20.GEM GEM4 Summer School: Cell and Molecular Biomechanics in Medicine: Cancer
Summer 2007

Space, Time and Energy Landscapes related to Life

Ju Li

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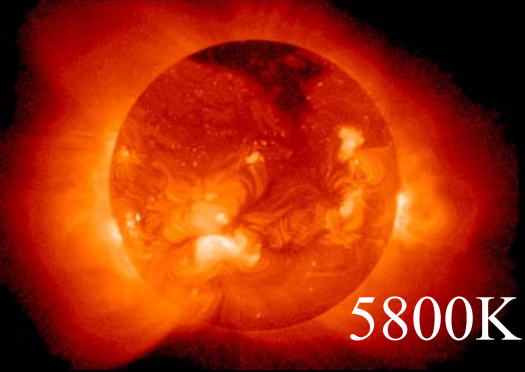
GLOBAL ENTERPRISE FOR MICRO-MECHANICS AND MOLECULAR MEDICINE

2nd GEM^4 Summer School
Cell and Molecular Mechanics in BioMedicine
with a focus on Cancer
June 25– July 6, 2007
National University of Singapore

Outline

- Earth as Heat Engine, Life as Information
- Energy Scales
- Spatial Pattern of Electrostatic Energy
- Spatial-Temporal Characteristics of Bending
- Rare Events and Timescale



Cosmic radiation
background: 2.7K

high-quality
energy in

low-quality
energy out

Images courtesy of NASA.

Carnot ideal
heat engine efficiency:
$(T_1-T_2)/T_1$

In terms of quantity: $E_{\text{in}} \approx E_{\text{out}}$
But in terms of quality or free energy,
earth enjoys (spends) huge drop

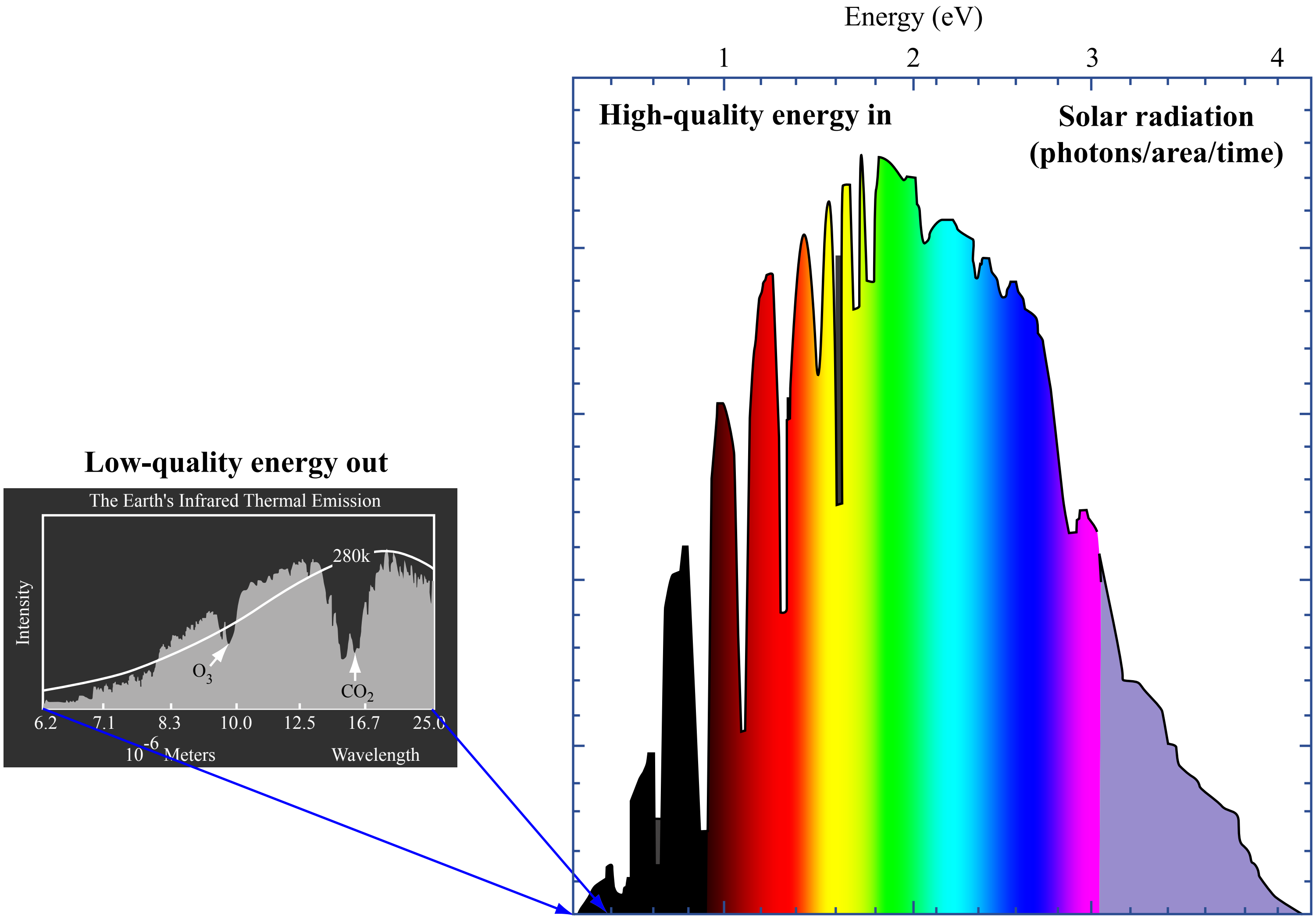
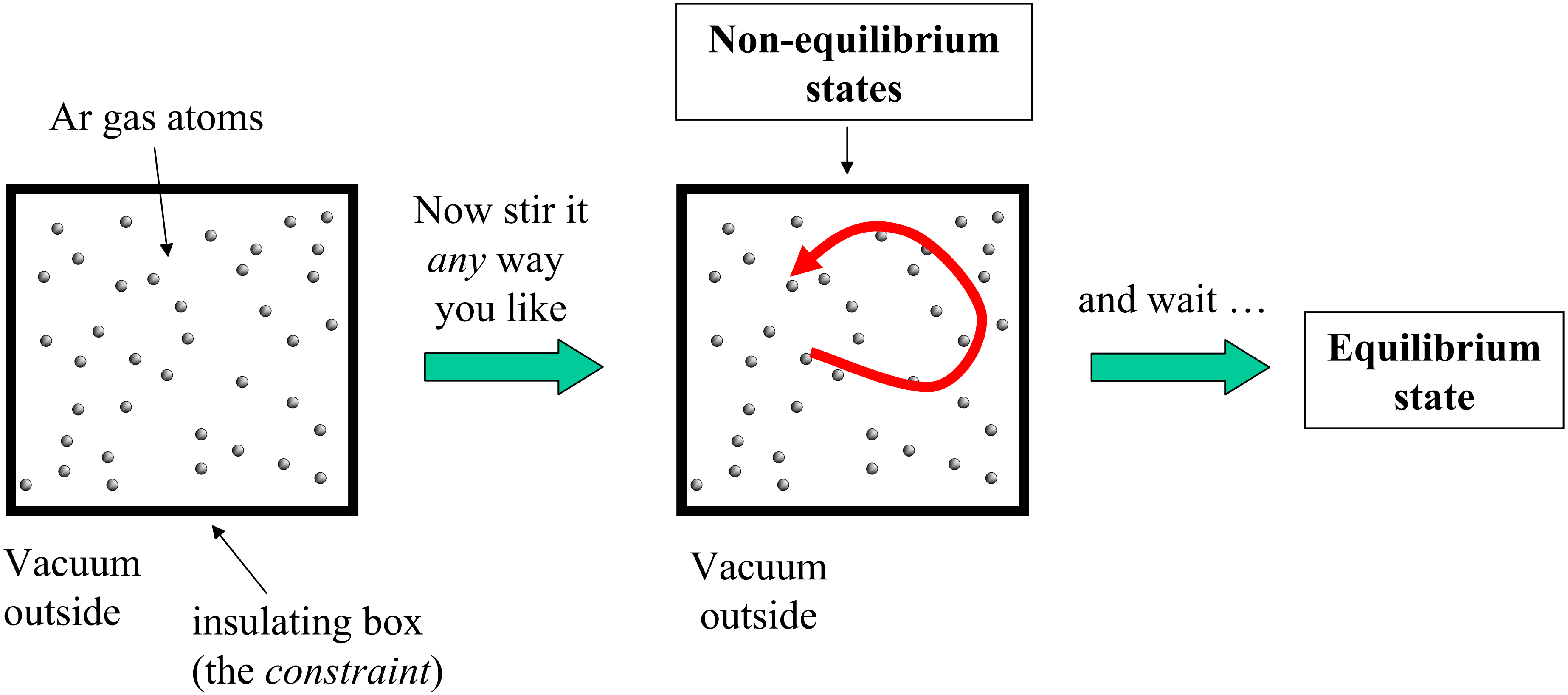


