

BIOLOGICAL PHYSICS
AND
BIOPHYSICS

Goals

Some examples from biological physics

GOALS OF BIOLOGICAL PHYSICS

CONCEPTS

AND

LAWS

OF COMPLEX SYSTEMS

BIOLOGICAL PHYSICS

Stan Ulam:

Ask not what physics can do for biology

Ask what biology can do for physics.

Vast field: Physics of

Proteins

Nucleic acids

Membranes

Energy transfer

Signaling

Networks

Neural Nets

....

THE GOOD OLD TIMES

In 1980, when biophysicist George Oster submitted a paper to an esteemed developmental biology journal, he received a reply with a rather Orwellian overtone. “The authors are attempting to apply Newton’s laws to embryos,” the anonymous reviewer wrote, “but as all biologists know, biological systems don’t obey the laws of physics.” Luckily, an astute editor found

BUT THINGS HAVE CHANGED

Biological numbers $\gg \gg$
astronomical numbers.

Primary sequence



20 letters

~ 200 in chain

$N \gg 10^{200}$

different
sequences



\rightarrow need $> 10^{100}$
universa !

[Are we the best solution ??]

BIOLOGICAL PHYSICS

Look at biosystems as physical systems.

Find concepts and laws.

Background : Physics, math, computing.

Learn biology, biochemistry.

BIOPHYSICS

How do the biosystems work?

Develop tools and methods

Background: Chemistry, biochemistry,
biology.

Some physics.

Tunneling in Ligand Binding to Heme Proteins

N. Alberding, R. H. Austin, K. W. Beeson, S. S. Chan, L. Eisenstein
H. Frauenfelder and T. M. Nordlund

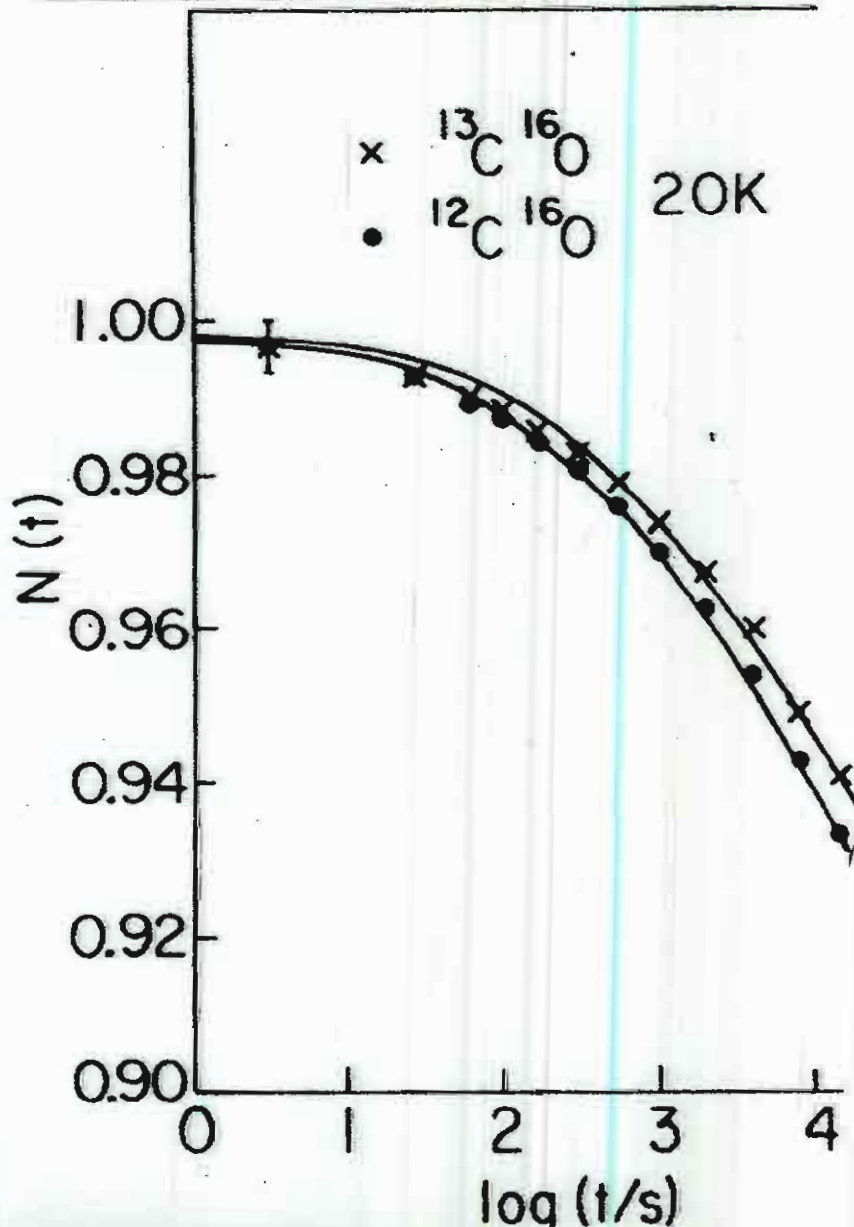
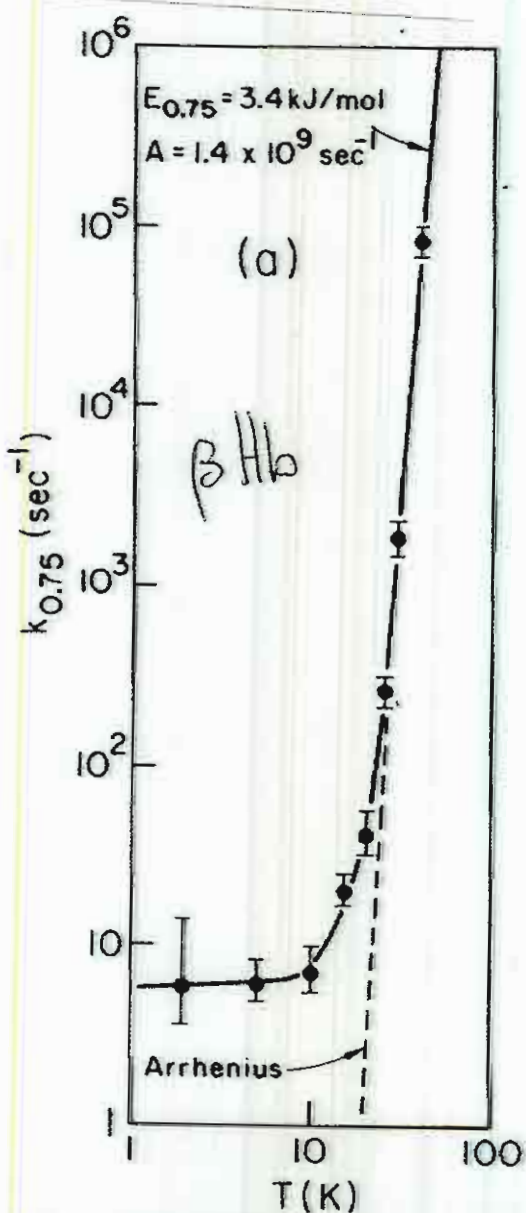
VOLUME 44, NUMBER 17

