Wah Chiu Baylor College of Medicine

National Center for Macromolecular Imaging (NCMI) (National Center for Research Resources, NIH)

Center for Protein Folding Machinery

(Nanomedicine Development Center, NIH Roadmap)

http://ncmi.bcm.edu

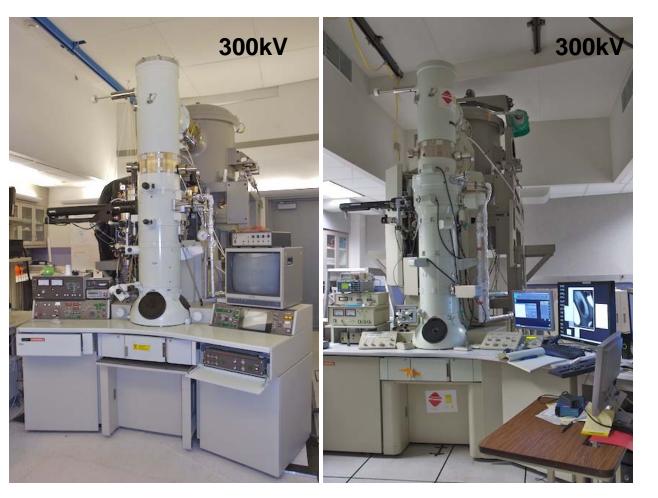


Research Missions at NCMI

- Develop and apply Cryo-EM for structure determinations of Molecular Nano-Machines in solution states towards atomic resolution; and of Whole Cells at molecular resolution
- Share our experimental and computational technology freely with the global academic community



