Content overview

I. Particle and continuum methods

1. Atoms, molecules, chemistry
2. Continuum modeling approaches and solution approaches
3. Statistical mechanics
4. Molecular dynamics, Monte Carlo
5. Visualization and data analysis
6. Mechanical properties – application: how things fail (and how to prevent it)
7. Multi-scale modeling paradigm
8. Biological systems (simulation in biophysics) – how proteins work and how to model them

Lectures 1-13

II. Quantum mechanical methods

1. It’s A Quantum World: The Theory of Quantum Mechanics
2. Quantum Mechanics: Practice Makes Perfect
3. The Many-Body Problem: From Many-Body to Single-Particle
4. Quantum modeling of materials
5. From Atoms to Solids
6. Basic properties of materials
7. Advanced properties of materials
8. What else can we do?

Lectures 14-26
Overview: Material covered so far…

- **Lecture 1:** Broad introduction to IM/S

- **Lecture 2:** Introduction to atomistic and continuum modeling *(multi-scale modeling paradigm, difference between continuum and atomistic approach, case study: diffusion)*

- **Lecture 3:** Basic statistical mechanics – property calculation I *(property calculation: microscopic states vs. macroscopic properties, ensembles, probability density and partition function)*

- **Lecture 4:** Property calculation II *(Monte Carlo, advanced property calculation, introduction to chemical interactions)*

- **Lecture 5:** How to model chemical interactions I *(example: movie of copper deformation/dislocations, etc.)*

- **Lecture 6:** How to model chemical interactions II *(EAM, a bit of ReaxFF—chemical reactions)*

- **Lecture 7:** Application to modeling brittle materials I

- **Lecture 8:** Application to modeling brittle materials II

- **Lecture 9:** Application – Applications to materials failure

- **Lecture 10:** Applications to biophysics and bionanomechanics
Lecture 10: Applications to biophysics and bionanomechanics

Outline:
1. Protein force fields
2. Single molecule mechanics
3. Fracture of protein domains – Bell model

Goal of today’s lecture:
- Force fields for organic materials, and specifically proteins
- Basic introduction into modeling of biological materials
- Fracture model for protein domains
1. Force fields for organic chemistry -
   how to model proteins
Significance of proteins

- Proteins are **basic building blocks of life**

- Define tissues, organs, cells

- Provide a **variety of functions and properties**, such as mechanical stability (strength), elasticity, catalytic activity (enzyme), electrochemical properties, optical properties, energy conversion

- Molecular simulation is an **important tool in the analysis of protein structures and protein materials**

**Goal here:** To train you in the fundamentals of modeling techniques for proteins, to enable you to carry out protein simulations

**Explain the significance of proteins (application)**
Human body: Composed of diverse array of protein materials

**Eye’s cornea**  
(collagen material)

**Skin**  
(complex composite of collagen, elastin)

**Cells**  
(complex material/system based on proteins)

**Muscle tissue**  
(motor proteins)

**Nerve cells**

**Blood vessels**

**Tendon**  
(links bone, muscles)

**Cartilage**  
(reduce friction in joints)

**Bone**  
(structural stability)

Image courtesy of NIH.


Image removed due to copyright restrictions.
Cellular structure: Protein networks

Cell nucleus

Actin network

Microtubulus (e.g. cargo)

Vimentin (extensible, flexible, provide strength)

= cytoskeleton

Image courtesy of NIH.
Protein structures define the cellular architecture

Intermediate filaments

Cell

Cytoskeleton

Full length filaments

Unit-length filaments (8 tetramers)

Tetramers (2 dimers)

Dimer (elementary building blocks)

>50 μm

>1 μm

>240 nm

~60 nm

~60 nm

~45 nm

Source: Fig. 2.17 in Buehler, Markus J. Atomistic Modeling of Materials Failure. Springer, 2008.