PHYSICAL REVIEW LETTERS

1980 28 APRIL 1980

Isotope Effect in Molecular Tunneling

J. O. Alben, D. Beece, S. F. Bowne, L. Eisenstein, H. Frauenfelder, D. Good, M. C. Marden,
P. P. Moh, L. Reinisch, A. H. Reynolds,^(a) and K. T. Yue



Human: Few Genes, Much Complexity

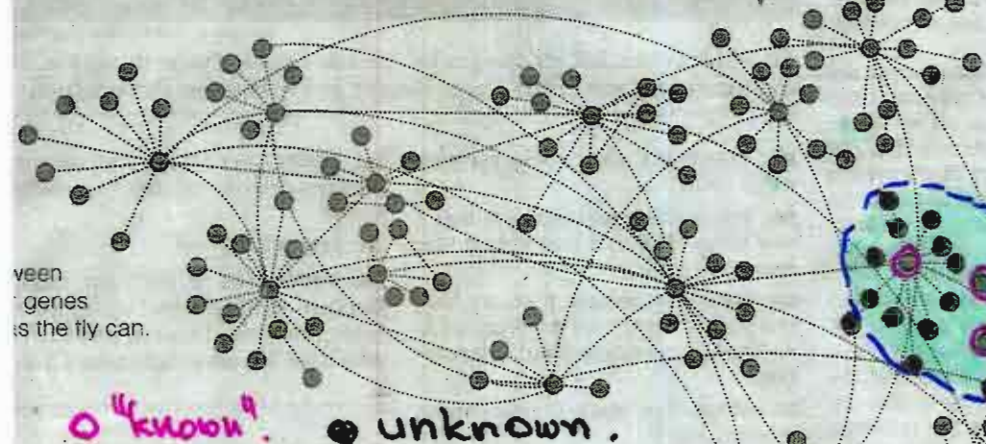
Humans have only about three times as many genes as the fly, but the complexity seems unlikely to come from a sheer quantity of genes. Rather, some scientists believe each human has a network with different parts like genes, proteins and groups of cells. These parts connect at different times and on different levels, and human complexity arises from the structure of the network and the dynamics of its interactions.

CAENORHABDITIS (Fruit fly)

HOMO SAPIENS



In this example the fly has 40 genes, and the human has 120.



between genes as the fly can.

