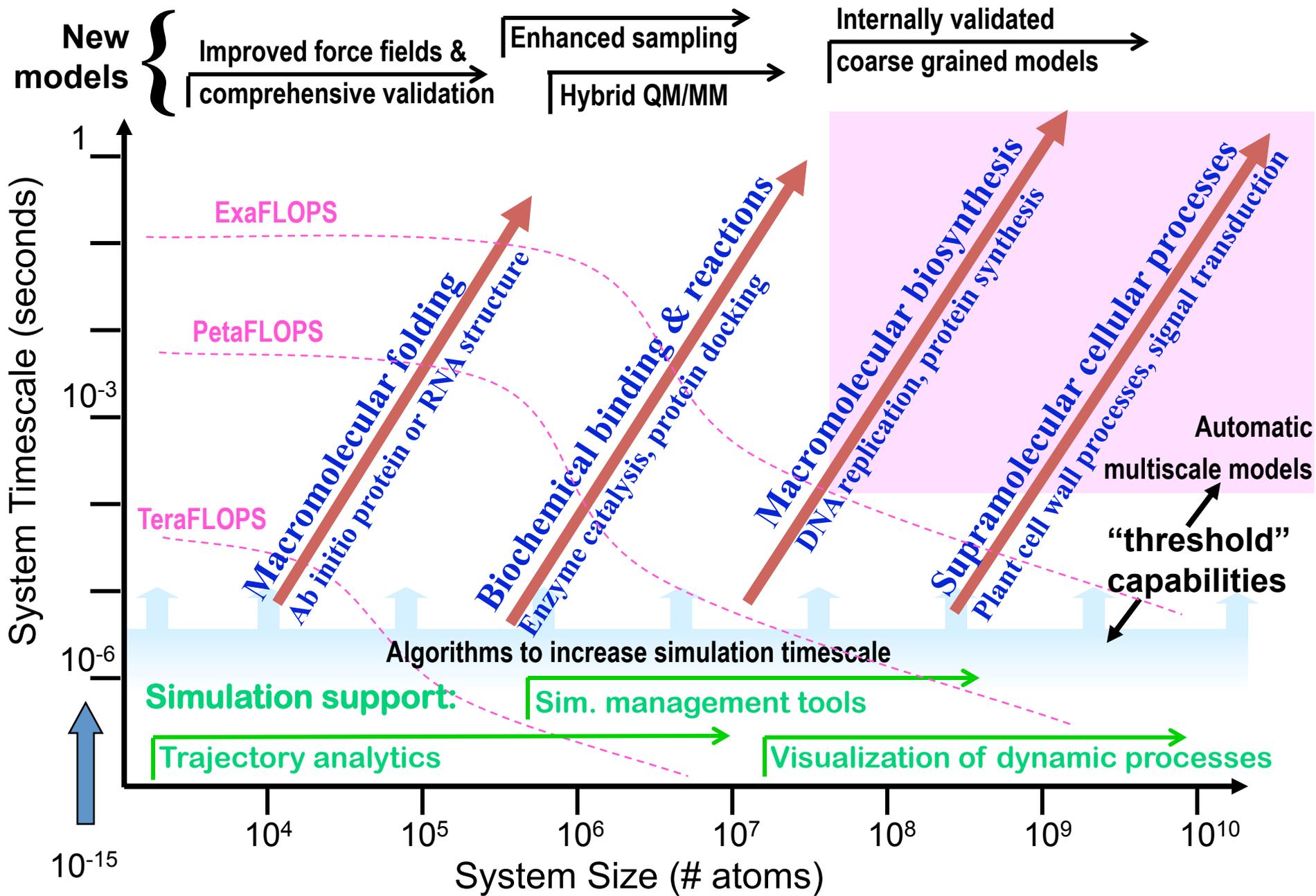
