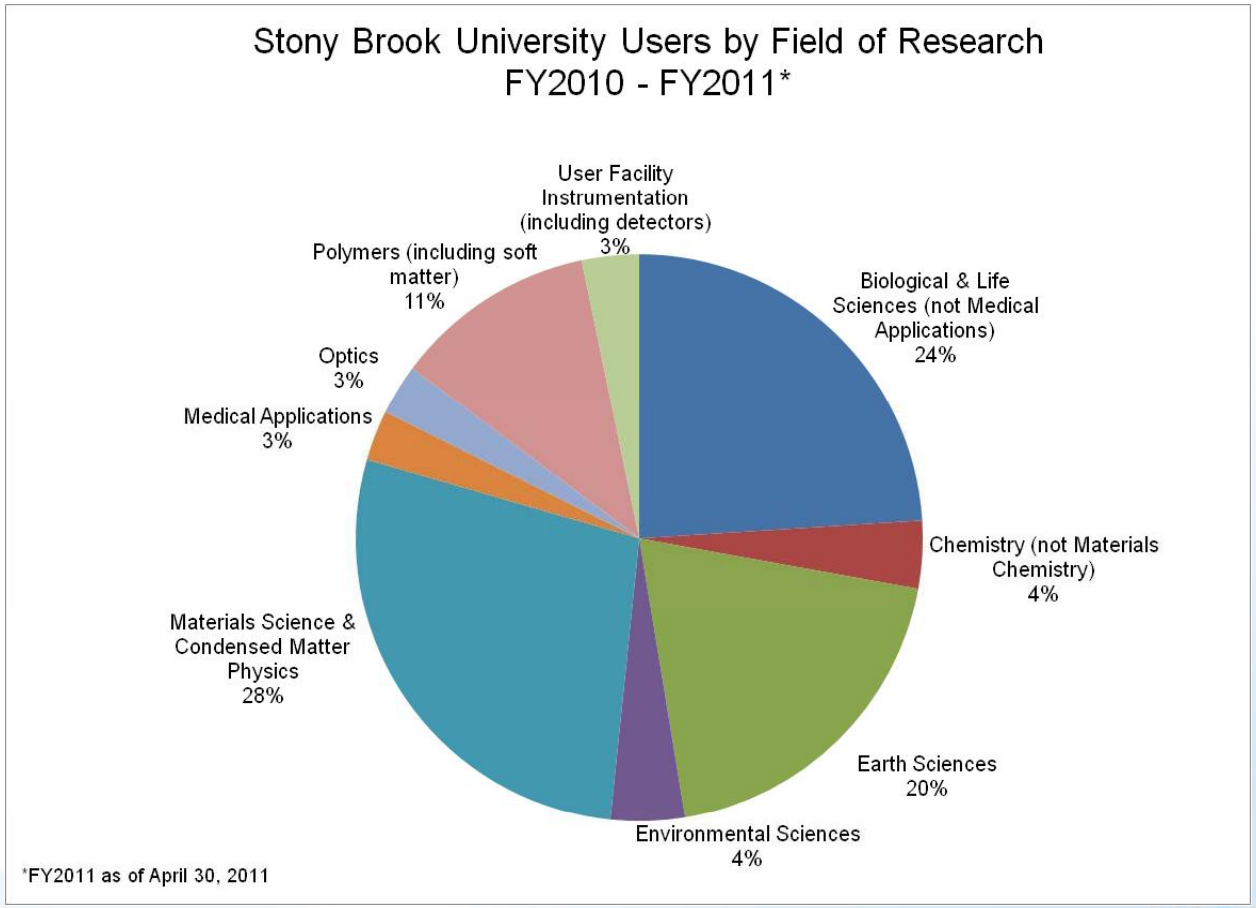
SBU Users in NSLS

- Physical Science Users ~ 70%
- Life Science Users ~ 30%



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Bio-Imaging at SBU

Arts & Science and Engineering:

- Chris Jacobsen (Physics)
- Stefan Judex (Biomed Eng)
- Yizhi Meng (Materials Sci & Eng)
- Yi-Xian Qin (Biomed Eng)
- Miriam Rafailovich (Materials Sci & Eng)
- Rich Reeder (Geosciences)
- Balu Sitharaman (Biomed Eng)

Medical School:

- Terry Button (Radiology)
- Patricia Coyle (Neurology)
- Don Harrington (Radiology)
- Allen Meek (Radiation Oncology)
- Bill Moore (Radiology)
- Rebecca Spiegel (Neurology
- Clint Rubin (Biomed Eng)
- Helmut Strey (Biomed Eng)

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Major Bio-Imaging Techniques

- Infrared Microspectroscopy (U2B, U10B)
  - Judex, Meng, Qian, Rafailovich, Rubin
- Scanning Transmission X-Ray Microscopy (X1A1, X1A2)
  - Jacobsen, Meng, Rafailovich
- X-Ray Microcomputed Tomography (X2B)
  - Judex, Rubin
- X-Ray Fluorescence Microscopy (X26A, X27A)
  - Reeder, Sitharaman
- Diffraction-Enhanced Imaging (X15A)
  - Button, Coyle, Harrington, Meek, Moore, Spiegel
- Microbeam Radiation Therapy (X17B1)
  - Button, Coyle, Harrington, Meek, Moore, Spiegel