○ "known" ● unknown

this week's... of human... use the cur-... to overpre-... r end of its... be the new

d their find-... yesterday in... a, too. Most

s can... ty.

es in the 75... essentially... ons of years... still active... chromosomes... ology. Large... been exten-... chromosome... archaean... which the... reconstruct

the history of the animal genome. As the modest number of human genes became apparent, biologists in both teams were forced to think how to account for the greater complexity of people, given that they seem to possess only 50 percent more genes than the roundworm. It is not foolish pride to suppose there is something more to Homo sapiens than Caenorhabditis elegans. The roundworm is a little tube of a creature with a body of 959 cells, of which 302 are neurons in what passes for its brain. Humans have 100 trillion cells in their body, including 100 billion brain cells.

Several explanations are emerging for how to generate extra complexity other than by adding more genes. One is the general idea of combinatorial complexity — with just a few extra proteins one could make a much larger number of different combinations between them. In a commentary in Science, Dr. Jean-Michel Claverie, of the French National Research Center in Marseille, notes that with a simple combinatorial scheme, a 30,000-gene organism like the human can in principle be made almost infinitely more complicated.

But Dr. Claverie suspects humans are not that much more elaborate than some of their creations. "In fact," he writes, "with

Continued on Page 4

PROTEINS ARE COMPLEX

>> 10^6 exist

>> 10^{200} possible

Heterogeneous in space and time

>> 10^{10} states of a given protein

Motions from femtoseconds to seconds

Fluctuations crucial

Proteins have functions

Control and feedback (networks).

.... Everything that living things do can be understood in term of the jiggings and wiggings of atoms.

R. P. FEYNMAN

GOAL : CONCEPTS, LAWS.

But we are very far away from such an understanding.

PHYSICS OF PROTEINS.

Structure

Energy landscape

Dynamics

(Function)

TOOLS : Physics
Chemistry
Biology
Computing

GLASS

Supercooled liquid.

Glass temperature: relaxation 0.01 s.

Properties:

Three relaxations

α Non-Arrhenius, nonexponential in t

β Arrhenius (?), nonexponential in t .

TLS (very low T).

Amorphous

Nonequilibrium

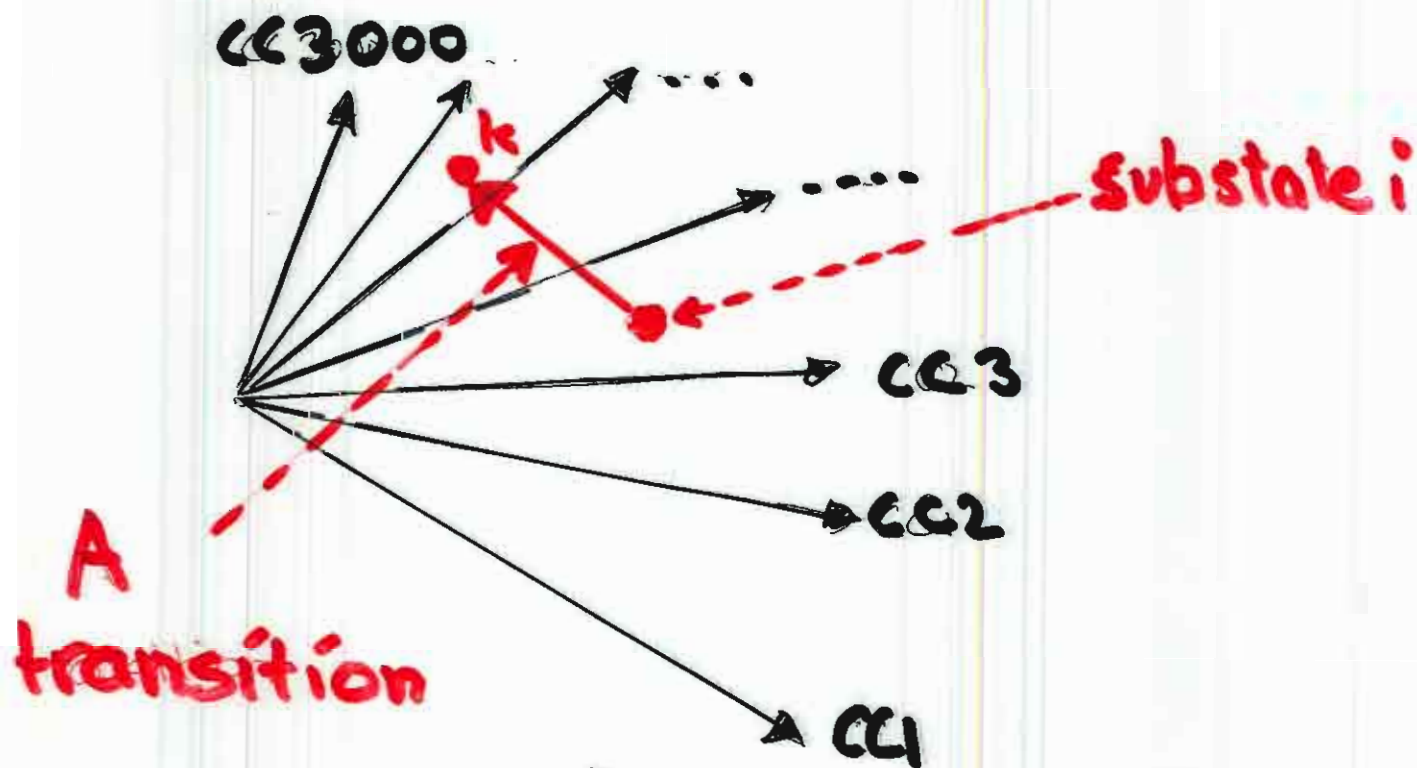
Energy landscape.