Image removed due to copyright restrictions; see image now: http://www.nanowerk.com/spotlight/id2878_1.jpg.
How protein materials are made – the genetic code

- Proteins: Encoded by DNA (three “letters”), utilize 20 basic building blocks (amino acids) to form polypeptides

- Polypeptides arrange in complex folded 3D structures with specific properties

1D structure transforms into complex 3D folded configuration

ACGT

Four letter code “DNA”

Combination of 3 DNA letters equals a amino acid

E.g.: Proline – CCT, CCC, CCA, CCG

Transcription/translation

Sequence of amino acids “polypeptide” (1D structure)

Folding (3D structure)
Chemical structure of peptides/proteins

Typically short sequence of amino acids

Longer sequence of amino acids, often complex 3D structure

Peptide bond

side chains

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R = side chain, one of the 20 natural amino acids

20 natural amino acids differ in their side chain chemistry
There are 20 natural amino acids

Difference in side chain, $R$

Forms peptide bond
Chemistry, structure and properties are linked

Presence of various chemical bonds:

- Covalent bonds (C-C, C-O, C-H, C-N..)
- Electrostatic interactions (charged amino acid side chains)
- H-bonds (e.g. between H and O)
- \( \text{vdW} \) interactions (uncharged parts of molecules)
Concept: split energy contributions

\[ U_{\text{total}} = U_{\text{Elec}} + U_{\text{Covalent}} + U_{\text{Metallic}} + U_{\text{vdW}} + U_{\text{H–bond}} \]

Covalent bond described as

1. Bond stretching part (energy penalty for bond stretching)
2. Bending part (energy penalty for bending three atoms)
3. Rotation part (energy penalty for bond rotation, \( N \geq 4 \))

Consider ethane molecule as “elastic structure”

\[ U_{\text{Covalent}} = U_{\text{stretch}} + U_{\text{bend}} + U_{\text{rotate}} \]
Force fields for organics: Basic approach

\[ U_{total} = U_{\text{Elec}} + U_{\text{Covalent}} + U_{\text{Metallic}} + U_{\text{vdW}} + U_{\text{H-bond}} \]

\[ U_{\text{Covalent}} = U_{\text{stretch}} + U_{\text{bend}} + U_{\text{rot}} \]

\[
\phi_{\text{stretch}} = \frac{1}{2} k_{\text{stretch}} (r - r_0)^2
\]

\[ U_{\text{stretch}} = \sum \phi_{\text{stretch}} \text{ pairs} \]

\[
\phi_{\text{bend}} = \frac{1}{2} k_{\text{bend}} (\theta - \theta_0)^2
\]

\[ U_{\text{bend}} = \sum \phi_{\text{bend}} \text{ triplets} \]

\[
\phi_{\text{rot}} = \frac{1}{2} k_{\text{rot}} (1 - \cos(\vartheta))
\]

\[ U_{\text{rot}} = \sum \phi_{\text{rot}} \text{ quadruplets} \]

=0 for proteins

Image by MIT OpenCourseWare.
Model for covalent bonds

\[ \phi_{\text{stretch}} = \frac{1}{2} k_{\text{stretch}} (r - r_0)^2 \]

\[ \phi_{\text{bend}} = \frac{1}{2} k_{\text{bend}} (\theta - \theta_0)^2 \]

\[ \phi_{\text{rot}} = \frac{1}{2} k_{\text{rot}} (1 - \cos(\vartheta)) \]

Courtesy of the EMBnet Education & Training Committee. Used with permission.

Images created for the CHARMM tutorial by Dr. Dmitry Kuznetsov (Swiss Institute of Bioinformatics) for the EMBnet Education & Training committee (http://www.embnet.org)

http://www.ch.embnet.org/MD_tutorial/pages/MD_Part2.html
Force fields for organics: Basic approach

\[ U_{total} = U_{\text{Elec}} + U_{\text{Covalent}} + U_{\text{Metallic}} + U_{\text{vdW}} + U_{\text{H\textendash}bond} \]

\[ \phi(r_{ij}) = \frac{q_i q_j}{\varepsilon_1 r_{ij}} \]

\[ F(r_{ij}) = -\frac{q_i q_j}{\varepsilon_1 r_{ij}^2} \]

\[ \varepsilon_1 = 4\pi\varepsilon_0 \quad \varepsilon_0 = 1.602 \times 10^{-19} \text{ C} \]
Force fields for organics: Basic approach

\[ U_{total} = U_{Elec} + U_{Covalent} + U_{Metallic} + U_{vdW} + U_{H-bond} \]