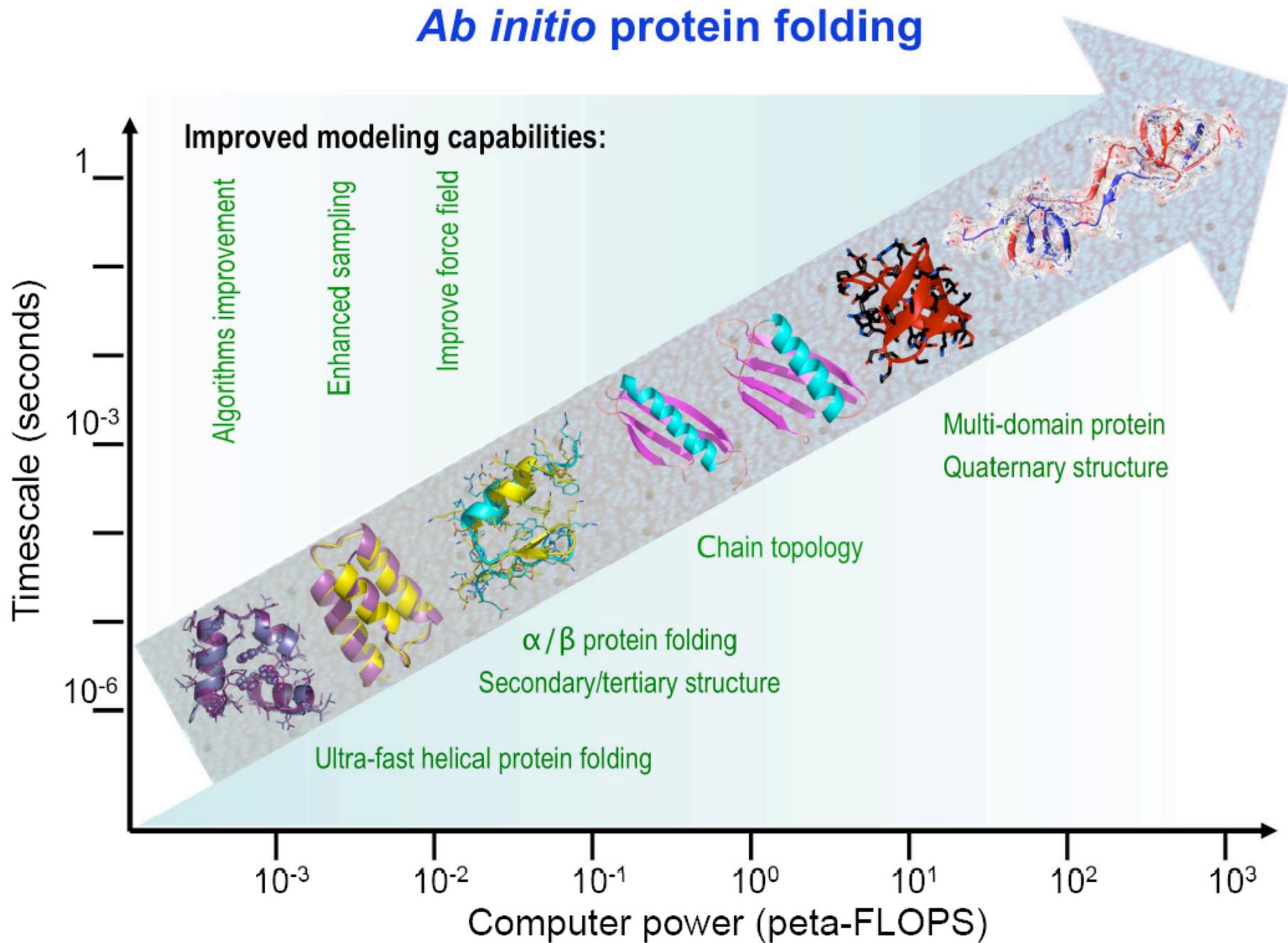