200kv Electron Cryo-Microscope at NCMI



NCMI Computer Clusters



Pipeline in Cryo-EM for Nano-Machine

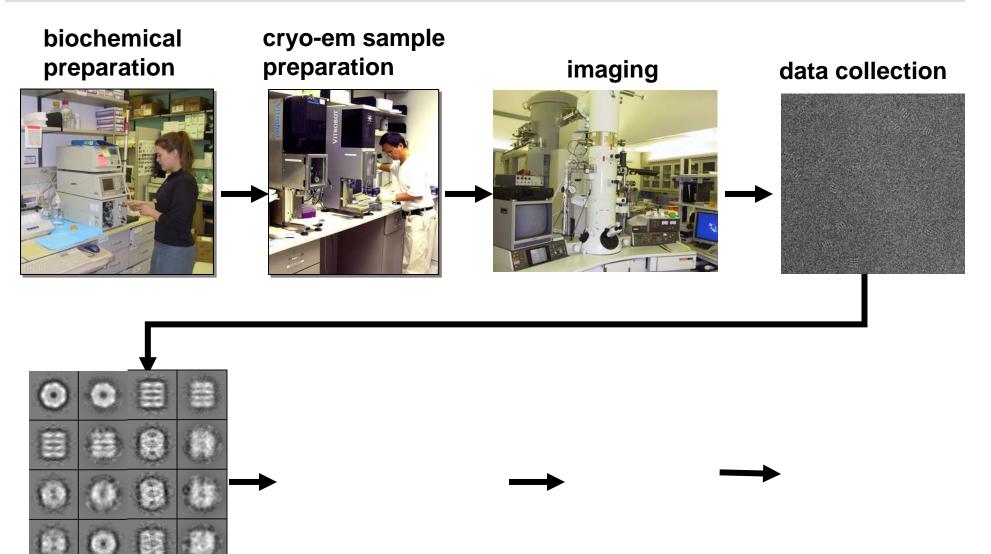


image processing

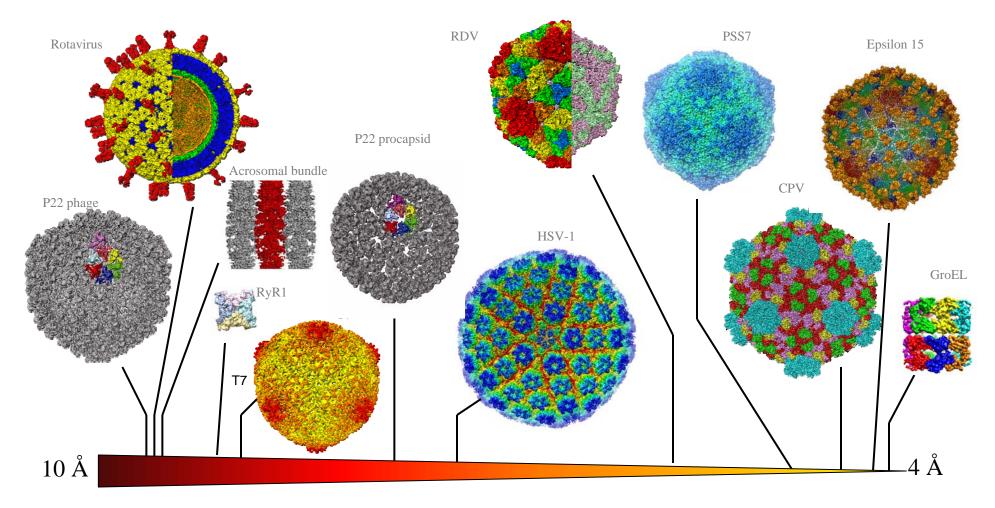
reconstruction structural analysis

model

NCMI Collaborators and Users



Subnanometer Resolution Cryo-EM Structures Determined at NCMI



Cryo-EM: A tool for Nano-Objects

Nanotubes Lon Wilson, Rice U

Nanowire Rick Smalley, Rice U

DPPC-Au Hollow Sphere Zasadzinski, UCSB

Membrane-copolymer Ka Yee Lee U Chicago

Nanoshell Naomi Halas, Rice U

Virus-like Particle and Au Core Lia Stanciu, Purdue University

Cryo-Electron Tomography of Platelet

Jose Lopez U Washington

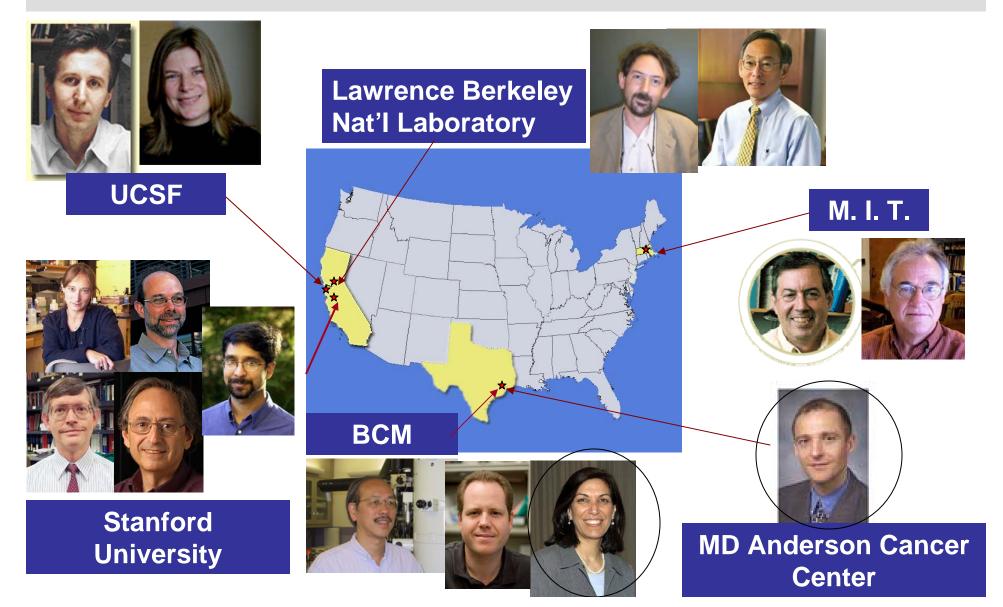


NIH Nanomedicine Development Center

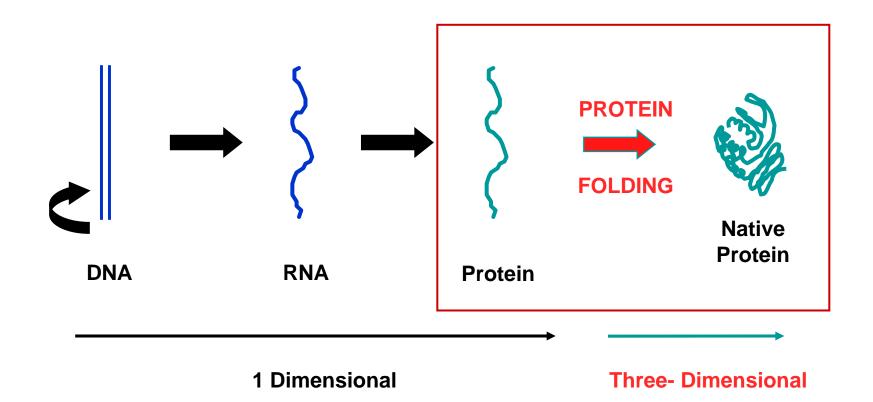
http://proteinfoldingcenter.org

PI: Wah Chiu

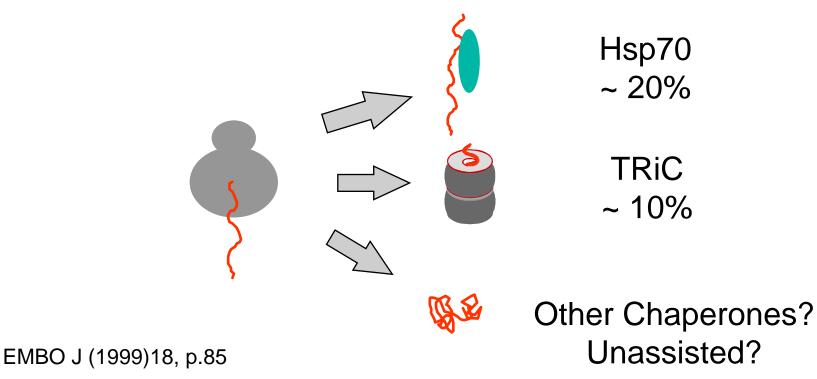
Protein Folding Machinery Center Investigators



Protein Folding is a Key Step in Gene Expression



Chaperone-mediated Folding in the Cell



A Large Fraction of Cellular Proteins Transits Through Chaperones During their Biogenesis