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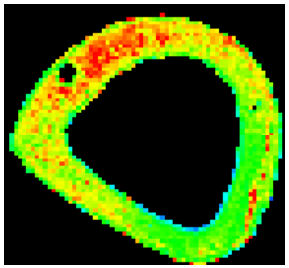
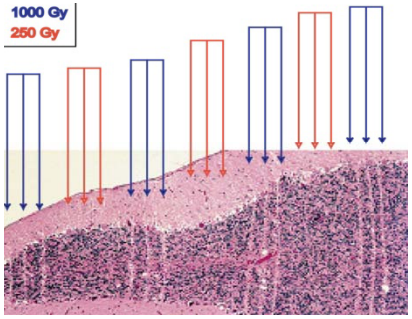
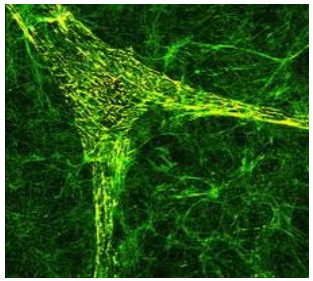
Applications



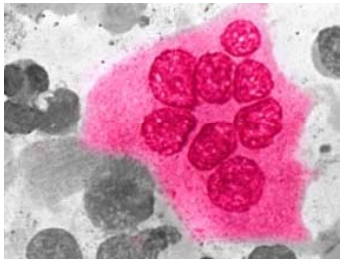
Identification of Chemical Factors that Determine Bone Strength (Judex)



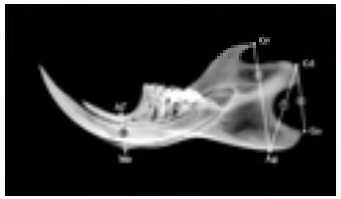
Microbeam radiation therapy for central nervous system research (Dilmanian, et al.)



Examination of the Biomineralized Self-Assembled Extracellular Matrix (Meng)

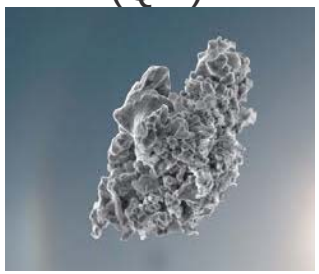


Characterization of biomineralized osteoblast-like cells (Qin)

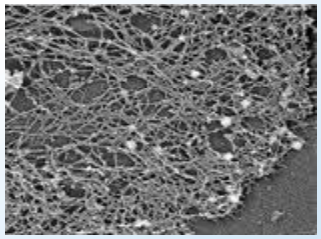


Low intensity vibrations improve the quality of bone aiding in tooth retention (Rubin)

Carbon XANES Analysis of Lignocellulose (Jacobsen)



Metal speciation in inhaled dust particles (Reeder)



Imaging of biomineralized protein networks (Rafailovich)

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Structural Biology at SBU

Biochemistry and Cell Biology:

- Steven Glynn (New Assistant Professor)
- Huilin Li (X25, X29)
  - Dale Deutsch (Biochemistry)
  - Robert Haltiwanger (Biochemistry)
  - Bill Lennarz (Biochemistry)
  - David Thanassi (Microbiology)

Pharmacological Sciences:

- Miguel Garcia-Diaz (X12C, X25, X29)
  - Peter Tong (Chemistry)
- Markus Seeliger (X12C)

Chemistry:

- Liz Boon (X3B)

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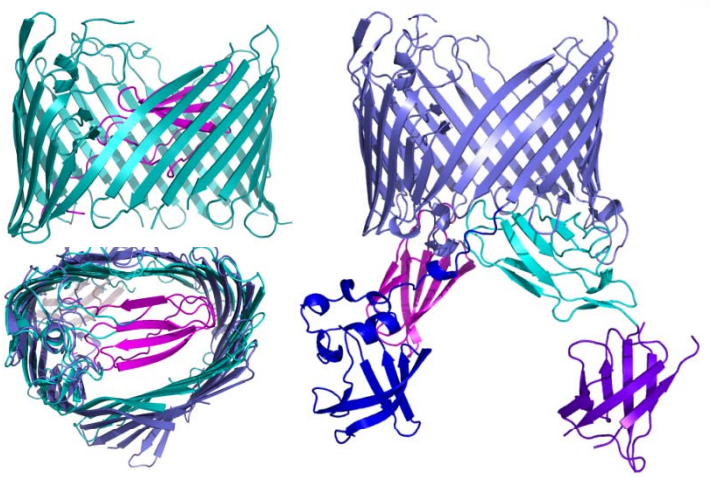
Assembly and Secretion of Bacterial Surface Fibril Visualized