Towards Exascale Biochemical Simulations



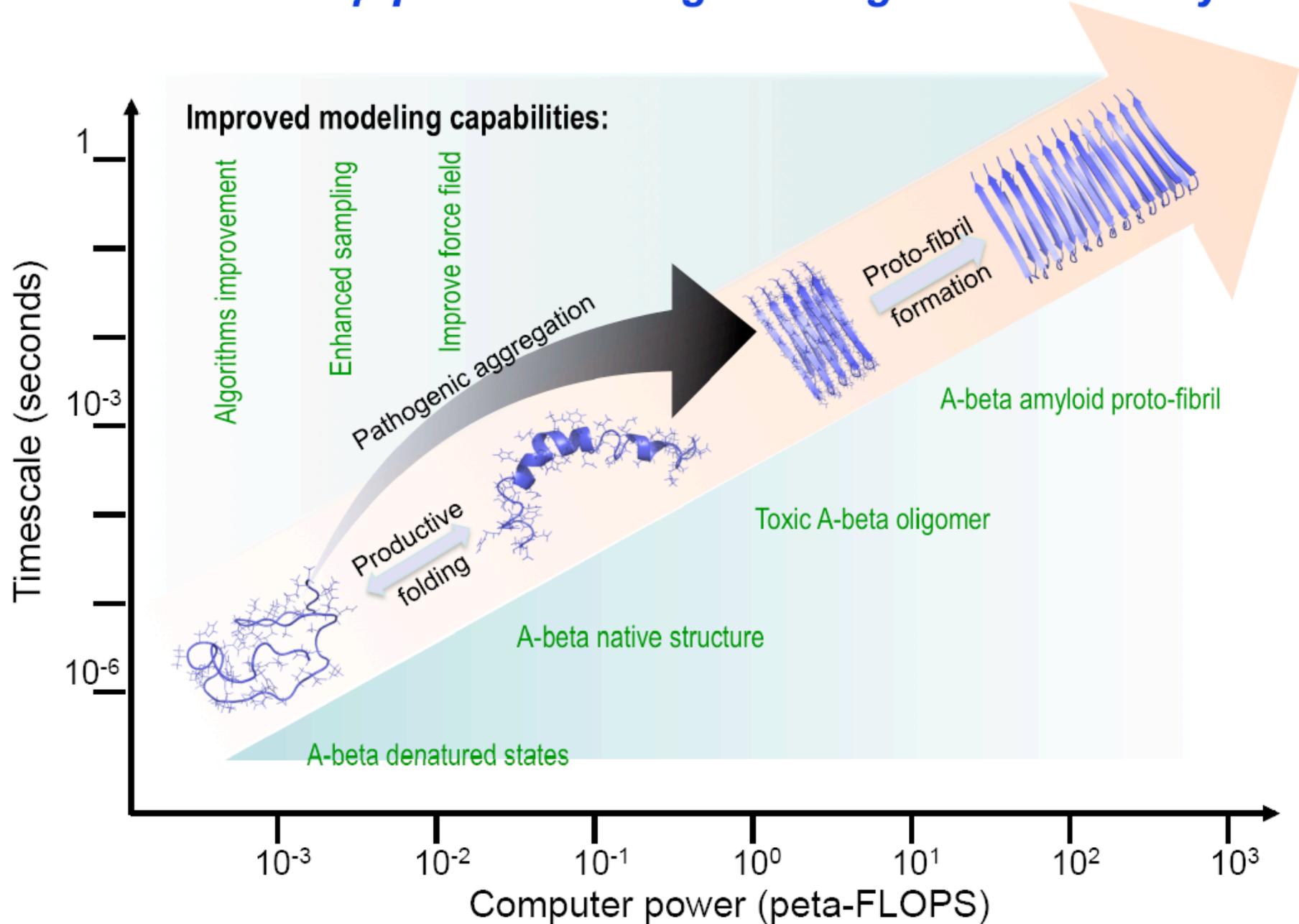
Scientific Grand Challenge I—Macromolecular Folding