=0 for proteins

\[ U_{vdW} \]

\[ \phi(r_{ij}) = 4\varepsilon \left( \frac{\sigma}{r_{ij}} \right)^{12} - \left( \frac{\sigma}{r_{ij}} \right)^{6} \]

LJ potential is particularly good model for vdW interactions (Argon)
H-bond model

\[ U_{total} = U_{Elec} + U_{Covalent} + U_{Metallic} + U_{vdW} + U_{H\text{-bond}} \]

Evaluated between acceptor (A) /donor(D) pairs

Between electronegative atom and a H- atom that is bonded to another electronegative atom

Slightly modified LJ, different parameters

\[ U_{H\text{-bond}} : \phi(r_{ij}) = D_{H\text{-bond}} \left[ 5 \left( \frac{R_{H\text{-bond}}}{r_{ij}} \right)^{12} - 6 \left( \frac{R_{H\text{-bond}}}{r_{ij}} \right)^{10} \right] \cos^4(\theta_{DHA}) \]

\( r_{ij} \) = distance between D-A
Summary

\[ U_{total} = U_{Elec} + U_{Covalent} + U_{Metallic} + U_{vdW} + U_{H-bond} \]

\[ U_{Elec} : \text{Coulomb potential} \quad \phi(r_{ij}) = \frac{q_i q_j}{\epsilon_1 r_{ij}} \]

\[ U_{Covalent} = U_{stretch} + U_{bend} + U_{rot} \]

\[ \begin{align*}
\phi_{stretch} &= \frac{1}{2} k_{stretch} (r - r_0)^2 \\
\phi_{bend} &= \frac{1}{2} k_{bend} (\theta - \theta_0)^2 \\
\phi_{rot} &= \frac{1}{2} k_{rot} (1 - \cos(\vartheta))
\end{align*} \]

\[ U_{vdW} : \text{LJ potential} \quad \phi(r_{ij}) = 4 \epsilon \left[ \left( \frac{\sigma}{r_{ij}} \right)^{12} - \left( \frac{\sigma}{r_{ij}} \right)^6 \right] \]

\[ U_{H-bond} : \quad \phi(r_{ij}) = D_{H-bond} \left[ 5 \left( \frac{R_{H-bond}}{r_{ij}} \right)^{12} - 6 \left( \frac{R_{H-bond}}{r_{ij}} \right)^{10} \right] \cos^4 (\theta_{DHA}) \]

=0 for proteins
The need for atom typing

- **Limited transferability** of potential expressions: Must use different potential for different chemistry

- Different chemistry is captured in different “tags” for atoms: **Element type** is expanded by **additional information** on particular chemical state

- Tags specify if a C-atom is in **sp³**, **sp²**, **sp** or in aromatic state (that is, to capture resonance effects)

- **Example atom tags**: CA, C_1, C_2, C_3, C…, HN, HO, HC, …
Atom typing in CHARMM

Example of the RTF for the Alanine residue:

RESI ALA0.00
GROUP
ATOM NNH1 -0.47 ! |
ATOM HNH  0.31 ! HN-N
ATOM CACT1 0.07 ! | HB1
ATOM HAHB  0.09 ! |   /
GROUP
    !HA--CA--CB-HB2
ATOM CBCT3 -0.27 ! |   \ 
ATOM HB1HA  0.09 ! |   HB3
ATOM HB2HA  0.09 !  O=C
ATOM HB3HA  0.09 !   |
GROUP
ATOM CC  0.51
ATOM OO-0.51
BONDCB CA N HN N CA
BOND C CA C +N CA HA CB HB1 CB HB2 CB HB3
DOUBLET O C
IMPR N -C CA HN C CA +N O
DONOR HN N
ACCEPTOR O C
IC -C CA *N HN  1.3551 126.4900 180.0000 115.4200 0.9996
IC -C N CA C   1.3551 126.4900 180.0000 114.4400 1.5390
IC N CA C +N   1.4592 114.4400 180.0000 116.8400 1.3558
IC +N CA *C O  1.3558 116.8400 180.0000 122.5200 1.2297
IC CA C +N +CA 1.5390 116.8400 180.0000 126.7700 1.4613
IC N C *CA CB   1.4592 114.4400 123.2300 111.0900 1.5461
IC N C *CA HA   1.4592 114.4400 -120.4500 106.3900 1.0840
IC C CA CB HB1  1.5390 111.0900 177.2500 109.6000 1.1109
IC HB1 CA *CB HB2 1.1109 109.6000 119.1300 111.0500 1.1119
IC HB1 CA *CB HB3 1.1109 109.6000 -119.5800 111.6100 1.1114
VMD analysis of protein structure
Common empirical force fields for organics and proteins