Figure by MIT OpenCourseWare.

Do Thermodynamics Govern Life?

Equilibrium: given the constraints, the macro-condition of system that is approached after sufficiently long time



Ar gas atoms

Now stir it *any* way you like

Non-equilibrium states

and wait …

Equilibrium state

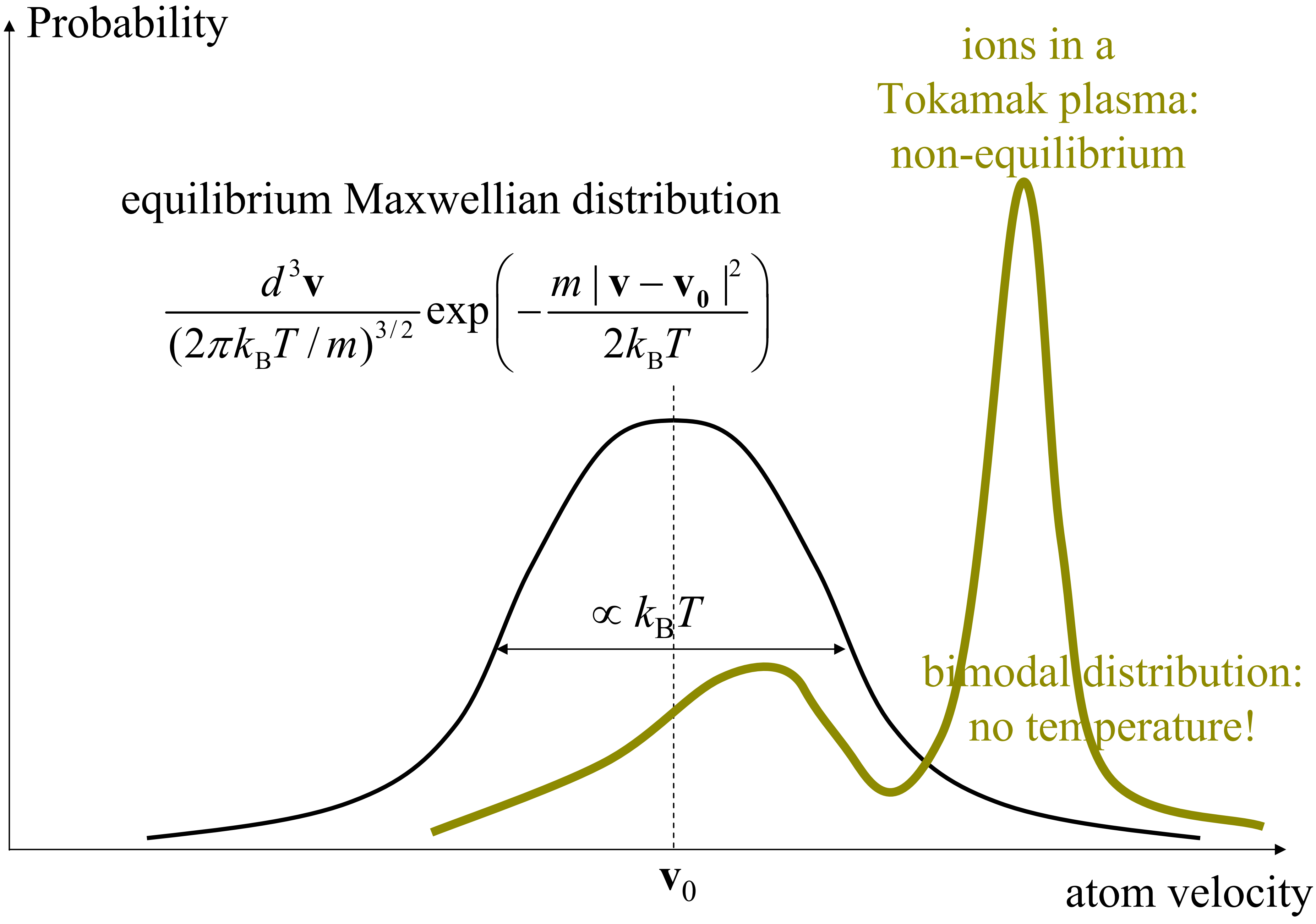
Vacuum outside

insulating box (the *constraint*)

Vacuum outside

Equilibrium system → T, S

Non-equilibrium system: no T, S



equilibrium Maxwellian distribution

$$\frac{d^3\mathbf{v}}{(2\pi k_\mathrm{B}T/m)^{3/2}}\exp\left(-\frac{m\,|\,\mathbf{v}-\mathbf{v_0}\,|^2}{2k_\mathrm{B}T}\right)$$

ions in a
Tokamak plasma:
non-equilibrium

bimodal distribution:
no temperature!

equilibrium is however yet
a bit more subtle:

It is possible to reach
equilibrium among a subset
of the degrees of freedom
(all atoms in a shot) or
subsystem, while this subsystem
is not in equilibrium with
the rest of the system.

This is why engineering &
material thermodynamics
is useful for cars and airplanes.

Image removed due to copyright restrictions.
Photograph of athlete catching a ball.

thermodynamics could apply to individual components, but not the entire machine.

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Simple schematic of an automobile.