Ab initio protein folding

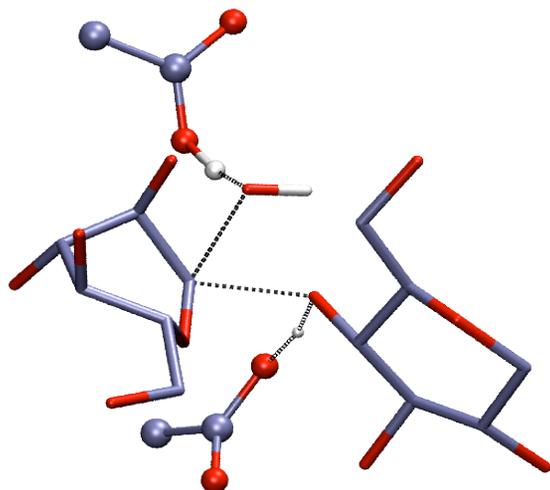


Scientific Grand Challenge I—Macromolecular Folding

Alzheimer- β protein folding and oligomer assembly



Scientific Grand Challenge II—Biochemical Binding and Reactions



Cellulase Transition State

Exascale will allow the determination of:

ligand binding modes and energies and enzyme reaction mechanisms to unprecedented accuracy

Major impact expected on:

Protein engineering (e.g., in bioenergy, bioremediation)

Drug/inhibitor discovery, Catalyst design.

Technical development required - software for efficient parallelisation of:

-quantum chemical and mixed quantum/molecular mechanical codes for reactions

-reaction path and free energy sampling methodologies (free energy perturbation, umbrella sampling, etc)

Scientific Grand Challenge III—Macromolecular Machinery

Challenge: Simulate a biomolecular complex on a physiologically meaningful timescale.

Definition

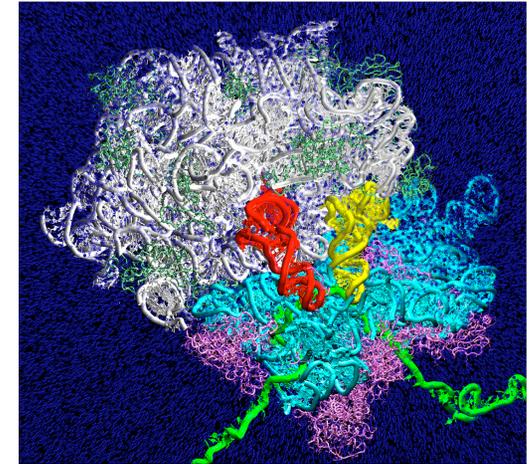
- ‘Holy Grail’ – using simulation to image dynamics at atomic resolution, ultimately with predictive capability.
- Combination of atomistic and coarse-grained techniques.
- Validate against experiment.
- Efficient methods for data mining