Class I (experiment derived, simple form)
- CHARMM
- CHARMm (Accelrys)
- AMBER
- OPLS/AMBER/Schrödinger
- ECEPP (free energy force field)
- GROMOS

Class II (more complex, derived from QM)
- CFF95 (Biosym/Accelrys)
- MM3
- MMFF94 (CHARMM, Macromodel…)
- UFF, DREIDING

Harmonic terms;
Derived from vibrational spectroscopy, gas-phase molecular structures
Very system-specific

Include anharmonic terms
Derived from QM, more general

http://www.ch.embnet.org/MD_tutorial/pages/MD.Part2.html
CHARMM force field

- Widely used and accepted model for protein structures

- Programs such as NAMD have implemented the CHARMM force field

Problem set #3, nanoHUB stretchmol module, study of a protein domain that is part of human vimentin intermediate filaments
Application – protein folding

Combination of 3 DNA letters equals a amino acid

*E.g.*: Proline – CCT, CCC, CCA, CCG

Sequence of amino acids “polypeptide” (1D structure)

.. - Proline - Serine – Proline - Alanine - ..

Folding (3D structure)

Goal of protein folding simulations:
Predict folded 3D structure based on polypeptide sequence
Movie: protein folding with CHARMM

- *de novo* Folding of a *Transmembrane fd Coat Protein*
  

*Polypeptide chain*

Images removed due to copyright restrictions.

Screenshots from protein folding video, which can be found here: [http://www.charmm-gui.org/?doc=gallery&id=23](http://www.charmm-gui.org/?doc=gallery&id=23).

**Quality of predicted structures quite good**

Confirmed by comparison of the MSD deviations of a room temperature ensemble of conformations from the replica-exchange simulations and **experimental structures** from both solid-state NMR in lipid bilayers and solution-phase NMR on the protein in micelles)
Movies in equilibrium (temperature 300 K)

Dimer

Tetramer
(increased effective bending stiffness, interaction via overlap & head/tail domain)

2. Single molecule mechanics

*Structure and mechanics of protein, DNA, etc. molecules*
Cooking spaghetti

stiff rods  cooking  soft, flexible rods
(like many protein molecules)
Single molecule tensile test – “optical tweezer”

Example 1: Elasticity of tropocollagen molecules

Entropic elasticity leads to strongly nonlinear elasticity

The force-extension curve for stretching a single type II collagen molecule. The data were fitted to Marko-Siggia entropic elasticity model. The molecule length and persistence length of this sample is 300 and 7.6 nm, respectively.

Image by MIT OpenCourseWare.

Example 2: Single protein molecule mechanics

Optical tweezers experiment

Protein structure (I27 multidomain titin in muscle)


http://www.nature.com/nature/journal/v387/n6630/pdf/387308a0.pdf
http://www.nature.com/nature/journal/v402/n6757/pdf/402100a0.pdf
Example 3: Single DNA molecule mechanics

Plots of stretching force against relative extension of the single DNA molecule (experimental results)

Plateau regime (breaking of bonds)

Structural makeup of protein materials

Although very diverse, all protein materials have universal “protocols” of how they are made
How protein materials are made—the genetic code

- Proteins: Encoded by DNA (three “letters”), utilize 20 basic building blocks (amino acids) to form polypeptides

- Polypeptides arrange in complex folded 3D structures with specific properties

1D structure transforms into complex 3D folded configuration

**Combination of 3 DNA letters (=codon) defines one amino acid**

*E.g.: Proline – CCT, CCC, CCA, or CCG*

**Sequence of amino acids “polypeptide” (1D structure)***

**Folding (3D structure)**
Concept: hydrogen bonding (H-bonding)
e.g. between O and H in H₂O
Between N and O in proteins
Drives formation of helical structures

AHs found in: hair, cells, wool, skin, etc.

