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Free Energy Landscape For Biological Systems
[Phys. Rev. Lett., 97, 018103 (2006)] using realistic values of all physical pa-
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A Brownian Dynamics model for describing the performance of
Massachusetts Institute of Technology, Cambridge, MA, USA.
Sheng Meng
Mechanism
Theoretical Models of Eumelanin Protomolecule and Its Photoprotection
Harvard University, Cambridge, MA, USA.
Sheng Meng, Efthimios Kaxiras.
Mechanism
The molecular structure of melanin, one of the most ubiquitous natural pig-
elaboratory behavior. We examine structural models for eumelanin protomolecules, based on
tetramers consisting of four monomer units (hydroquinone, indolequinone and
its two tautomers), in arrangements that contain an interior porphyrin ring.
These models reproduce convincingly many aspects of eumelanin’s experiment-
tally observed behavior. In particular, we present a plausible synthetic pathway
of the tetramers and their further complexation through interlayer stacking, or
through formation of helical superstructures, into eumelanin macromolecules.
The unstructured nature of C-C bonds in indolequinone units and the finite size of
protomolecules introduce covalent bond formation between stacked layers.
We employ Time-dependent Density Functional Theory to calculate the optical
absorption and the relaxation dynamics of melanin model constituents. The re-
sults explain the ability of these molecules to transform photon energy into
thermal energy in a remarkably short time scale of ~100 femtoseconds (fs).
We find that following electronic excitation by light absorption, ultrafast en-
ergy conversion takes place through two novel mechanisms: proton
transfer on a timescale of 10 fs and state mixing upon oligomerization on a
time scale of ~50 fs. These results are in good agreement with available ex-
periments and help elucidate melanin’s role in photoprotection during ultra-
velot radiation.
A Brownian Dynamics model of separation-by-partitioning in nanofluidic
devices
Ghassan N. Fayad, Nicolas G. Hadjiconstantinou.
Massachusetts Institute of Technology, Cambridge, MA, USA.
We present a Brownian Dynamics model for describing the performance of
nanofluidic devices used for biological molecule separation. Our present
work focuses on the process of separation of electric-field-driven DNA mole-
cules by partitioning, using periodic nanofilter arrays. Our results show that ex-
perimental results for molecules up to 20 persistence lengths can be modeled
using the worm-like-chain model, provided free draining behavior is appropri-
ately accounted for in the model.
In particular, our model is able to capture the experimental results of Fu et al.
[Phys. Rev. Lett., 97, 018103 (2006)] using realistic values of all physical pa-
rameters while being more efficient than explicit molecular dynamics methods.
Free Energy Landscape For Biological Systems
Hanbing Lin, Jian-min Yuan.
Drexel University, Philadelphia, PA, USA.
We have investigated methods of constructing free energy landscape of
a few biological systems. For simple enzyme kinetics reaction, using
a method developed by A0 and coworkers, we have constructed the energy
landscape around the stable fixed point. However the landscape resembles
that of a saddle point. The discrepancy may come from the slow convergent
property of the series used. We also tried solving the master equation for
equilibrium statistical distribution, and based on this distribution we can
construct the energy landscape which looks qualitatively correct. Following
the latter procedure and based on stochastic dynamics we can construct en-
ergy landscape of a minimal model for immune response which shows bist-
ability. Finally, a similar procedure is applied to construct the energy land-
scape for a minimal model of p53 oscillating loops which exhibits limit cycle behavior.
Primary Electronic Response In Biomolecules Exposed To X-ray Laser Radiation
Carl Burmeister, Helmut Grubmueller, Gerrit Groenhof.
MPI for Biophysical Chemistry, Goettingen, Germany.
The ultra intense femtosecond X-ray pulses from free electron lasers that are
being developed in Hamburg and Stanford hold the promise to obtain X-ray
scattering information from single molecules, even from proteins [1]. This
technique could enable monitoring ultrafast atomistic dynamics in proteins
and other biomolecules at the single molecule level. At such short wavelengths
the X-ray photons will eject electrons from the sample. This will lead to
a coulomb explosion of the nuclei. Thus it is crucial how much time-resolved
structural information can be expected from a single molecule diffraction
experiment. To address this question, we have begun to develop a method to
simulate the electronic response of biomolecular systems subject to electron
emission. Due to their strong binding to the nuclei, the inner shell electrons
show significantly larger X-ray cross section than the outer electrons, such
that the initial event will be the nearly instantaneous partial removal of the inner
shell. The resulting fast re-filling dynamics by electrons of the outer shells
will critically determine the atomic dynamics and the pace of the Coulomb ex-
losion.
In our simulations, a stochastic criterion is used to generate an initial open shell
system based on the cross sections. We use Hartree-Fock level of theory and
gaussian basis sets to treat the initial state. The expansion coefficients of the
basis functions are taken to be time-dependent. Thus the expansion coefficients
are propagated by the time-dependent Schroedinger equation. This time-depen-
dent approach is currently applied to a one dimensional model system. We plan
to apply it to real molecular systems. Our goal is to treat systems up to the size
of a peptide.
Revisiting Anomalous Diffusion Due To Molecular Crowding
Yoshisuka Kubota, Neal Waxham.
University of Texas Medical School, Houston, Houston, TX, USA.
Molecular diffusion is called anomalous when the mean-squared displacement
of a moving particle does not increase linearly with time. Several simulation
works demonstrated anomalous diffusion, as opposed to normal (i.e., Brown-
ian) diffusion, in crowded environments with fixed and/or mobile obstacles.
Experimental measurements often report a reduction of molecular diffusion
but not necessarily anomalous diffusion in the cytoplasm. Here we propose
two possible reasons for the discrepancy between simulations and experiments
on diffusion in crowded environments.
First, some of the previously developed algorithms might not accurately simu-
late three-body or higher order molecular collisions in the crowded environ-
ment. To this end, we have developed an event-driven, exact collision detection
algorithmic scheme and systematically studied the impact of crowding on mol-
ecular diffusion. When these higher-order collisions are explicitly taken into
account, the anomalous diffusion in 3D seen with the previously developed al-
gorithms becomes less prominent or disappears.
Second, experimental analyses that suggested anomalous diffusion might have
been problematic. This is particularly relevant to fluorescence correlation spec-
troscopy (FSC). Unlike single-particle tracking (SPT), FCS does not provide
direct information about trajectories of individual molecules. It relies on the
analysis of fluctuations in the number of fluorescent particles in a focused laser
spot. The diffusion of molecule is inferred from the shape of the autocorrelated
fluorescent signals fitted to a mathematical formula purportedly representing
anomalous diffusion. However, the latter formula was derived from a modified
diffusion equation, which may not have physical basis, thus leading to poten-
tially erroneous data analysis. We propose a new FCS autocorrelation formula
based on continuous time random walk theory and fractional diffusion
equation.
Finally, we use this new FCS formula and the novel event-driven algorithm to
simulate diffusion in crowded environments and discuss possible reconcili-
ation of discrepancies between previous simulations and experimental
data.