Examples

- Cellulose-related (Bioenergy), Ribosome (Biothreat), DNA polymerase

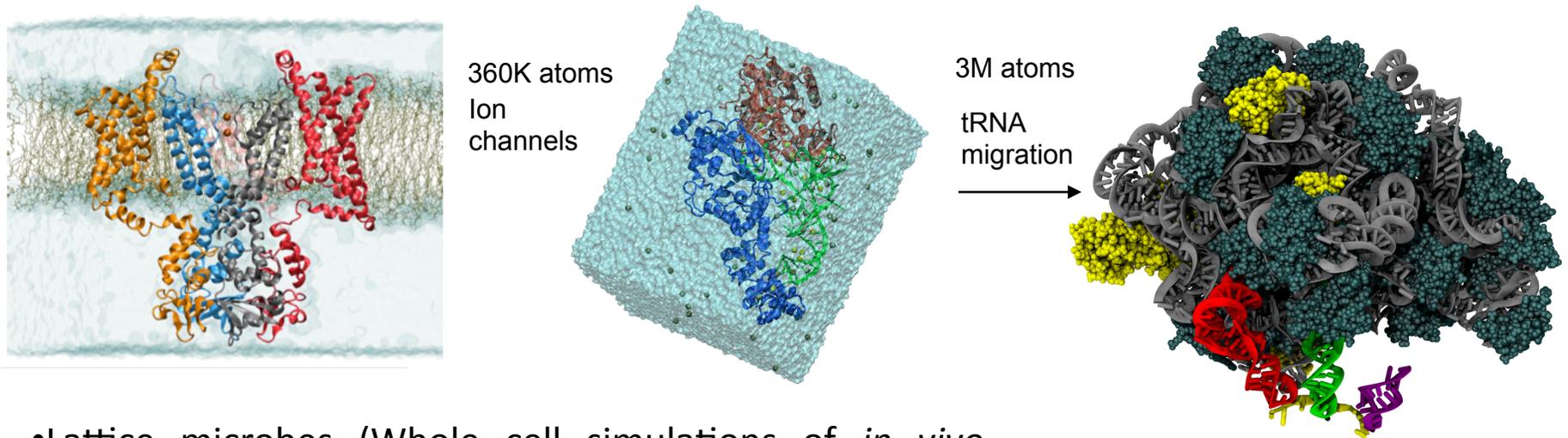
Technical gaps

- Scaling of electrostatics for charged systems (FFT, Generalized reaction field, other novel methods)
- Development for advanced architectures
- Integration and validation of atomistic and coarse-grained techniques
- Detailed validation against experiment
- Determining convergence for the simulation



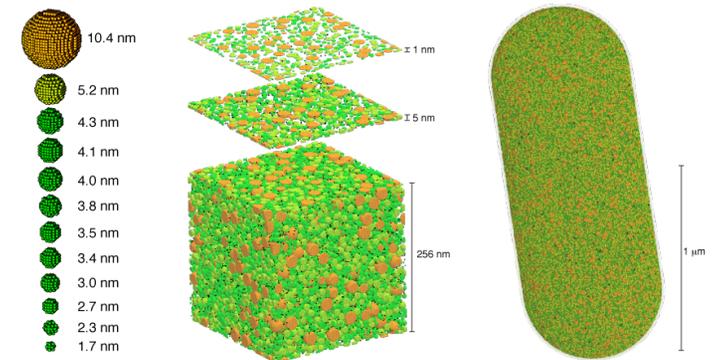
Scientific Grand Challenge IV: Supramolecular Assemblies & Cellular Processes

- MD all atom and coarse-grained simulations: signaling (membrane/proteins), universal processes of translation, transcription, replication (RNA/protein)



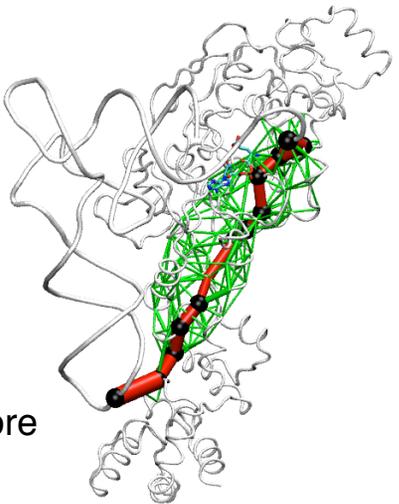
- Lattice microbes (Whole cell simulations of *in vivo* processes): Present state (with 1 GPU=1teraflop, resolution 2-8nm, 30s) : Realistic molecular crowding based on size distributions and populations from proteomics and cryo-electron tomography, tens of biochemical reactions for specific networks

- Technical Challenges: Legitimate decoupling of complex systems. Connect simulations of cellular processes and energy networks to systems biology models

