Welcome and introduction to GEM4

- International, interdisciplinary, inter-institutional initiative started early 2006
- MIT, NSU, Harvard, Institut Pasteur
- Engineering, biology, medicine & public health intersected
- Paradigm for global cooperation through research, training & translation
- Networking opportunities
- Infrastructure capabilities

- Training program: Summer school (2007 in Singapore, focus on cancer)*
- Also offered by GEM4: Distinguished lecture series
- Junior scientist program

*With the newly announced SMART: Singapore-MIT Alliance for Research and Technology Center in Singapore

GEM4 co-sponsors the next worldwide meeting on biomechanics in 2010.

- Cell and molecular mechanics in biomedicine, with a focus on infectious diseases.
- From a course developed at MIT by Prof. Patrick Doyle, Allan Grodzinsky & R. Kamm.
- Lab info: http://www.opennetware.org/wiki/GEM4 Labs
- Breakdown of participants: 30% life scientists, 70% engineers
- Poster sessions to share research knowledge.
- Research proposals to be developed during the summer schools, presented in 3-4 pages.
- Direct questions to Maggie Sullivan or Roger Kamm: msullmag@mit.edu

Simple statistical mechanics for biological systems

- Questions: What is the goal?
- Starting with the central dogma in biology: DNA → RNA → protein → organelles
  (Crick)
- Ecosystem → organism → tissue → cell →
  (and feedback!), essentially increasing length scale
Hence, length and time scales and "out of equilibrium" principles matter.

**Length scales:**

- \( \phi \text{ DNA} \)
- \( \text{cell size} \)
- \( \text{DNA length} \)

**Time scales:**

- Chemical reaction
- Action potential of E. Coli
- Cell mobility

**Energy scales:**

- Thermal energy used as a rule: \( E / \text{mole} / ^\circ K \sim RT \) (of ideal gas) \( = \frac{1}{2} RT \) per degree of freedom (3 d.o.f. for ideal gas)

- Energy / molecule (and per degree of freedom) \( \sim RT / \text{mol} = k_B T \)

- Avogadro's number \( \text{mol} \sim 6 \times 10^{23} \) and Boltzmann's constant \( k_B = 1.38 \times 10^{-23} \text{J/molecule} / ^\circ K \)

- Force scale of \( \text{pN} \) and length scale of \( \text{nm} \). (spice Newtons, nanometers)

**Coupled interactions:**

- Chemical (physical)
- Electrical
- Mechanical

**Grand goal is to understand how these interact (are organized) in space and time.**
Energy scales:

\[
\begin{align*}
\text{RT} & \quad 10^1 \\
\text{ATP hydrolysis} & \quad 10^3 \\
\text{photosynthesis (green light)} & \quad 10^5 \\
\text{glucose oxidation} & \quad 10^9 \\
\end{align*}
\]

Over the past decade, much progress has been made experimentally and technically.

Down on small scales, biology is geometrically dominated by filaments and membranes which is connected with chemical molecular which makes for physical complexity (nonlinearity).

Outline:

- random walks & diffusion
- drag, mobility, Boltzmann's law, Stokes-Einstein
- biological forces & energies
- physics, mechanics and mechano-chemistry of polymers and membranes


...a bacteria tumble randomly in a homogeneous environment, then more directedly in the presence of a chemotactant (response to a stimulus); when the chemotactant diffuses away, randomness reappears (adaptation).

Sensing and movement are coupled:

- in the absence of any active processes, what happens to a bolus of chemotactant?

Carnot, Helmholtz, Boltzmann, Gibbs: maximize the disorder, statistical probability

random walks (in 1-D) and diffusion

microscopic macroscopic

\[t = 0 \quad t \to \infty\]
• from kinetic energy: 
\[ \frac{1}{2} k_B T = \frac{1}{2} m \langle v^2 \rangle \]
\[ \langle v^2 \rangle = k_B T / m \]
mean squared velocity

for a lysozyme \( m \sim 14 \) kg / mole and \( 6 \times 10^{23} \) molecules / mole
\[ \sqrt{\langle v^2 \rangle} \sim 14 \text{ m/s very high!} \]

but collisions and dissipation \( \Rightarrow \) no net motion of the lysozyme velocity \( v \), step size \( \delta = \pm v \tau \) with \( \tau \): time between collisions.

\[ -2\delta - \delta \quad 0 \quad +\delta \quad 2\delta \]

1. probability of going in either direction \( p = 1 / 2 \)
2. each step independent of others