Defects in Protein Folding lead to Human Disease

Amyloid Deposits: Prions, Alzheimers

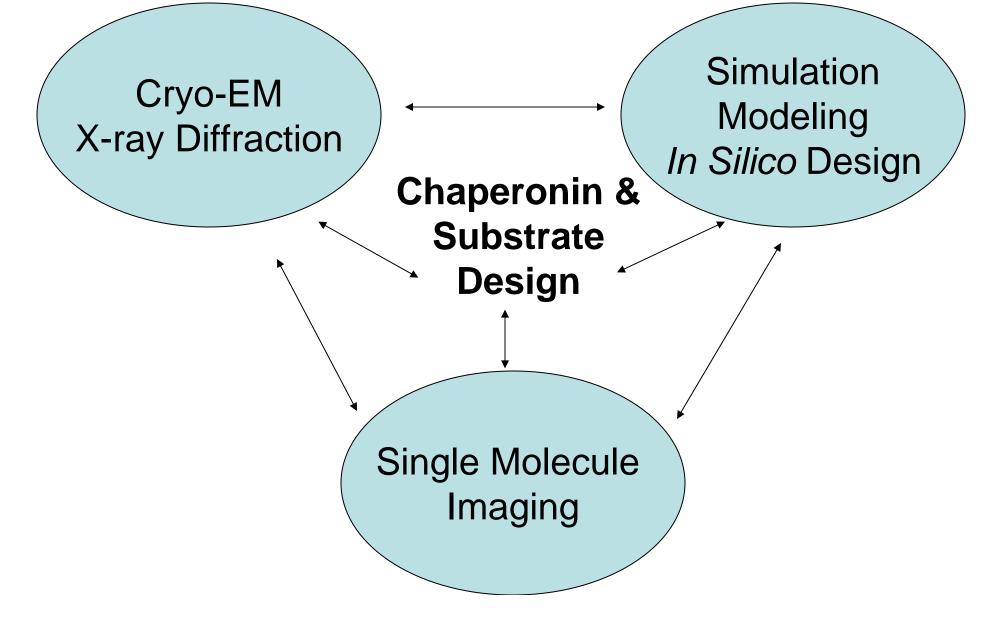
Mutations: Cancer, Metabolic Diseases

Denaturing Stress: Ischemia, Stroke

Our Nanomedicine Center Goals

- Engineer chaperonin variants optimized to fold proteins of biomedical importance *in vitro*.
- Engineer chaperonin variants that promote folding/unfolding of specific proteins *in vivo*.
- Engineer an "adaptor" molecule to turn "on" or "off" substrate targeted to the chaperonin
- Design a versatile nano-cage based on the chaperonin platform to encapsulate and release ligands of choice.
- Develop and disseminate a pipeline of measurement and simulation tools for characterizations of nanomachines.
- Develop an educational curriculum on nanomedicine

Multi-Disciplinary Approach to Design New Chaperonin and Substrate



Protein Folding Machinery Center

- Continuously seeking for clinical partners for exploring our unique capability for treating diseases related to protein misfolds
- Actively engaging in bridging translational and biophysical/computational research