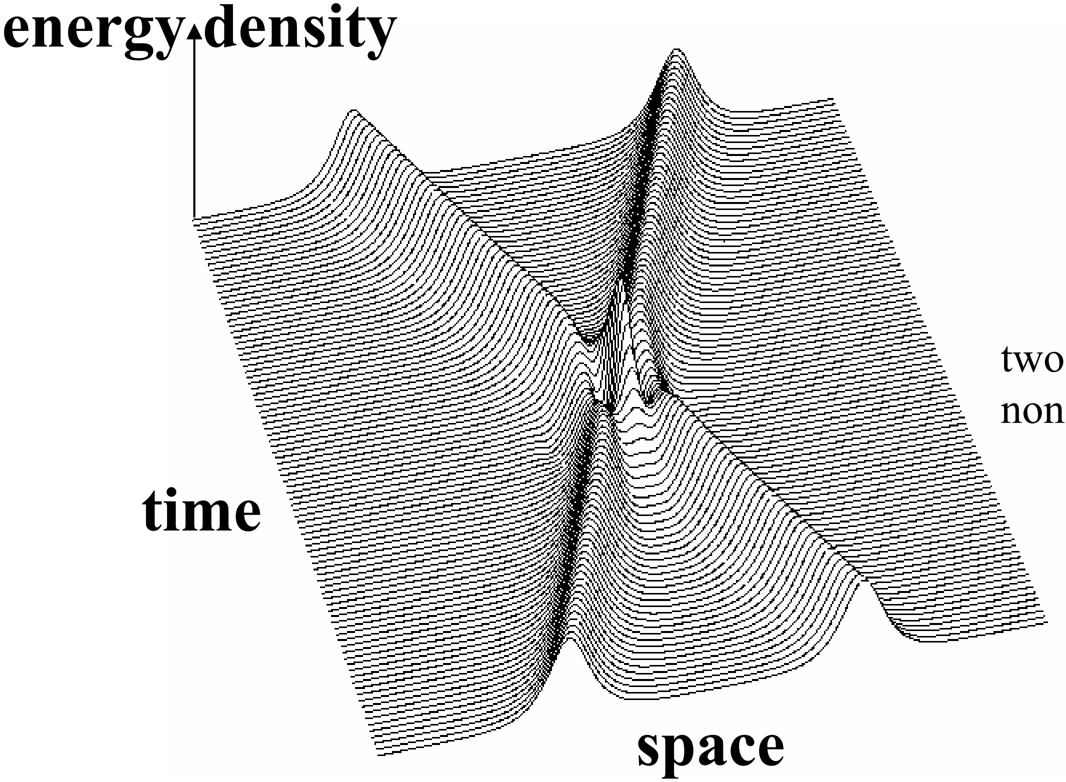
Life on earth are soft carbonaceous machines, that **consume** high-quality energy (metabolism) to achieve functions impossible from **totally equilibrium** systems.

But biomachines differ from cars and airplanes in one aspect: the dominance of **information**.

Fact: in few months, 90% of my physical self (atoms) becomes CO_2, urine, etc.

Life as solitons.

Soliton is a nonlinear local excitation (energy pack) that conserves character (non-dispersive) when traveling in a medium.



two-soliton collision in cubic nonlinear Schrödinger system

Life is a very specific program stored in DNA to consume free energy in the physical world. (acquire and spend)

I caught a rabbit and ate it. One week later, the atoms that caught the rabbit become CO_2, while some of the rabbit's atoms gets incorporated into new "me". Why "I ate the rabbit", instead of "the rabbit ate me"?

Information triumph over matter

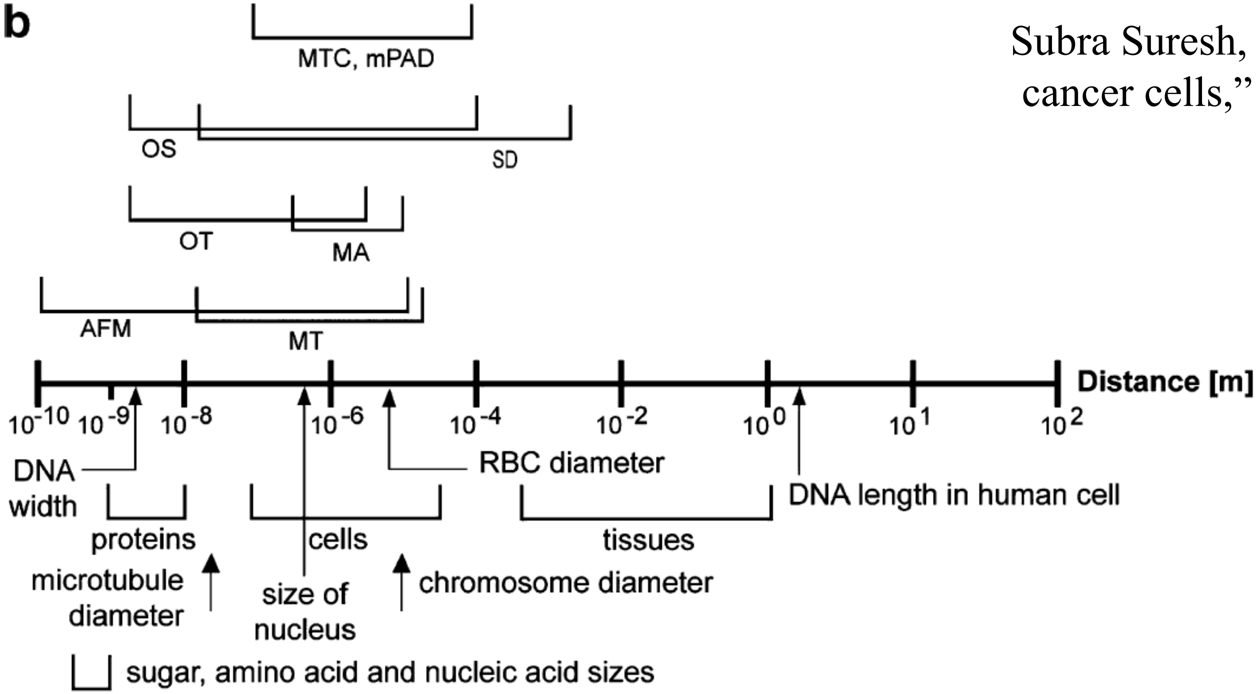
Image removed due to copyright restrictions.
Cover of textbook: Nelson, Philip, Marko Radosavljevic, and Sarina Bromberg.
Biological Physics: Energy, Information, Life. New York, NY: W. H. Freeman and Co., 2004. ISBN: 9780716743729.

Life is information organizing energy.

Courtesy of American Institute of Physics. Used with permission.

Rob Phillips and Stephen R. Quake, “The biological frontier of physics,” *Physics Today* **59** (2006) 38.

Subra Suresh, "Biomechanics and biophysics of cancer cells," *Acta Materialia* **55** (2007) 3989.