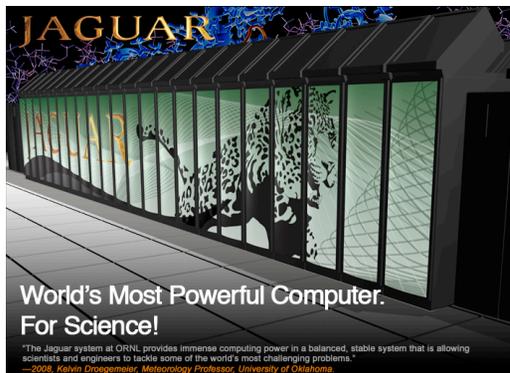


Scientific Grand Challenge IV: Supramolecular Assemblies & Cellular Processes

Technical Gap: Accelerating Visualization of Dynamical Processes

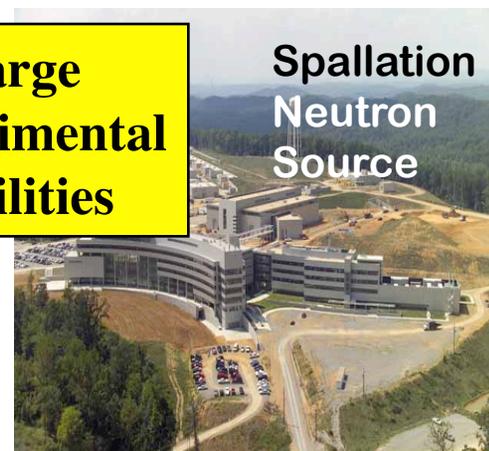
- Multiscale representations - coarse-grained and all atom
 - Visualizing Correlation/Interaction Data - Networks
- 
- Accelerating visualization of very large simulations, e.g. 100 million atom chromatophore in photosynthetic bacteria, large cellular automata, arbitrary particle systems
 - Challenge: Develop new visualization algorithms that fully leverage both multi-core X86 CPUs and multiple accelerators (e.g. GPUs), so that a single high-end desktop machine with say 16 X86 cores and 4 accelerators can become an effective platform for working with systems of this size and complexity.
 - Goal - Extract low-level properties of the structure and use them to dynamically update graphical representations, e.g. the ring pucker for the carbohydrates, dynamically updating H-bonds, multi-core X86 CPUs and accelerators to visualize molecular orbital in QM/MM simulations
 - Parallelize secondary structure determination on GPUs to handle dynamics of large structures.
 - GPU-accelerated analysis techniques on implicit ligand sampling work that was originally developed for collaboration with NREL for synthetic biology efforts related to alternative energy. Current GPU code is 30x faster than the CPU version
 - Graphical connections between real particles and arbitrary coarse-grained particles

Biomolecular simulations enable many DOE Missions



Supercomputing

**Large
Experimental
Facilities**

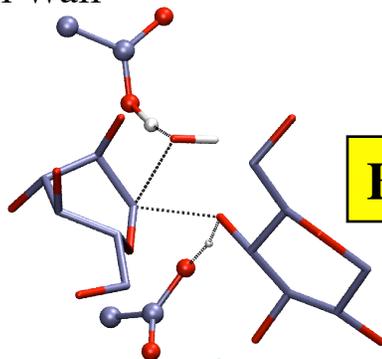


Synergy with Neutron and
X-ray developments.

Algorithm Development for
Exascale Simulation



Plant Cell Wall



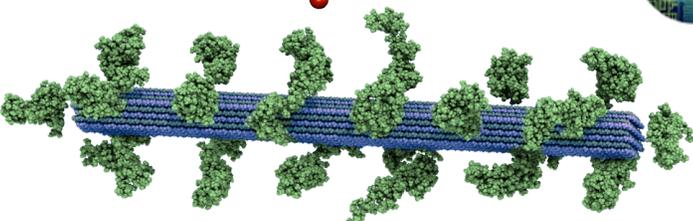
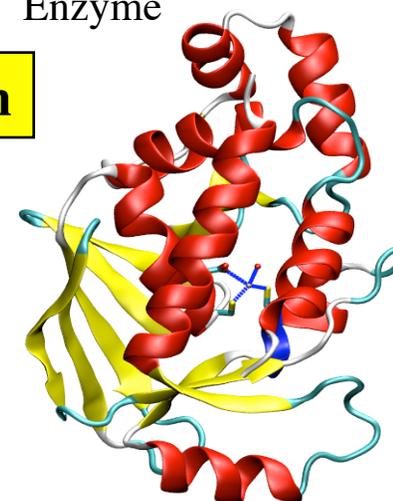
Bioenergy