Google: “glass”	26 000 000
“glass transition”	68 000

THE ENERGY LANDSCAPE

A protein, including the hydration shell and the close solvent, can assume a vast number of different conformation.

A given conformational substate is a point in a hyperspace of $\approx 3N$ (> 3000) dimensions.

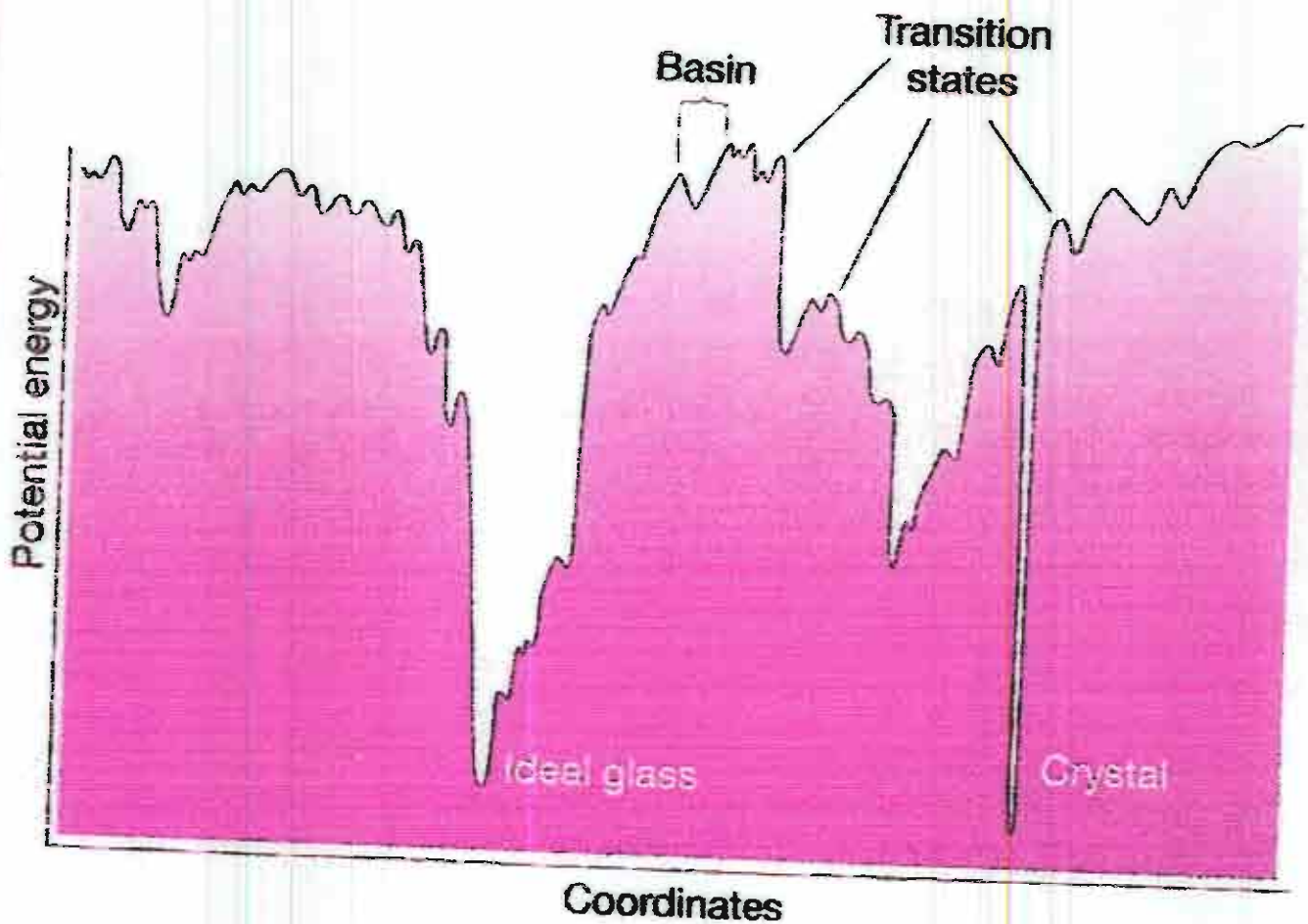


EVIDENCE: EXPERIMENT, COMPUT.