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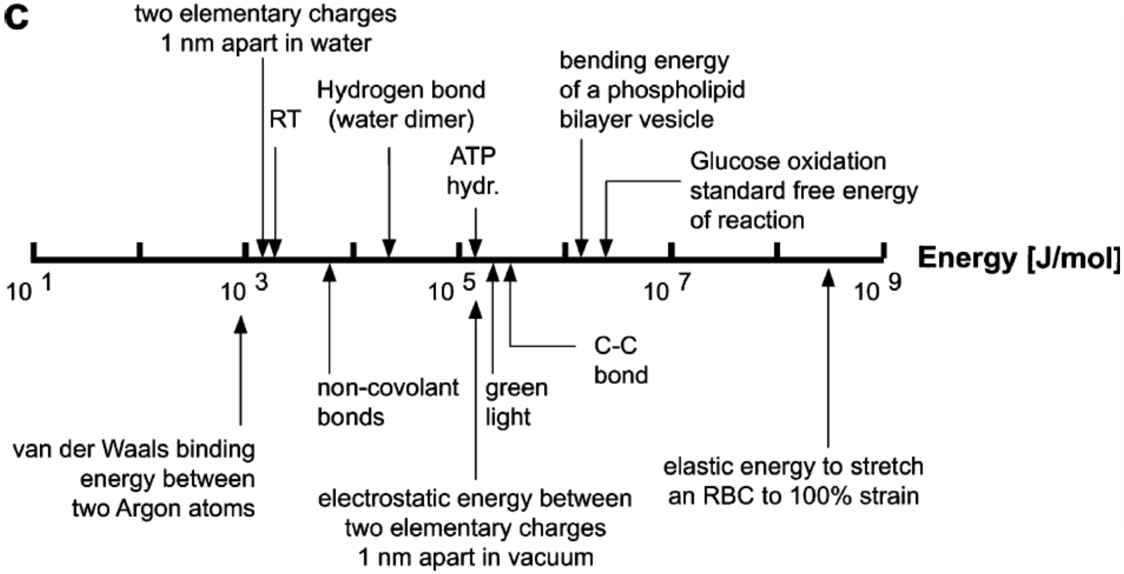
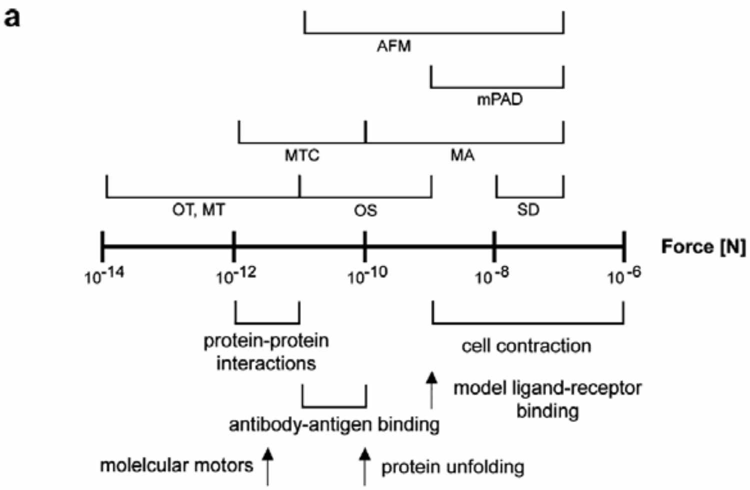




Last philosophical question: which are more *magical*, biomachines or engineered machines ?

Biomachines are severely confined in energy scale.

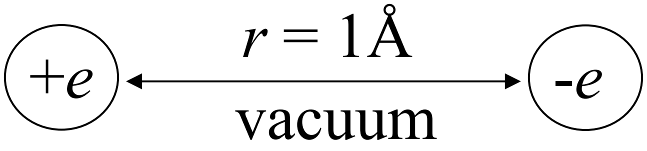
Engineers: No bird flies faster than the plane I took to Singapore
No animal went to the Moon with bio power
No laser in bio-systems, no nuclear reactor
No purified silicon to augment computation

Biologists: answer 1: efficiency, complexity, adaptivity
of ATP burning soft nano-machines
answer 2: All hard machines are made by one *self-aware* soft machine,
Cro-Magnon.

Modelers: modeling is the ultimate self-awareness.

Correct answer: the most potent magic belongs to nano-bio-engineers
who know how to do modeling! (information + energy scales)

Spatial Organization of Electrostatic Energy



$$U = \frac{q_1 q_2}{4\pi\varepsilon_0 r} = 14.4 \text{ eV}$$

This is huge! ($k_\mathrm{B}T_\mathrm{room} = 0.025$ eV, $U = 560 k_\mathrm{B}T_\mathrm{room}$)

Now add water:

$$U = \frac{q_1 q_2}{4\pi\varepsilon_\mathrm{r}\varepsilon_0 r} = \frac{14.4}{80} = 0.18 \text{ eV} \quad = \quad 7 k_\mathrm{B}T_\mathrm{room}$$

$$\exp\left(-\frac{U}{k_\mathrm{B}T_\mathrm{room}}\right) = 10^{-3}$$

this is good for life

Screening by bound charge vs Screening by mobile charge:

Screening by bound charges reduces the magnitude of the long-range electric field but can never kill it.

Screening by mobile charges completely kills the long-range tail of electric field.

Poisson's equation in dielectric medium:

pH-7 water is strong
dielectric but weak electrolyte:
[hydronium]=[hydroxyl]=10^{-7}

$$\nabla^2 \phi = -\frac{\rho_{\text{total}}}{\varepsilon_{\text{r}} \varepsilon_0}$$

electrolyte

$$\rho_{\text{total}} = e\delta\left(\mathbf{x}\right) + Ze\rho_{\text{p-ion}}(\mathbf{x}) - Ze\rho_{\text{n-ion}}(\mathbf{x})$$

Define $\phi(\mathbf{x} \to \infty) = 0,$ we know also that

$$\rho_{\text{p-ion}}(\mathbf{x} \to \infty) = \rho_{\text{n-ion}}(\mathbf{x} \to \infty) = \rho_0$$

At $\mathbf{x} \neq \infty$, p-ion has energy $Ze\phi(\mathbf{x})$, and

n-ion has energy $-Ze\phi(\mathbf{x})$ compared to at infinity,

So if thermal equilibiurm is reached,

$$\rho_{\text{p-ion}}(\mathbf{x}) = \rho_0 \exp\left(-\frac{Ze\phi(\mathbf{x})}{k_{\mathrm{B}}T}\right),$$

$$\rho_{\text{n-ion}}(\mathbf{x}) = \rho_0 \exp\left(\frac{Ze\phi(\mathbf{x})}{k_{\mathrm{B}}T}\right)$$

$$\rho_{\text{total}} = e\delta\left(\mathbf{x}\right) - 2Ze\rho_0 \sinh\left(\frac{Ze\phi(\mathbf{x})}{k_{\mathrm{B}}T}\right)$$

$$\nabla^2\phi = -\frac{e\delta\left(\mathbf{x}\right) - 2Ze\rho_0 \sinh(Ze\phi / k_{\mathrm{B}}T)}{\varepsilon_{\mathrm{r}}\varepsilon_0} : \text{ nonlinear}$$

Suppose $Ze\phi(\mathbf{x}) << k_\mathrm{B}T$, linearize the equation:

$$\rho_\mathrm{total} \approx e\delta\left(\mathbf{x}\right) - \frac{2Z^2e^2\rho_0}{k_\mathrm{B}T}\phi(\mathbf{x})$$

$$\nabla^2\phi = -\frac{e\delta\left(\mathbf{x}\right)}{\varepsilon_\mathrm{r}\varepsilon_0} + \frac{2Z^2e^2\rho_0}{k_\mathrm{B}T\varepsilon_\mathrm{r}\varepsilon_0}\phi(\mathbf{x})$$

$$\lambda_\mathrm{D}^{-2} \equiv \frac{2Z^2e^2\rho_0}{k_\mathrm{B}T\varepsilon_\mathrm{r}\varepsilon_0}: \quad \nabla^2\phi = -\frac{e\delta\left(\mathbf{x}\right)}{\varepsilon_\mathrm{r}\varepsilon_0} + \frac{\phi}{\lambda_\mathrm{D}^2}$$

$$\phi = \frac{e}{4\pi\varepsilon_\mathrm{r}\varepsilon_0}\frac{\exp(-r/\lambda_\mathrm{D})}{r}$$

For water solvent (ε_r=80) at 298 K:

$$\lambda_{\mathrm{D}} = \frac{0.3\mathrm{nm}\sqrt{\mathrm{M}}}{\sqrt{I}}, \quad I \equiv \frac{1}{2}\sum_i Z_i^2 c_i$$

ionic strength [M]

mobile ion concentration [M]

λ_D is how much free charges can be separated (local breakdown of electro-neutrality) spatially by thermal fluctuation energy.