Tao Wang[1,3], Nadine Henderson[2], Huilin Li[1,3] and David Thanassi[2]
1. Department of Biochemistry and Cell Biology, 2. Department of Molecular Genetics and Microbiology, Stony Brook University; 3. Biology Department, Brookhaven National Laboratory

- Bacteria use surface fibrils called pili to adhere to the host in order to gain initial foothold for subsequent establishment of colonies. The Thanassi lab and the Li lab have been collaborating to elucidate how the bacterial outer membrane usher FimD assembles and secrets the type 1 pili.
- Using beamlines X25 and X29, the Thanassi and Li labs recently solved the crystal structure of the FimD usher in the resting state.
- The Waksman group at University College London recently solved the crystal structure of FimD usher that is already activated by the chaperone-subunit.
- Comparison of the same FimD protein in two functional states reveals how the initially blocked secretion channel is activated and opened up; and how the usher catalyzes the assembly of the pilus subunits.



The bacterial membrane protein FimD usher in the resting (top left) and the activated state (right). Comparison of the usher in the two states reveal unexpected large conformational changes in the membrane-embedded translocation domain (bottom left); and how the initially plugged translocon is opened up for pilus assembly and secretion.

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G Phan, H Remaut, T Wang, W Allen, K Pirker, A Lebedev, N Henderson, S Geibel, E Volkan, J Yan, M Kunze, J Pinkner, B Ford, C. Kay, H Li, S Hultgren, D Thanassi, G Waksman*, "Crystal structure of the FimD usher bound to its cognate FimC:FimH substrate", Nature, 2011, in press.*
H Remaut, C Tang, N Henderson, J Pinkner, T Wang, S Hultgren, D Thanassi, G Waksman, H Li. "Fiber formation across the bacterial outer membrane by the chaperone/usher pathway", Cell. 2008, 133, 640.

Work performed on beamlines X25 and X29.

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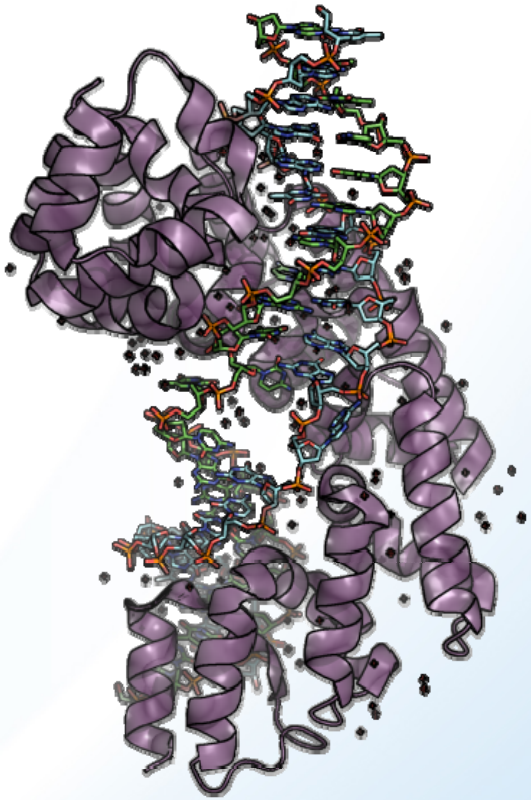
Structural Insight into Mitochondrial Transcription

Yakubovskaya, E., Mejia, E., Guja, K., Byrnes, J, Hambardjieva, E. Garcia-Diaz, M.
[1]Stony Brook University



Deficiencies in mitochondrial gene expression affect a large proportion of the population and can cause or contribute to disease development. We are studying the molecular mechanisms responsible for transcription, a central process in gene expression, and the mechanisms by which deficiencies in this process can lead to mitochondrial pathologies. We have recently solved the structure of the human mitochondrial termination factor (MTERF1) bound to dsDNA containing the termination sequence. The structure revealed unexpected insight into the mechanism of MTERF1 binding and transcription termination. MTERF1 adopts a unique DNA binding mechanism in which a handful of critical interactions mediate the recognition of the termination sequence and association of MTERF1 with the major groove of the double-helix, leading to helix unwinding. Helix unwinding, together with a few key protein-DNA interactions, destabilizes the central base pairs of the termination sequence, promoting base-flipping of three nucleotides. Base-flipping plays a key role to facilitate termination, and interfering with any of the critical protein-DNA contacts severely impairs termination. Consistently, we have demonstrated that several pathogenic mtDNA point mutations that occur in the termination sequence and affect key interactions for sequence recognition result in a strong reduction in termination, suggesting a link between mitochondrial disease and the regulation of mitochondrial transcription.

*Yakubovskaya, E., Mejia, E., Byrnes, J., Hambardjieva, E., Garcia-Diaz, M. (2010) Helix unwinding and base flipping enable human MTERF1 to terminate mitochondrial transcription. Cell **141**, 982-993.*

*Byrnes, J., and Garcia-Diaz, M. (2010) Mitochondrial transcription, how does it end? Transcription **2**, 32-36*

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Work performed on beamlines X12C, X25 and X29

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