GLASS : THE ENERGY

LANDSCAPE

Stillinger



High dimensional.

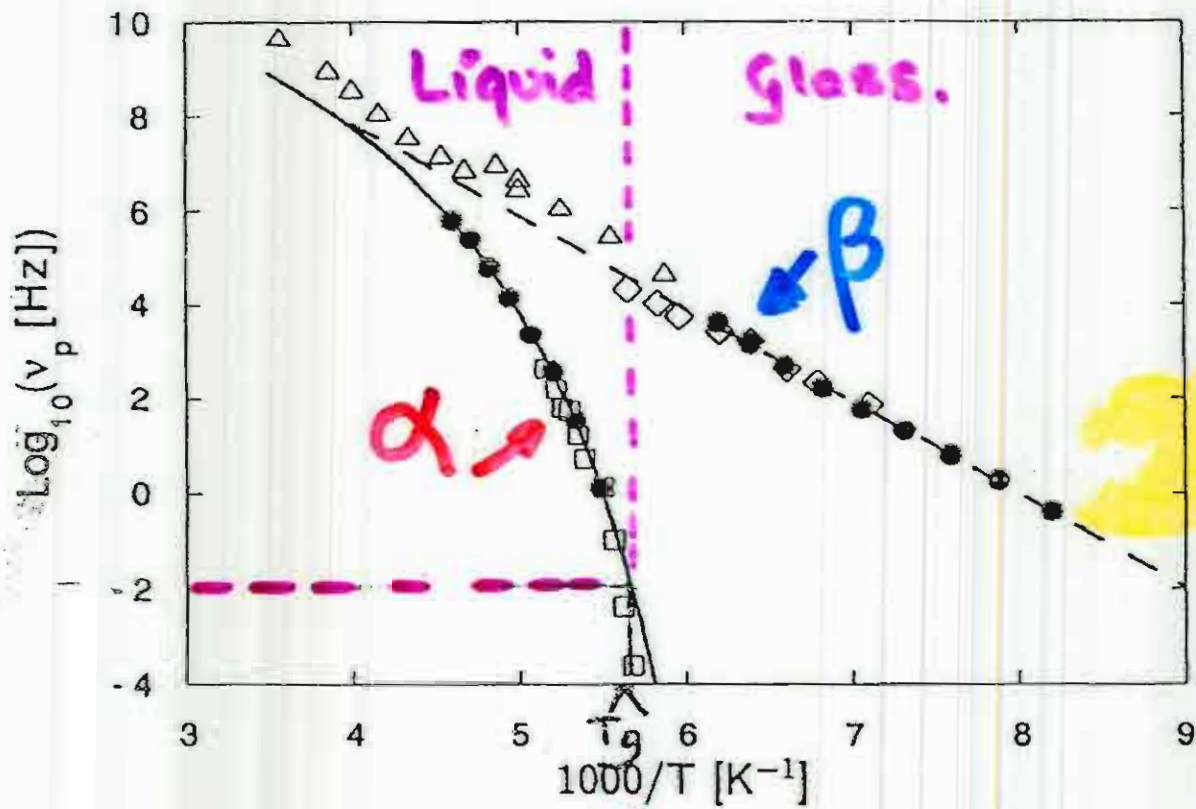
RELAXATIONS IN GLASSES

Glasses show two major types of relaxations:

α - relaxations : large-scale; Not Arrhenius (VTF)

β - relaxations : ?? Arrhenius (Ferry?)

An example from Deegan and Nagel (polybutadiene):