Unless you are doing Van de Graaff particle accelerator where MeV energy are involved

Image removed due to copyright restrictions.
Van der Graaff generator.

The most you can do in ordinary electrochemical system is to separate a bit of charge (∝area) λ_D (typically few nms) away from the balancing counter ions.

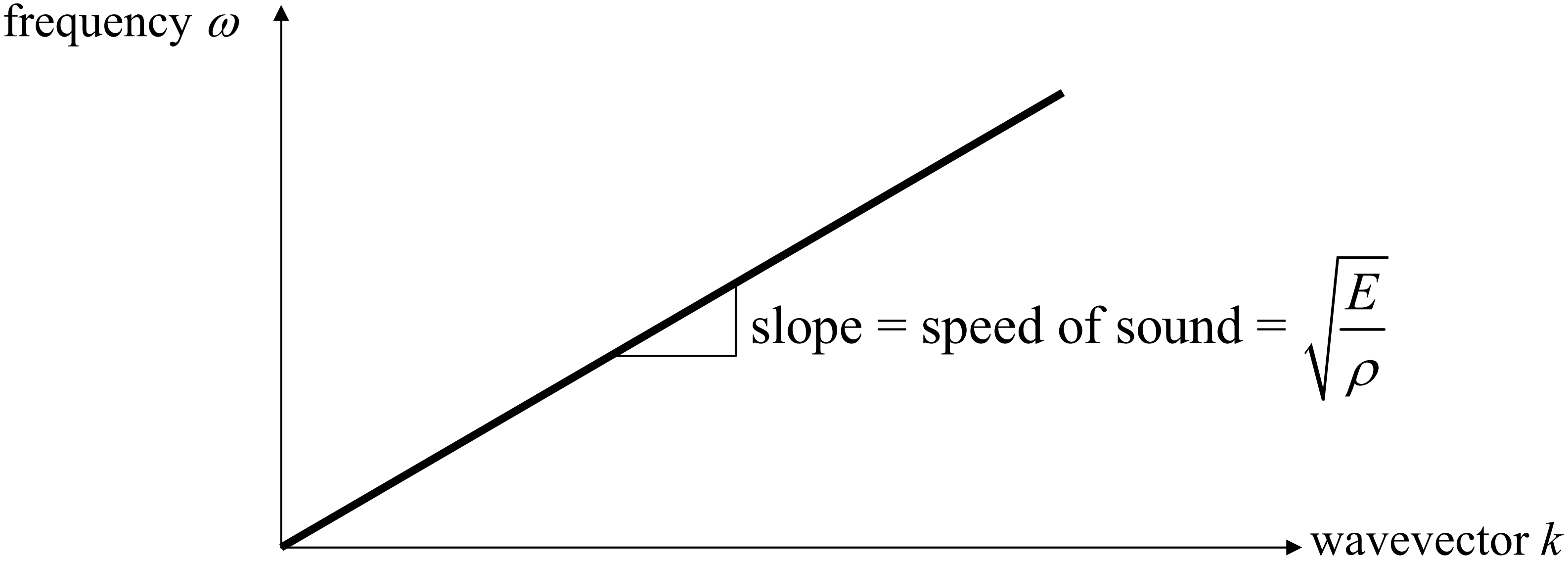
Spatial-Temporal Characteristics of Uniaxial Compression

$$\text{Strain energy } U = \int dx dA \frac{E\varepsilon_{xx}^2}{2} = A\int dx \frac{E}{2}\left(\partial_x u\right)^2$$

$$\text{Kinetic energy } K = A\int dx \frac{\rho(\partial_t u)^2}{2}$$

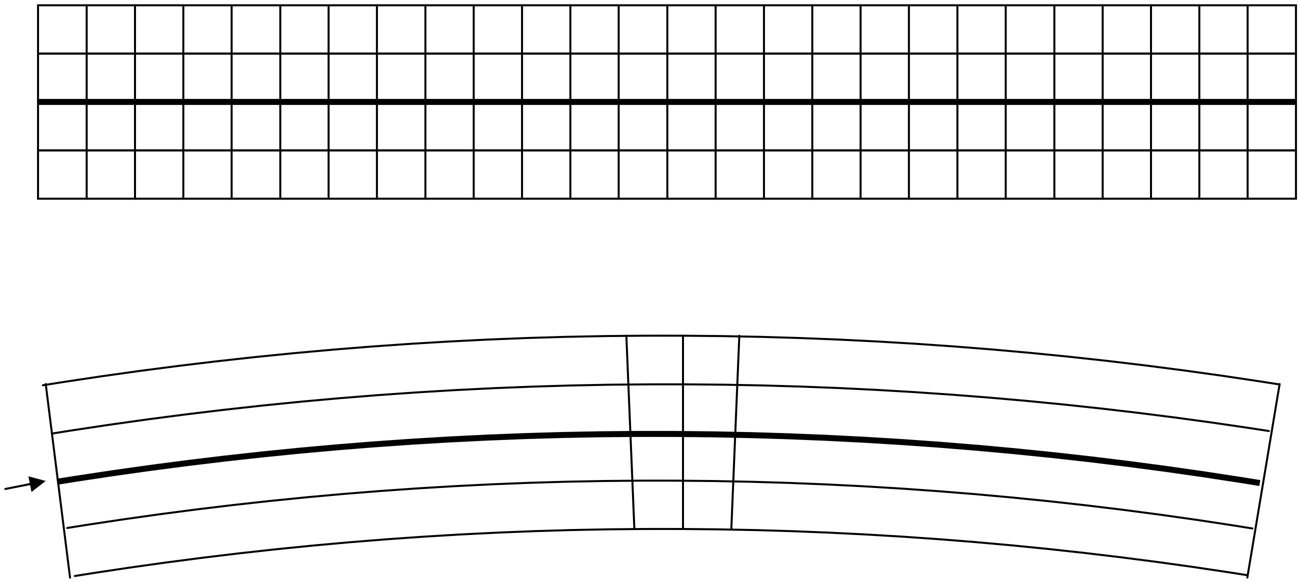
$$A\rho\partial_t^2 u = AE\partial_x^2 u$$

$$\text{Plug in } u(x,t) = \exp(ikx - i\omega t), \quad \omega^2 = \frac{E}{\rho}k^2$$