Source: Qin, Z., L. Kreplak, and M. Buehler.
“Hierarchical structure controls
nanomechanical properties of vimentin
License CC BY.
Primary, secondary, tertiary structure

Beta-sheets (abbreviated as BS)

Beta-sheet

Found in many mechanically relevant proteins

Spider silk
Fibronectin
Titin (muscle tissue)
Amyloids (Alzheimer’s disease)

Images removed due to copyright restrictions.
Amyloid proteins (Alzheimer’s disease)

Please see Fig. 8 from http://web.mit.edu/mbuehler/www/papers/final_JCTN_preprint.pdf.
3. Fracture of protein domains – Bell model
How to apply load to a molecule

(in molecular dynamics simulations)
Steered molecular dynamics (SMD)

Steered molecular dynamics used to apply forces to protein structures

Virtual atom moves w/ velocity $\vec{v}$

end point of molecule
Steered molecular dynamics (SMD)

Steered molecular dynamics used to apply forces to protein structures

\[ f = k(v \cdot t - x) \]
\[ \vec{f} = k(\vec{v} \cdot t - \vec{x}) \]

SMD spring constant

Virtual atom moves with velocity \( \vec{v} \)

Distance between end point of molecule and virtual atom

end point of molecule

SMD deformation speed vector

time
SMD mimics AFM single molecule experiments

Atomic force microscope
SMD is a useful approach to probe the nanomechanics of proteins (elastic deformation, “plastic” – permanent deformation, etc.)

Example: titin unfolding (CHARMM force field)
Unfolding of titin molecule

Titin I27 domain: Very resistant to unfolding due to parallel H-bonded strands

Keten and Buehler, 2007
Protein unfolding - ReaxFF

AHs

F

PnIB 1AKG

Breaking C-S

Breaking S-S

Breaking C-C

ReaxFF modeling

Protein unfolding - CHARMM

Covalent bonds don’t break

CHARMM modeling

Comparison – CHARMM vs. ReaxFF

Application to alpha-helical proteins
Vimentin intermediate filaments

Vimentin intermediate filament

Intermediate filaments – occurrence

- Neuron cells (brain)
  - Image of neuron and cell nucleus © sources unknown. All rights reserved. This content is excluded from our Creative Commons license. For more information, see http://ocw.mit.edu/fairuse.

- Hair, hoof

- Fibroblast cells (make collagen)

- Cell nucleus
Alpha-helical protein: stretching

A: First H-bonds break (turns open)
B: Stretch covalent backbone
C: Backbone breaks

ReaxFF modeling of AH stretching

M. Buehler, JoMMS, 2007
What about varying pulling speeds?
Variation of pulling speed

Image by MIT OpenCourseWare. After Ackbarow and Buehler, 2007.
Force at angular point \( f_{AP} \) = fracture force

\[ f_{AP} \sim \ln \nu \]

See also Ackbarow and Buehler, *J. Mat. Sci.*, 2007
General results…
Rupture force vs. pulling speed

$ f_{AP} $
How to make sense of these results?
A few fundamental properties of bonds

- Bonds have a “bond energy” (energy barrier to break)

- **Arrhenius relationship** gives probability for energy barrier to be overcome, given a temperature

\[ p = \exp \left( -\frac{E_b}{k_B T} \right) \]

- All bonds **vibrate at frequency** \( \omega \)
Bell model

Probability for bond rupture (Arrhenius relation)

\[ p = \exp \left( -\frac{E_b}{k_B T} \right) \]

Boltzmann constant \( k_B \)
temperature

“bond”

distance to energy barrier \( x_b \)

height of energy barrier \( E_b \)
Bell model

Probability for bond rupture (Arrhenius relation) \( f = f_{AP} \)

\[
p = \exp\left( - \frac{E_b - f \cdot x_B}{k_B T} \right)
\]