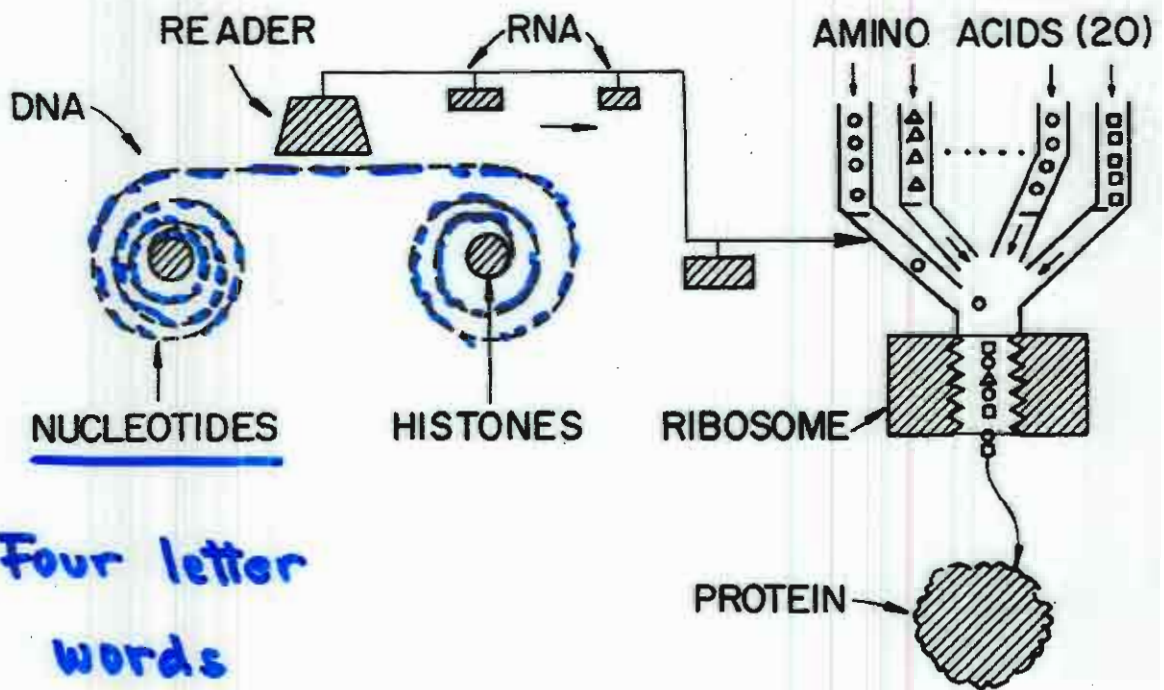


Glass temperature.