Spatial-Temporal Characteristics of Bending

Bending is special



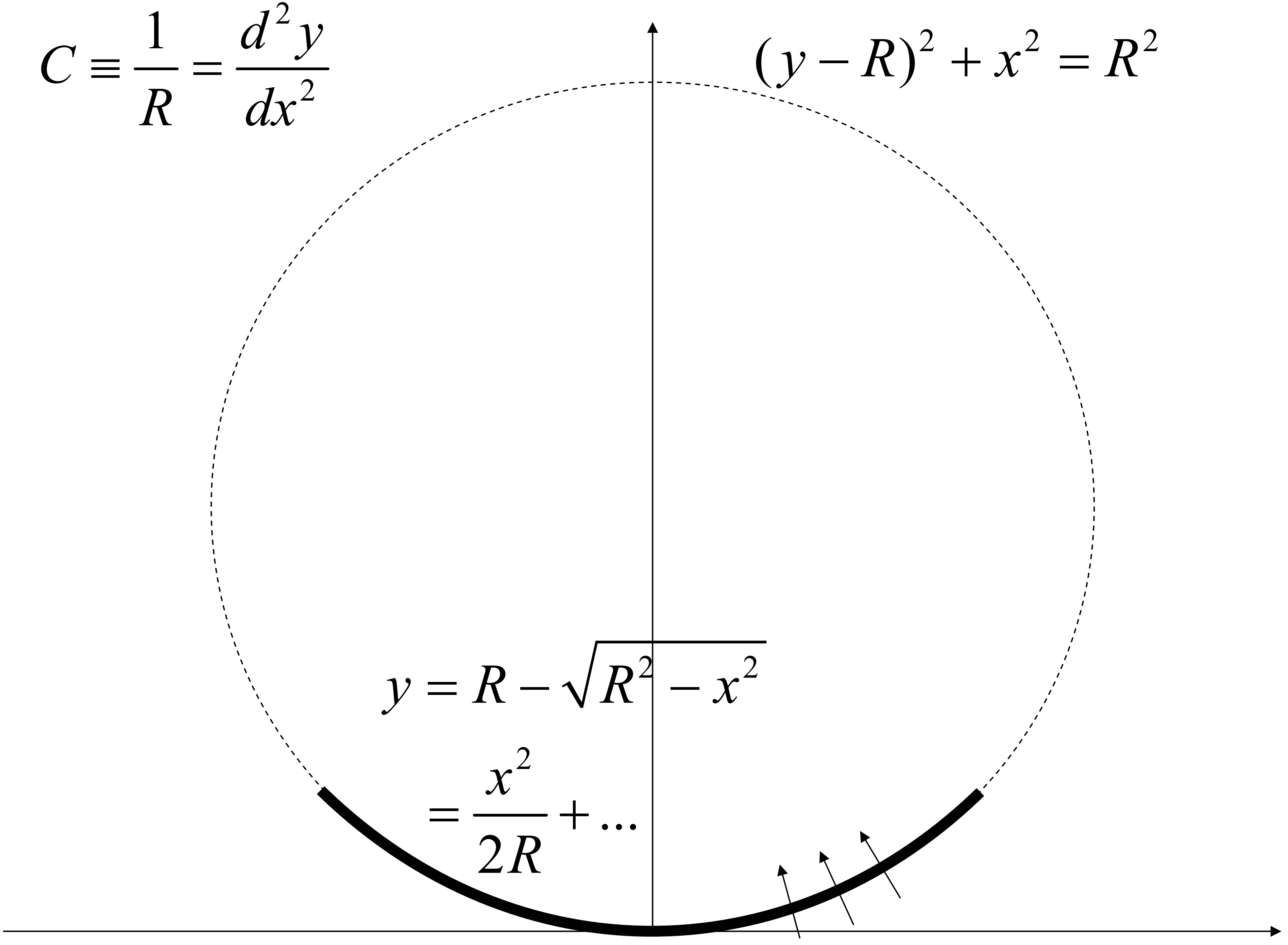
Strain energy $U = \int dxdA \frac{E\varepsilon_{xx}^2}{2} = \int dxdA \frac{Ey^2}{2R^2}$

Moment of inertia: $I \equiv \int y^2 dA: \quad U = \int dx \frac{EI}{2R^2} = \int dx \frac{\kappa C^2}{2}, \ \kappa \equiv EI, \ C \equiv \frac{1}{R}$

for cylindrical rod of radius a : $I = \frac{1}{2}\int r^2 2\pi r dr = \frac{\pi a^4}{4}$