- Boltzmann constant
- Temperature
- "bond"
- Force applied (lower energy barrier)
- Distance to energy barrier
- Height of energy barrier
Bell model

Probability for bond rupture (Arrhenius relation)

\[ p = \exp \left( -\frac{E_b - f \cdot x_B}{k_B T} \right) \]

Off-rate = probability times vibrational frequency

\[ \chi = \omega_0 \cdot p \]

\[ \omega_0 = 1 \times 10^{13} \text{ 1/sec} \]

bond vibrations
Bell model

Probability for bond rupture (Arrhenius relation)

\[ p = \exp \left( -\frac{E_b - f \cdot x_B}{k_B T} \right) \]

Off-rate = probability times vibrational frequency

\[ \chi = \omega_0 \cdot p = \omega_0 \cdot \exp \left( -\frac{(E_b - f \cdot x_b)}{k_b \cdot T} \right) \]

“How often bond breaks per unit time”

\[ \omega_0 = 1 \times 10^{13} \text{ 1/ sec} \]
Bell model

Probability for bond rupture (Arrhenius relation)

\[ p = \exp \left( - \frac{E_b - f \cdot x_B}{k_B T} \right) \]

Off-rate = probability times vibrational frequency

\[ \chi = \omega_0 \cdot p = \omega_0 \cdot \exp \left( - \frac{(E_b - f \cdot x_b)}{k_b \cdot T} \right) = \frac{1}{\tau} \]

\[ \omega_0 = 1 \times 10^{13} \text{ 1/sec} \]

\[ \tau = \text{bond lifetime (inverse of off-rate)} \]
Bell model

\[ \frac{\Delta x}{\Delta t} = v \] pulling speed (at end of molecule)
Bell model

\[ \Delta x / \Delta t = v \]

pulling speed (at end of molecule)
Structure-energy landscape link

\[ \Delta x = x_b \]
\[ \Delta t = \tau \quad \tau = \left[ \omega_0 \cdot \exp \left( - \frac{(E_b - f \cdot x_b)}{k_b \cdot T} \right) \right]^{-1} \]
Bell model

Bond breaking at $x_b$ (lateral applied displacement):

$$\chi \cdot x_b = \omega_0 \cdot \exp\left(-\frac{(E_b - f \cdot x_b)}{k_b \cdot T}\right) \cdot x_b = \Delta x / \Delta t = v$$

$= 1 / \tau$

pulling speed
Bell model

\[ \omega_0 \cdot \exp \left( - \frac{(E_b - f \cdot x_b)}{k_b \cdot T} \right) \cdot x_b = v \]

Solve this expression for \( f \):
Bell model

\[ \omega_0 \cdot \exp \left( - \frac{(E_b - f \cdot x_b)}{k_b \cdot T} \right) \cdot x_b = \nu \]

Solve this expression for \( f \):

\[
- \frac{(E_b - f \cdot x_b)}{k_b \cdot T} + \ln(\omega_0 \cdot x_b) = \ln \nu \quad \leftarrow \ln(\cdot) \\
- E_b + f \cdot x_b = k_b \cdot T(\ln \nu - \ln(\omega_0 \cdot x_b))
\]

\[
f = \frac{E_b + k_b \cdot T(\ln \nu - \ln(\omega_0 \cdot x_b))}{x_b} = \frac{k_b \cdot T}{x_b} \ln \nu + \frac{k_b \cdot T}{x_b} \left( \frac{E_b}{k_b \cdot T} - \ln(\omega_0 \cdot x_b) \right)
\]

\[
f = \frac{k_b \cdot T}{x_b} \ln \nu - \frac{k_b \cdot T}{x_b} \left( \ln(\omega_0 \cdot x_b) - \frac{E_b}{k_b \cdot T} \right)
\]

\[
f = \frac{k_b \cdot T}{x_b} \ln \nu - \frac{k_b \cdot T}{x_b} \ln \left( \omega_0 \cdot x_b \cdot \exp \left( - \frac{E_b}{k_b \cdot T} \right) \right)
\]
Simplification and grouping of variables

\[ f(v; x_b, E_b) = \frac{k_b \cdot T}{x_b} \cdot \ln v - \frac{k_b \cdot T}{x_b} \cdot \ln \left( \omega_0 \cdot x_b \cdot \exp\left( - \frac{E_b}{k_b \cdot T} \right) \right) \]

\[ = v_0 = \omega_0 \cdot x_b \cdot \exp\left( - \frac{E_b}{k_b \cdot T} \right) \]