ASSEMBLY

LEGISLATIVE

EXECUTIVE

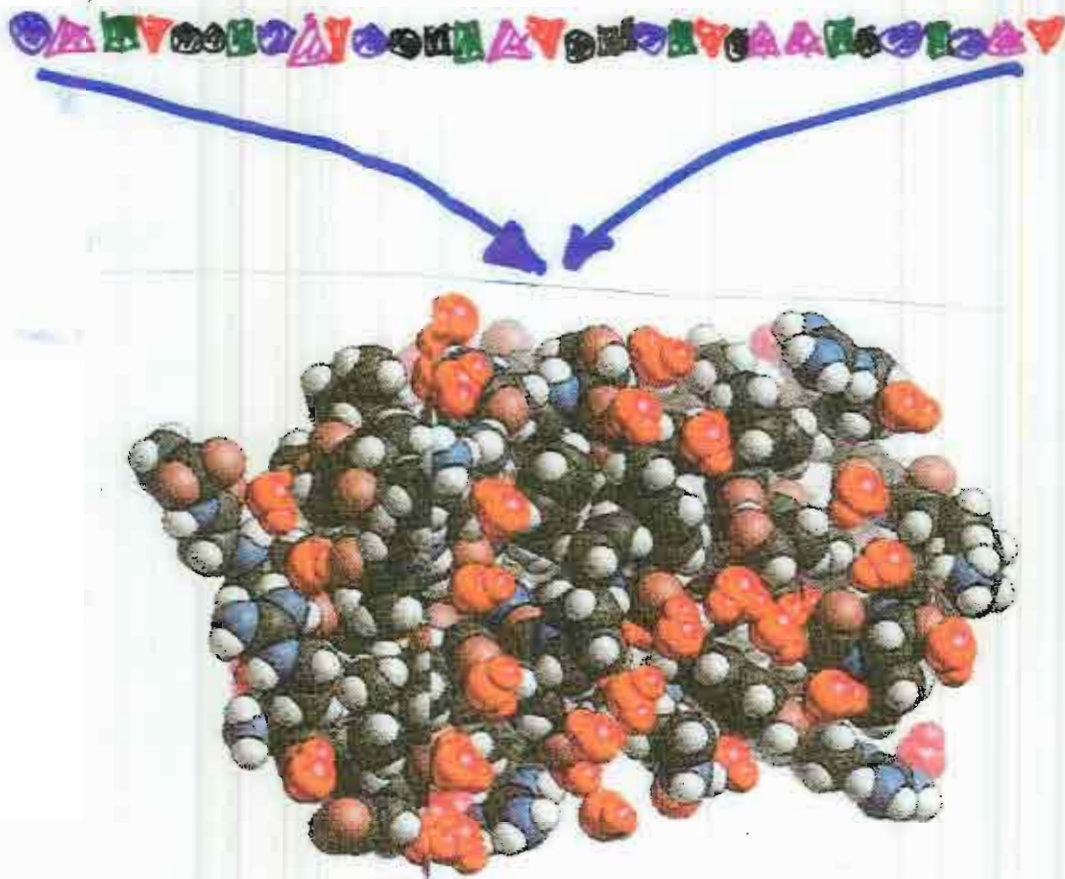


CAU → HIS

PROTEIN STRUCTURE

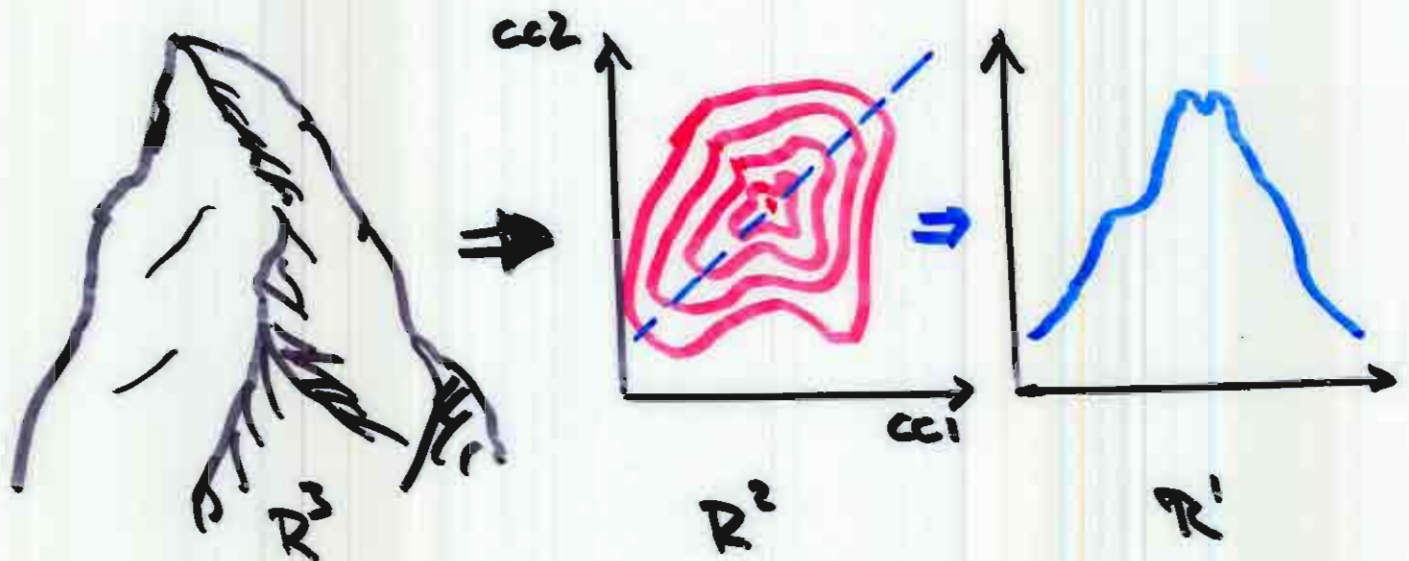
THE OLD TEXTBOOK PICTURE

“The primary sequence folds into a unique tertiary structure.”



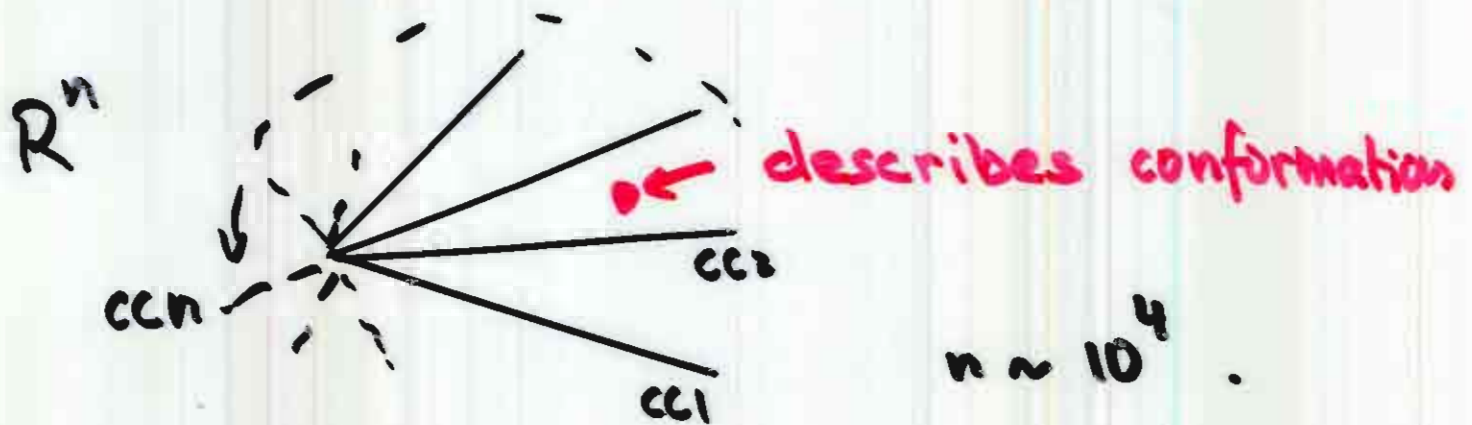
“Every atom in its proper place!”