$$C \equiv \frac{1}{R} = \frac{d^2 y}{dx^2}$$

$$(y - R)^2 + x^2 = R^2$$

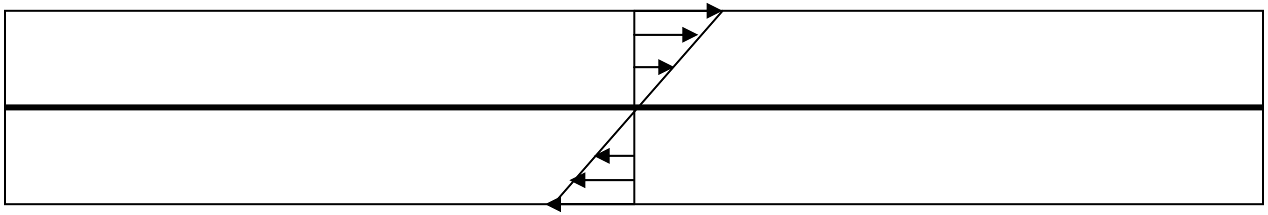


$$y = R - \sqrt{R^2 - x^2}$$

$$= \frac{x^2}{2R} + \dots$$

Spatial-Temporal Characteristics of Bending

Bending is special

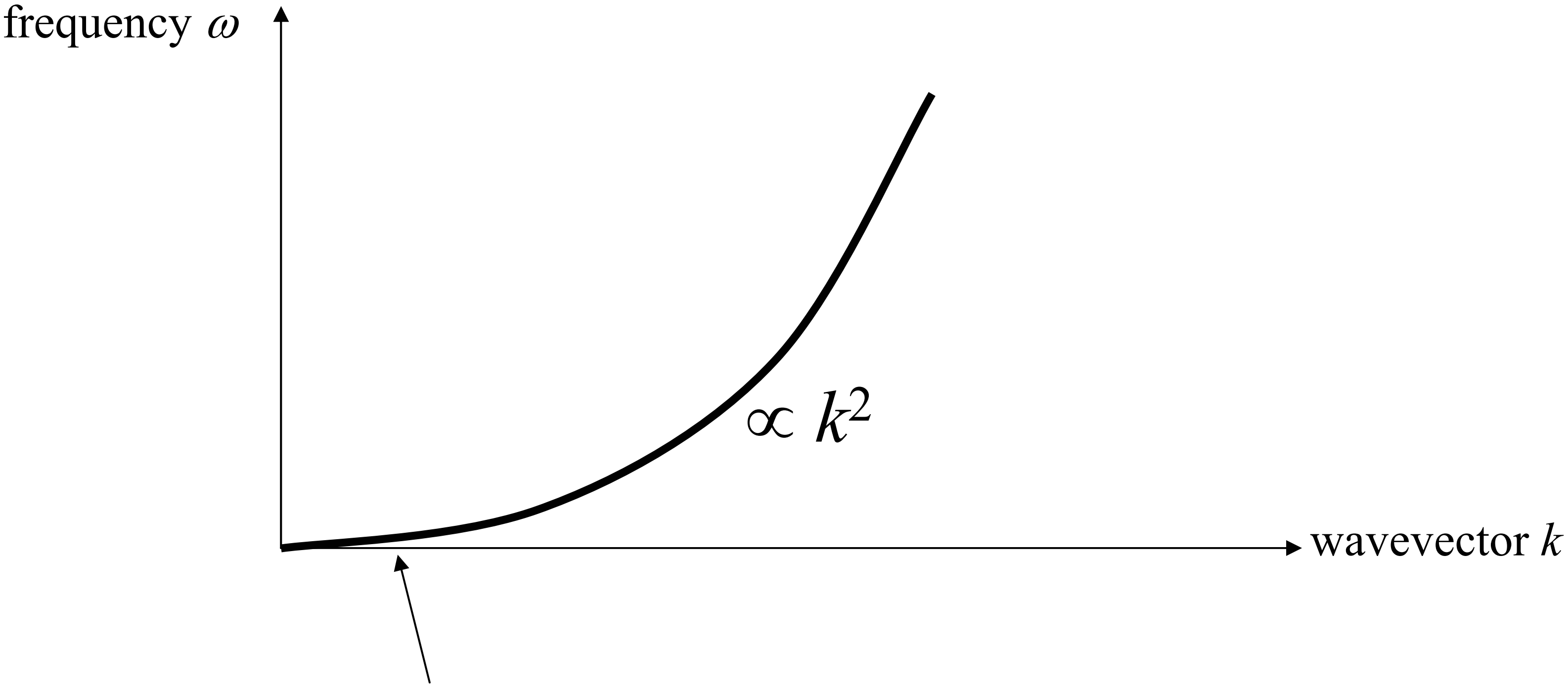


Strain energy $U = \int dx \frac{\kappa C^2}{2} = \int dx \frac{EI}{2} \left(\partial_x^2 y \right)^2$

Kinetic energy $K = A \int dx \frac{\rho (\partial_t y)^2}{2}$

$$A\rho \partial_t^2 y = EI \partial_x^4 y$$

Plug in $u(x,t) = \exp(ikx - i\omega t)$, $\omega^2 = \frac{EI}{\rho A} k^4$



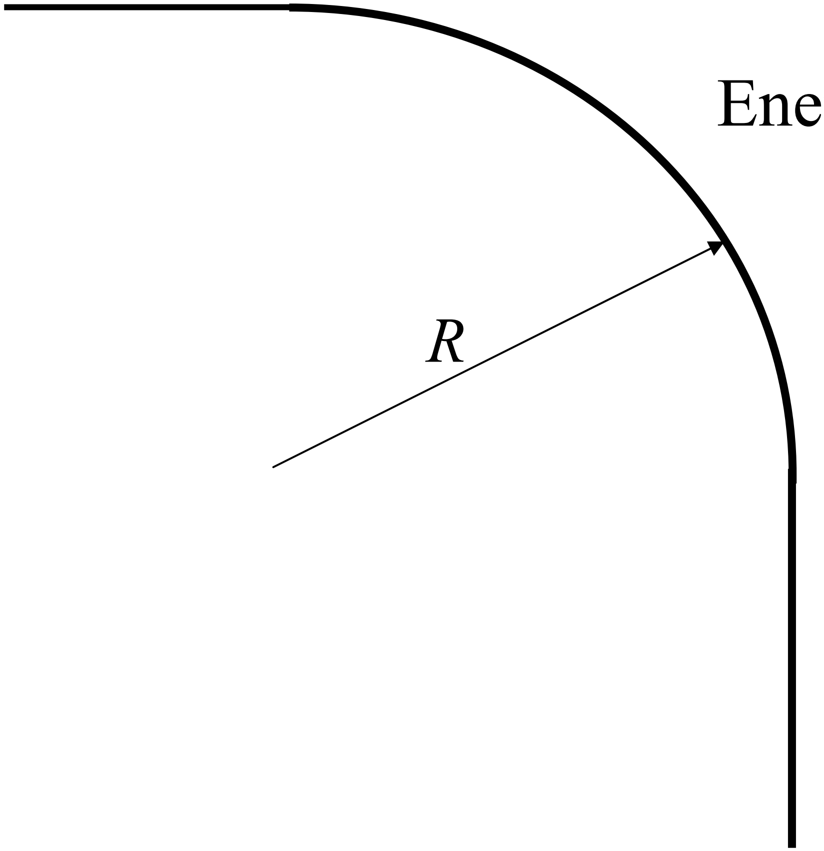
Long-wavelength free bending waves are extra-soft.

If tension σ is applied, $\omega^2 = \dfrac{\sigma A k^2 + EIk^4}{\rho A}$

If compression σ is applied, a long enough rod always buckle:

buckling wavelength $\propto k_{\min}^{-1} \propto \sqrt{\dfrac{EI}{\sigma A}}$: Euler buckling formula

Consider a quarter-circle:



Energy required: $$\frac{2\pi R}{4}\frac{\kappa}{2R^2} = \frac{\pi\kappa}{4R} \sim k_{\mathrm{B}}T$$

Smallest loop radius
thermal fluctuation can bend:

$$R \sim \frac{\pi\kappa}{4k_{\mathrm{B}}T}$$

Persistence length: longest separation that orientation correlation can be survive

Rare Events and Timescale: Harmonic Transition State Theory

Potential energy landscape: $U(\mathbf{x}^{3N})$

N is total number of atoms

$$\text{Force} = -\frac{\partial U}{\partial \mathbf{x}^{3N}}$$

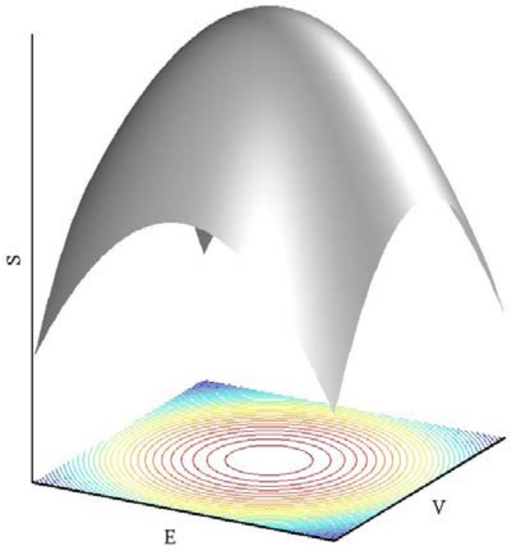
$$\text{Hessian} = \frac{\partial^2 U}{\partial \mathbf{x}^{3N} \partial \mathbf{x}^{3N}}$$