• with \( N \) particles at origin at \( t = 0 \)
\[ x_i(n) = x_i(n-1) \pm \delta \]
\( \{ i: \text{particle label} \} \)
\( \{ n: \text{number of steps} = t / \tau \} \)

\[ \langle x(n) \rangle = \frac{1}{N} \sum_{i=1}^{N} x_i(n) = \langle x_i(n-1) \rangle = \ldots = \langle x_i(0) \rangle = 0 \]

\[ \langle x(n) \rangle = 0 \]
mean location of particles

• spread of distribution: variance
\[ x_i^2(n) = x_i^2(n-1) + \delta^2 + 2 \delta x_i(n-1) \]
\[ \langle x_i^2(n) \rangle = \langle x_i^2(n-1) \rangle + \delta^2 = n \delta^2 \]
\[ \langle x^2(t / \tau) \rangle = \frac{1}{2} \cdot 2 \delta^2 / \tau \cdot t = 2 \delta^2 t \]
with \( \delta = \frac{1}{2} \frac{\delta^2}{\tau} \)

mean square proportional to time

\[ \sqrt{\langle x^2(t / \tau) \rangle} \propto t^{1/2} \quad \text{slow (diffusion)} \]

\( \delta \sim \sqrt{\langle v^2 \rangle} \) \( \delta \sim 10 \text{ m/s} \)
\[ 10^{-10} \text{ m} \sim 10^{-9} \text{ m}^2 / \text{s} \text{ or } 10^{-5} \text{ cm}^2 / \text{s} \]

\( \tau \mid 10^{-4} \text{ cm} \sim 1 \mu \text{m} \sim (10^{-6} \text{ m}) \div (10^{-9} \text{ m}^2 / \text{s}) \sim 10^{-3} \text{ s} \)
quick on small scale

\( t \mid 1 \mu \text{m} \sim 10^4 \text{ s} \text{ or } 10 \text{ hours} \)
slow on large scale
Newton's law \( \mathbf{F} = m \frac{d\mathbf{v}}{dt} \) was noted to be the most important human discovery. It is at the core of biology (force & velocity related).

A major part of mechanics today is to understand and measure forces.

**Forces**

What should the mass \( m \) be in biology? Neighboring cells influence one cell by interaction between discrete identifiable objects.

A more general definition of force/interaction is needed in biology.

**Stress**

\[
\begin{align*}
\Delta S & \quad \text{Surface area} \\
\mathbf{v} & \quad \text{outer normal} \\
\Delta T & \quad \text{force exerted}
\end{align*}
\]

\[
\lim_{\Delta S \to 0} \frac{\Delta T}{\Delta S} = \mathbf{v}^T
\]

and with \( \mathbf{v}^T \parallel x_1 \) axis :

\[
\mathbf{v}^T_{(1)} = \begin{pmatrix}
\tau_1 \\
\tau_{12} \\
\tau_{13}
\end{pmatrix}
\]

**Stress tensor**

\[
\begin{pmatrix}
\tau_{11} & \tau_{12} & \tau_{13} \\
\tau_{12} & \tau_{22} & \tau_{23} \\
\tau_{13} & \tau_{23} & \tau_{33}
\end{pmatrix}
\]

**Stress per unit area**

\[
\tau_n \tau_{22} \tau_{33} \quad \text{normal stress}
\]

\[
\tau_{12} \tau_{13} \tau_{21} \quad \text{shear stress}
\]

**Pressure**

\[
\text{Pressure} = -\frac{1}{3} (\tau_{11} + \tau_{22} + \tau_{33})
\]

...from outer world onto cubic element

**Principal stress**

Starting with an analogy with vectors, coordinates depend on set of axes. In principle coordinates system (one and only one exists):

\[
\begin{pmatrix}
\tau_1 \\
0 \\
0
\end{pmatrix}
\]

**Stress deviators**

The solutions to certain problems are independent of normal stresses.

\[
\begin{align*}
\delta_{ij} &= 0 \quad \text{if } i \neq j \\
n & \quad \text{and } 1 \quad \text{if } i = j
\end{align*}
\]

\[
\begin{align*}
\tau_{ij}' &= \tau_{ij} - \frac{1}{3} (\tau_{11} + \tau_{22} + \tau_{33}) \delta_{ij} \\
\end{align*}
\]

**Mean normal stress**
Residual stress

Deformation strain strain rate

Displacement $u^i = \xi^i - \alpha^i$

in 1-D motion

Deformation gradients $
\frac{\partial x}{\partial x'}$

$E_{12} \approx \tan \alpha$

Reference states in biology are debatable, difficult to define (because deformable materials)

In a fluid, what quantity is proportional to the applied stress? strain rate