Only system parameters, [distance/length]
Bell model

\[ \omega_0 \cdot \exp \left( - \frac{(E_b - f \cdot x_b)}{k_b \cdot T} \right) \cdot x_b = v \]

Results in:

\[ f(v; x_b, E_b) = \frac{k_b \cdot T}{x_b} \cdot \ln v - \frac{k_b \cdot T}{x_b} \cdot \ln v_0 = a \cdot \ln v + b \]

\[ a = \frac{k_B \cdot T}{x_b} \]

\[ b = -\frac{k_B \cdot T}{x_b} \cdot \ln v_0 \]
$f \sim \ln \nu$ behavior of strength

$$f(\nu; x_b, E_b) = a \cdot \ln \nu + b$$

$E_b = 5.6 \text{ kcal/mol}$ and $x_b = 0.17 \text{ Å}$ (results obtained from fitting to the simulation data)
Scaling with $E_b$: shifts curve

\[ f(v; x_b, E_b) = a \cdot \ln v + b \]

\[ a = \frac{k_B \cdot T}{x_b} \quad b = -\frac{k_B \cdot T}{x_b} \cdot \ln \nu_0 \quad \nu_0 = \omega_0 \cdot x_b \cdot \exp \left( -\frac{E_b}{k_B \cdot T} \right) \]
Scaling with $x_b$: changes slope

\[ f(v; x_b, E_b) = a \cdot \ln v + b \]

\[
\begin{align*}
a &= \frac{k_B \cdot T}{x_b} \\
b &= -\frac{k_B \cdot T}{x_b} \cdot \ln v_0 \\
v_0 &= \omega_0 \cdot x_b \cdot \exp\left( -\frac{E_b}{k_b \cdot T} \right)
\end{align*}
\]
Simulation results


Bertaud, Hester, Jimenez, and Buehler, J. Phys. Cond. Matt., 2010
Mechanisms associated with protein fracture
Change in fracture mechanism

FDM: Sequential HB breaking

SDM: Concurrent HB breaking (3..5 HBs)

Simulation span: 250 ns
Reaches deformation speed O(cm/sec)

Analysis of energy landscape parameters

Table 1. Summary of the differences between the SDM and FDM, for AH1, AH2, and BS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SDM</th>
<th>FDM</th>
<th>SDM</th>
<th>FDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulling speed, m/s</td>
<td>$v &lt; 0.4$ (4)</td>
<td>$v &gt; 0.4$ (4)</td>
<td>$v &lt; 10$</td>
<td>$v &gt; 10$</td>
</tr>
<tr>
<td>Unfolding force, pN</td>
<td>$F &lt; 350$ (400)</td>
<td>$F &gt; 350$ (400)</td>
<td>$F &lt; 4,800$</td>
<td>$F &gt; 4,800$</td>
</tr>
<tr>
<td>$E_b$, kcal/mol</td>
<td>11.1 (9.11)</td>
<td>4.87 (3.08)</td>
<td>11.08</td>
<td>1.82</td>
</tr>
<tr>
<td>$x_b$, Å</td>
<td>1.2 (1.19)</td>
<td>0.2 (0.11)</td>
<td>0.138</td>
<td>0.019</td>
</tr>
<tr>
<td>HB-breaking mechanism</td>
<td>Simultaneous</td>
<td>Sequential</td>
<td>Simultaneous</td>
<td>Sequential</td>
</tr>
</tbody>
</table>

The values in parentheses in the AH columns represent the results for AH2.

Energy single H-bond: $\approx$3-4 kcal/mol

What does this mean???
H-bond rupture dynamics: mechanism

H-bond rupture dynamics: mechanism

I: All HBs are intact
II: Rupture of 3 HBs – simultaneously; within $\tau \approx 20$ ps
III: Rest of the AH relaxes – slower deformation…