Diagonalize Hessian to get normal mode frequencies

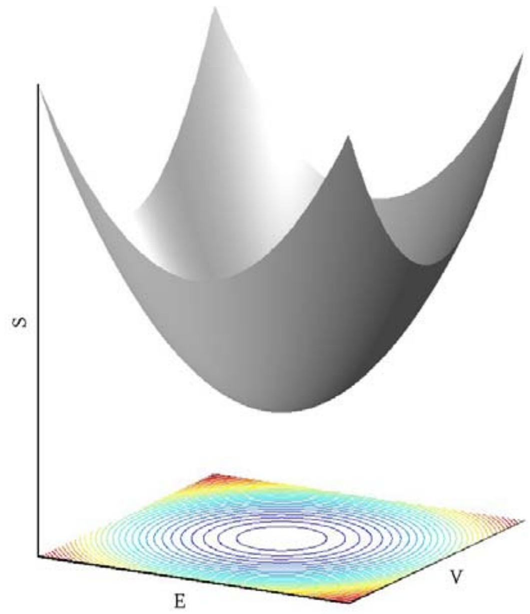
$$\nu_1, \nu_2, \nu_3, \ldots, \nu_{3N}$$

local minima: $\nu_1, \nu_2, \nu_3, \ldots, \nu_{3N}$ are all real

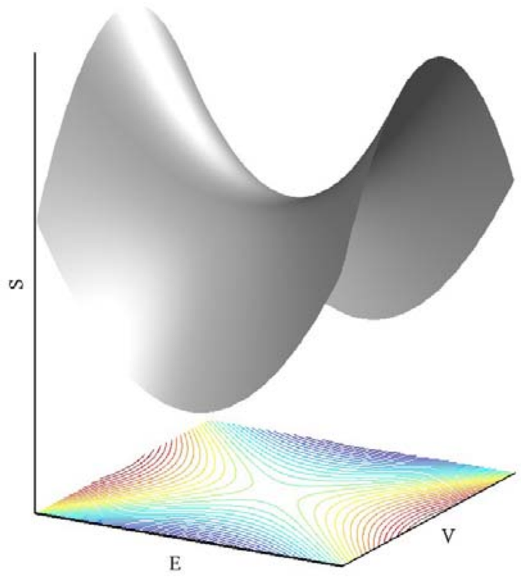
saddle point: $\nu_2, \nu_3, \ldots, \nu_{3N}$ are real



Maximum



Minimum



Saddle

$$R = \frac{\nu_1 \nu_2 \nu_3 \ldots \nu_{3N}}{\nu_2{}' \nu_3{}' \ldots \nu_{3N}{}'} \exp\left(-\frac{U' - U}{k_\mathrm{B} T} \right)$$

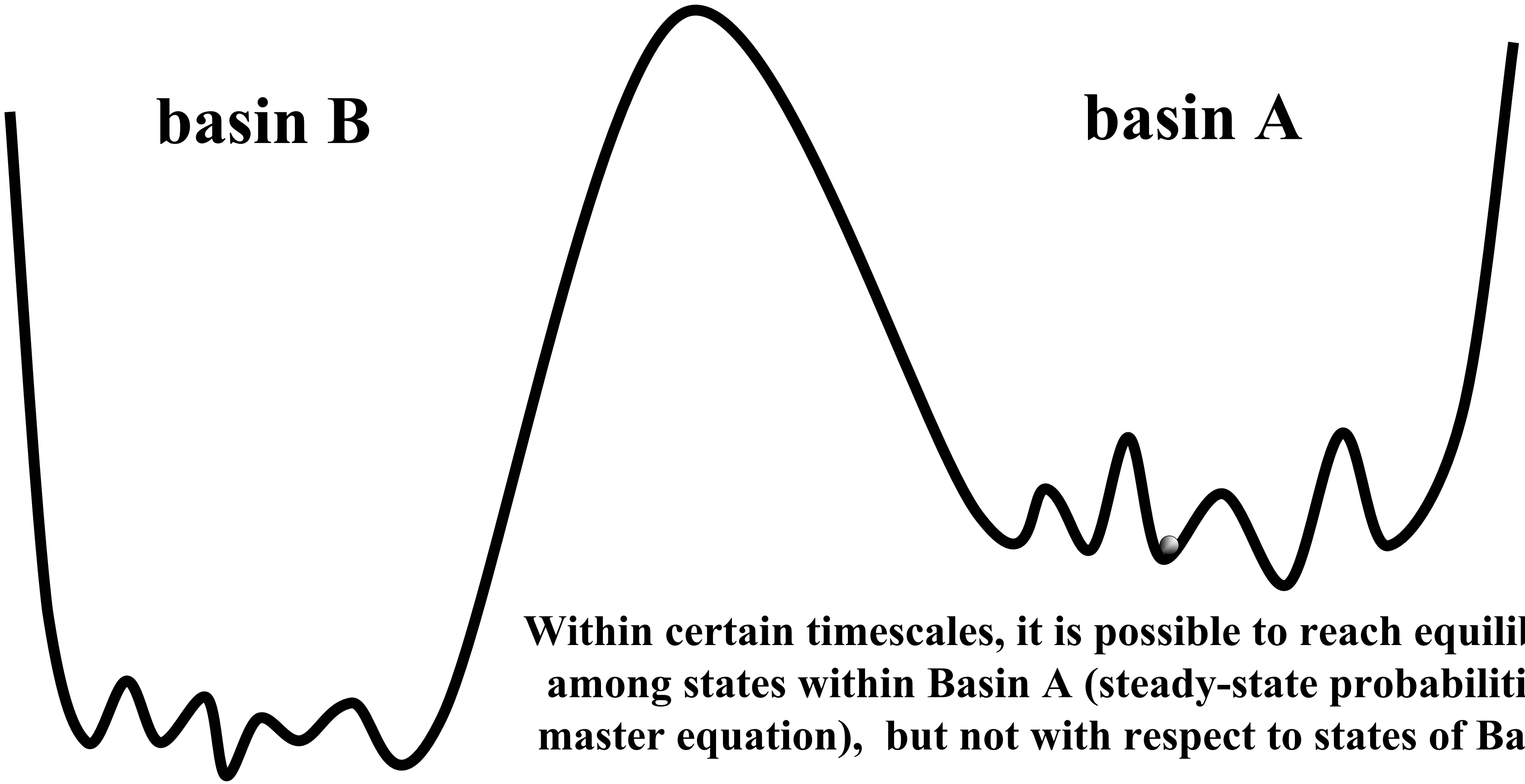
$$= \nu_1 \exp\left(-\frac{F' - F}{k_\mathrm{B} T} \right), \text{ where } F' = U' + k_\mathrm{B} T \ln \nu_2{}' \nu_3{}' \ldots \nu_{3N}{}'$$

$$F' = U + k_\mathrm{B} T \ln \nu_2 \nu_3 \ldots \nu_{3N}$$

In quantum mechanics, free energy of one oscillator is

$$-k_{\mathrm{B}}T\ln(e^{-h\nu/2k_{\mathrm{B}}T}+e^{-3h\nu/2k_{\mathrm{B}}T}+e^{-5h\nu/2k_{\mathrm{B}}T}+\ldots)=-k_{\mathrm{B}}T\ln\frac{e^{-h\nu/2k_{\mathrm{B}}T}}{1-e^{-h\nu/k_{\mathrm{B}}T}}$$

In the semiclassical limit ($h\to 0$), $F\to k_{\mathrm{B}}T\ln\dfrac{h\nu}{k_{\mathrm{B}}T}$



Within certain timescales, it is possible to reach equilibrium among states within Basin A (steady-state probabilities in master equation), but not with respect to states of Basin B.