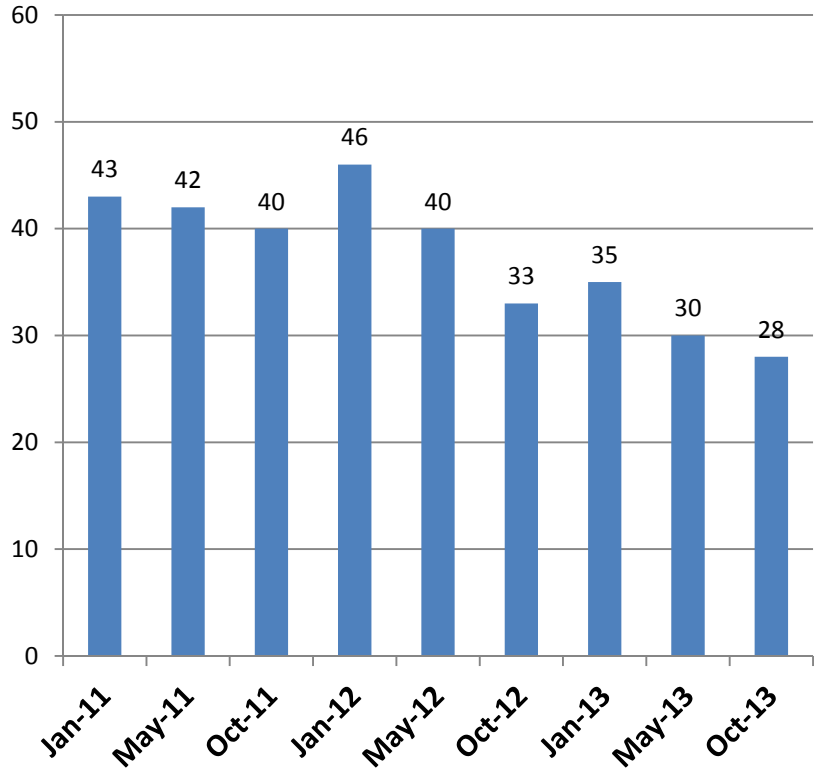
- 2004 – Panel on Scientific Boundaries in Review (PSBR)
  – MSFA (metallobiochemistry, metalloenzymes, mechanistic enzymology)

- 2006 – Working Group in response to concerns from mechanistic enzymology community regarding inadequate clustering and low representation/influence in MSFA membership
  – MSFA split into
    - MSFA – metallobiochemistry
    - MSFE– mechanistic enzymology

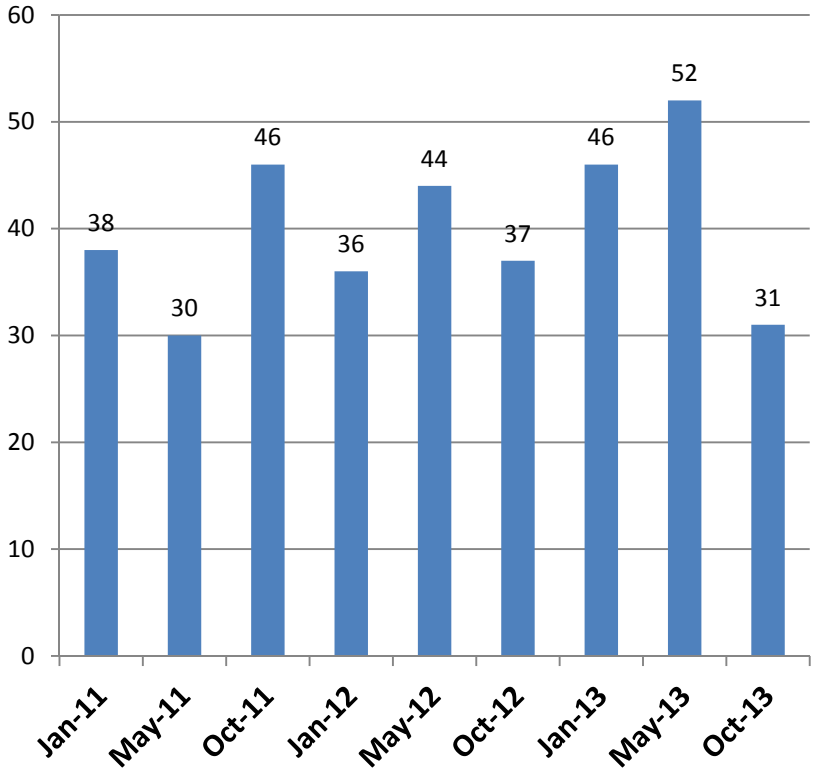
Continuing Problem: Low Workloads

Number of R01 applications, 2011/01-2013/10

MSFA
Avg 37



MSFE
Avg 40



Proposed Solution: Merged Study Section

- Mechanistic enzymology involving protein and nucleic acid catalysts.
- Metalloenzymes and their mechanisms: biochemical, spectroscopic, genetic, kinetic and structural methods applied to understand the mechanism of the metal center.
- The design, synthesis and use of enzyme inhibitors where the primary interest is to understand or modulate enzyme mechanism/function. Biochemical mechanism based drug development
- Protein-ligand interactions and dynamics.
- Macromolecular studies of metabolic pathways and networks.
- Computational and theoretical studies of biochemical reactions, application of quantum mechanics and molecular mechanics to studies of enzyme mechanisms, genomic enzymology, sequence-structure analysis to uncover mechanistic strategies of superfamilies.
- Synthetic and theoretical models of metallo-active sites: small molecule complexes and designed peptides intended to mimic an enzyme active site reactivity or metal center specificity.
- Chemistry of metal centers and organic redox active cofactors: redox chemistry of oxygen/nitrogen species. Chemistry of reactive oxygen/nitrogen metabolism: methods of generation and mitigation as well as it undesired side reactions.
- Metal ion homeostasis and metabolism: regulation of influx, efflux and transport of iron, copper, zinc and manganese as well as other metals ions whose concentration must be closely controlled or limited. Mechanisms of metal ion toxicity.

2013 – BCMB IRG Review

- Evaluation Panel endorsed the proposal to merge MSFA and MSFE.
- Scientifically logical
- Counseled attention to appropriate expertise and perspective for increased scientific scope of the new study section

Would mechanistic enzymology community's concerns from 2006 be an issue again? Not likely

- Main concern: "mechanistic enzymology is underrepresented" in the membership of the study section
  - Merged study section has 20 chartered members -- 8 from MSFA (metallobiochemistry), 10 from MSFE (mechanistic enzymology)
- Additional concern: Mechanistic enzymology applications are reviewed in multiple study sections/not clustered adequately
  - Clustering in MSFE maintained in the merged study section
- Based on current workloads, over half the applications would be from MSFE
- SRO and Chair of merged study section from MSFE

BCMB IRG Review Evaluation Panel

- Lorena Beese, Duke
- Tadhg Begley, Texas A&M
- William Tolman, Minnesota
- Shelagh Ferguson-Miller, Michigan State
- James Nelson, Stanford
- Andrew Murray, Harvard (CSRAC)
- George Phillips, Rice
- Keith Yamamoto, UCSF – observer (CSRAC)

CSR Staff:
John Bowers, Chief, BCMB IRG
George Chacko, Director, OPAE

Discussion