Monitoring and Control of Bio-Molecular Interactions

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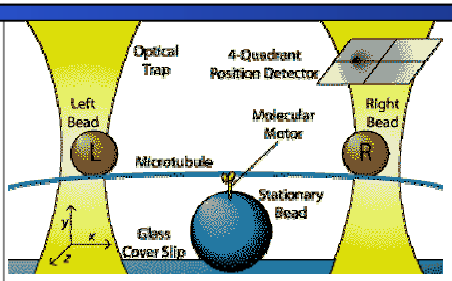
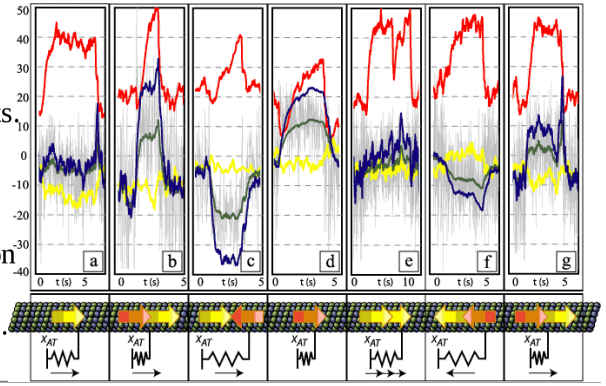
Goals and Potential Impact

Knowledge discovery and the development of nanoscale devices and processes requires the interaction between heterogeneous components of a system and with human operators. A key challenge is the real-time interpretation of measurements obtained from molecular and nanoscale systems. Offline interpretation prohibits automatic control as a function of random nanoscale events. Therefore, there is a need for real-time, customizable, model-based analysis of measurements on a biomolecular level, their automatic interpretation to detect nanoscale events, and automatic control of experimental conditions to achieve the problem-specific objectives.



Optical tweezers are used to bring microtubule and Ncd into close proximity. The bead position is measured using a 4-quadrant position detector. Motor attachments and strokes are inferred from position.

Results of filtering identification and classification of single molecular motor events. Some events were not previously observed. Real-time control of optical taps is needed for direct confirmation of findings. Note 0.1 signal-to-noise ratio of many events.



Approach and/or Accomplishments

-- Model-based, single-realization interpretation of biomolecular measurements.
-- Use of stochastic models with input, parametric and structural discontinuities.
-- We use meso-scale models, which combine the elements of continuums and discrete event models.
-- Automatic classification of molecular events is used to characterize molecular interactions.
-- Current application: Analysis and model-based interpretation of measurements obtained using optical traps to study the interactions between a single non-processive molecular motor (Ncd) and its complementary filament (microtubule).
-- This application indicates a clear need for feedback control to study biomolecular interactions on a single molecular level.

Bottlenecks and Open Research Questions

-- We need to learn how to model processes at the interface of continuum and countable processes.
-- The resulting models are likely to be continuous systems with discontinuities. Thus the need for non-smooth analysis and control methods.
-- New emphasis on control of stochastic systems (e.g. control on average) is needed.
-- Since interface between nano/micro- and macro-level will introduce interferences, it is desirable to process the measurements and generate controls at the source.
-- The networking and coordination between multiple nano/micro-devices is needed, which would allow us to instrument and actuate the environment, including that of the human body.
-- The research must be multidisciplinary with a strong emphasis on demonstrations.
-- High cost of equipment is a problem.