Bioremediation



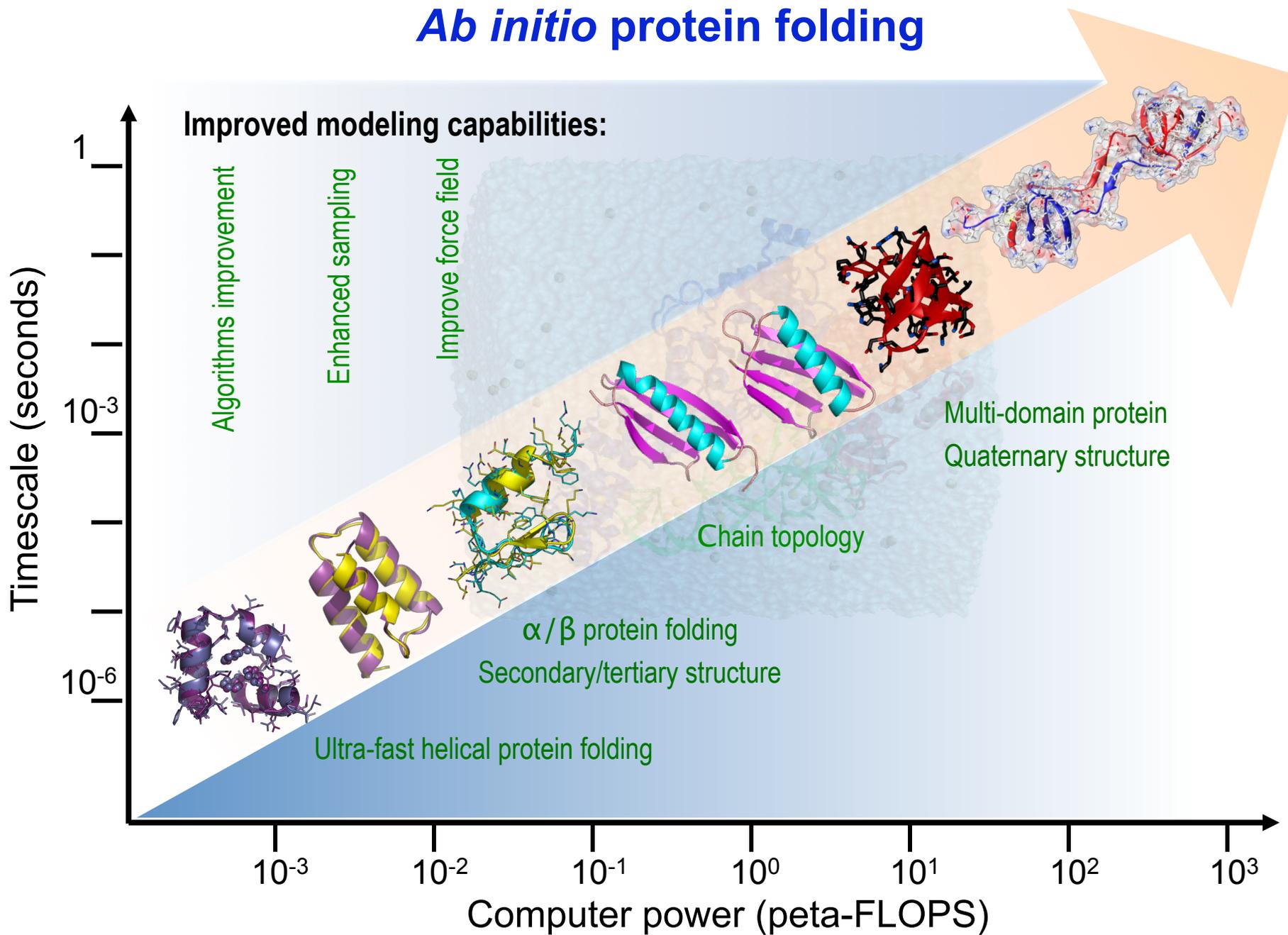
Mercury
Detoxification
Enzyme



Cellulase Active Site

Scientific Grand Challenge I—Macromolecular Folding

Ab initio protein folding



Scientific Grand Challenge I—Macromolecular Folding

Alzheimer- β protein folding and oligomer assembly

