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**Biology**

**Chemistry**

\[ E_{\text{total}} = E_{\text{inner}} + E_{\text{outer}} \]
\[ E_{\text{inner}} = \sum K_s (b-b_0)^2 + \sum K_s (\theta-\theta_0)^2 + \sum K_s (1 + \cos \eta_p - \eta) \]
\[ E_{\text{outer}} = \sum \frac{q_i q_j}{4\pi \epsilon_0 r_{ij}} + \epsilon \left( \frac{R_{\min}}{r_{ij}} \right)^{12} - 2 \left( \frac{R_{\min}}{r_{ij}} \right)^6 \]

**Physics**

\[ F_i = m_i a_i = m_i \frac{d^2 r_i}{dt^2} = -\nabla E(R) \]

**Mathematics**

\[ r_i(t + \delta t) = 2r_i(t) - r_i(t + \delta t) + \delta t^2 \frac{F_i(t)}{m_i} \]
What can we **directly** see?

Experiments

Simulations

Unfolded  Folded

Unfolded  Folded
Computer Simulations of Biological Systems

- **Electronic Level**: Quantum Mechanical (QM)

- **Molecular Level**: Molecular Dynamics (atomistic)

- **Coarse-Grained Simulations**: Assembly Level

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**Time (real)**
- fs
- ps
- ns
- ms
- s
- mins

**Size of the System (# of atoms)**
- $0, 10, 10^2, 10^3, 10^4, 10^5, 10^6, 10^7, \ldots$
Many-core GPU performance is faster and increasing more quickly than single-core CPUs.
GPU Hardware Setup
**Group In the News**

**Video games take role in treating cancer at Wake Forest**

*S. Roberts*  
*By Olivia Siler*  
*17 February 12*

**Can a video game cure cancer?**

*By ALICIA ROBERTS*

Angi Zhou (12) never thought she would thank video gamers for showing her the way to exciting discoveries in molecular biology. But here she is, acknowledging that the technology she uses to show the inner workings of cells was originally perfected to create realistic images on gaming screens worldwide.

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**NEW RNA SIMULATION KNOWS WHEN TO FOLD**

Riboswitches are RNA molecules that control gene expression. They detect specific small molecules and change how a cell reacts to them. These molecules fold into precise, active structures that enable or prevent gene activity. A team of researchers from Wake Forest University has developed a new algorithm to simulate how riboswitches fold and unfold, allowing them to predict which structures are most likely to be active.

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**Rapid, Real-Time Cell Secretion Assay System**

Cytoplasm—proteins involved in communication between cells and important markers for medical diagnosis—are essential to immunological research. Many synthesis methods take a long time, must be repeated for each marker, or cannot be used in large-scale studies. Now, Matthew J. Luchansky and Ryan C. Bailey have developed a fast and simple new system that allows concentrations of multiple analyte molecules to be detected in real time (DOI: 10.1021/acs.jacs.9b08761). The team used their biosensor chip to simultaneously quantify several human cytokines from cell culture supernatants.

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**Spotlights on Recent JACS Publications**

**Video game GPUs reappropriated for biological simulations**

By Olivia Siler  
*17 February 12*

**ABSTRACT:** Globally, RNA folding occurs in multiple stages involving chain compaction and subsequent rearrangement by a number of parallel routes to the folded state. However, the sequence-dependent details of the folding pathways and the interplay between collapse and folding are poorly understood. To obtain a comprehensive picture of the thermodynamics and folding kinetics we used molecular simulations of coarse-grained model of a pseudoknot found in the conserved core domain of the human telomerase (hTR) by varying both temperature (T) and ion concentration (C). The phase diagram in the [T,C] plane shows that the boundary separating the folded and unfolded state for the fixed 4T-motif is system is relatively sharp, implying that a thermodynamic transition is present in the system. However, the folding kinetics following single C-jump or T-quench is complicated, involving multiple channels to the native state. Although globally folding kinetics are similar, the kinetics of chain compaction are vastly different, which reflects the role of initial conditions in directing folding and collapse. Remarkably, even after substantial reduction in the overall size of hTR, the ensemble of compact conformations are far from being mutually exclusive, suggesting that the search for the folded state occurs among the ensemble of low-energy flexible global states. This result implies that unfolding, which occurs in a single step, is faster upon C-decrease compared to a T-jump in temperature. To identify "hidden" states that are visited during the folding process we performed simulations by periodically interrupting the approach to the folded state by lowering C. Two simulations show that hTR reaches the folded state through a single route of compact clusters that are repeatedly visited during the pulse sequence in which the unfolding is interrupted. The results from interrupted unfolding simulations, which are in accord with our equilibrium single-molecule folding of a large ribosome, show that multiple precursors are needed to reveal the available states that are sampled by RNA as it folds. Although we have illustrated the complexity of RNA folding using hTR as a case study, general arguments and qualitative comparisons to time-resolved scattering experiments on analogous group I ribozyme and single-molecule non-equilibrium periodic ion-quench experiments establish the generality of our findings.

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**Foldin of Human Telomerase RNA Pseudoknot Using Ion-Jump and Temperature-Quench Simulations**

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**JACS**

*Journal of the American Chemical Society*

*www.jacs.org*
Current Biophysics Projects

Protein-RNA Interactions
- Collaborator: Rebecca Alexander (Wake Forest Univ., Dept. of Chemistry)
- Level: Undergraduate

Protein-Nanoparticle Interactions
- Collaborator: Pu-Chun Ke (Clemson Univ., Dept. of Physics)
- Level: Undergraduate, Graduate

Fibrinogen Elasticity
- Collaborators: Martin Guthold (Wake Forest Univ., Dept. of Physics), Valeri Barsegov (University of Massachusetts)
- Level: Graduate

Qualifications:
- Interest in Biophysics, Computer Science, and/or Biochemistry.
- Some computer programming experience preferred.
- Unafraid to talk to people outside your discipline about your research.
- Must commit to one year of research (undergraduate only).
PHY 320/620: Physics of Biological Macromolecules

• TuTh 9:30-10:45am

• Manchester 244

• Pre-/Co-requisites:
  – PHY 113/114

• Questions?
  Contact me: choss@wfu.edu

Alexander D. MacKerell, Jr.
University of Maryland, Baltimore School of Pharmacy
November 7, 2012

Charles Brooks, III
University of Michigan Departments of Chemistry and Biophysics
January 30, 2013