LANDSCAPES



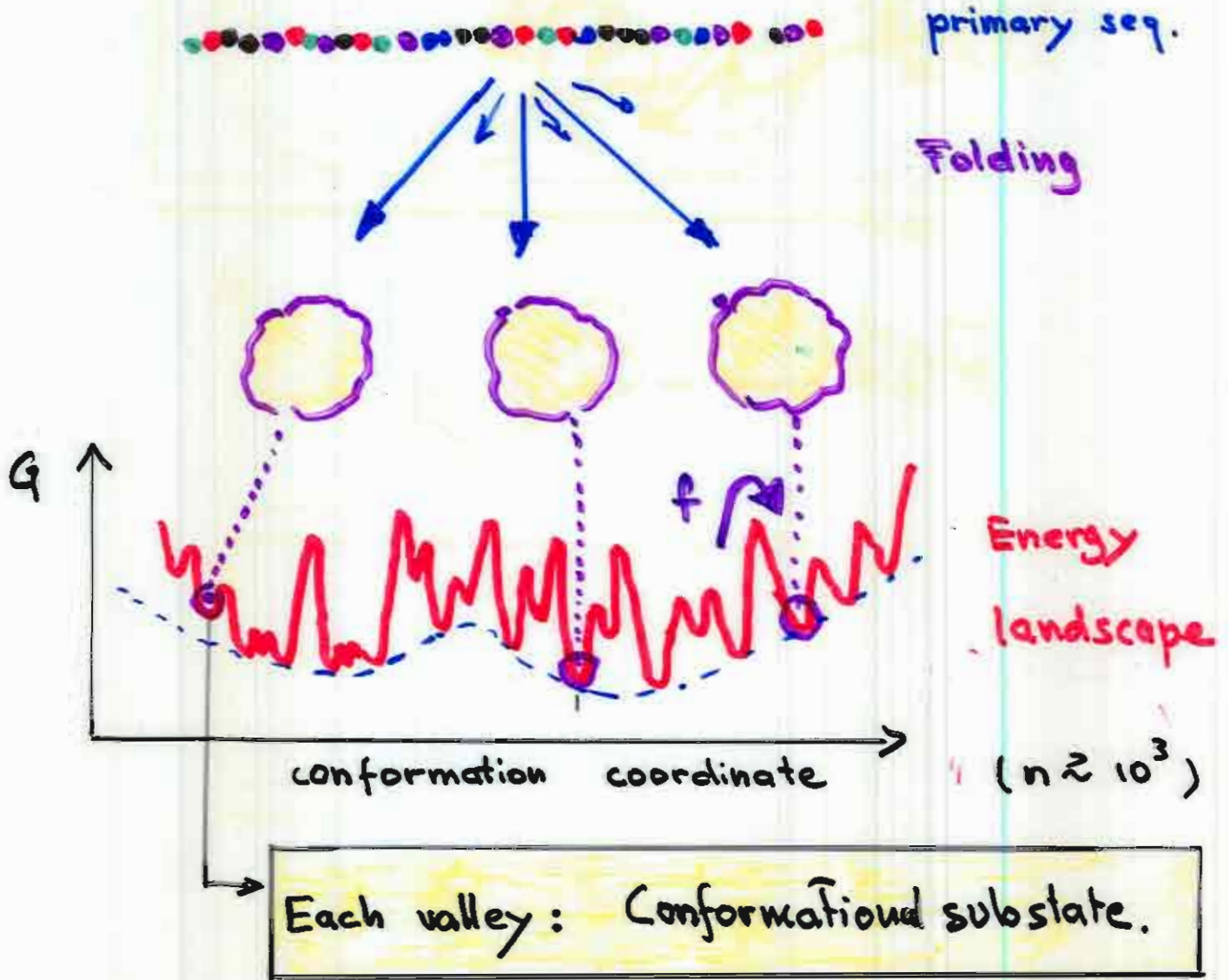
PROTEINS

$n \gg 3000$ coordinates



$n \sim 10^4$.

THE EL OF PROTEINS (CS) (Energy landscape)

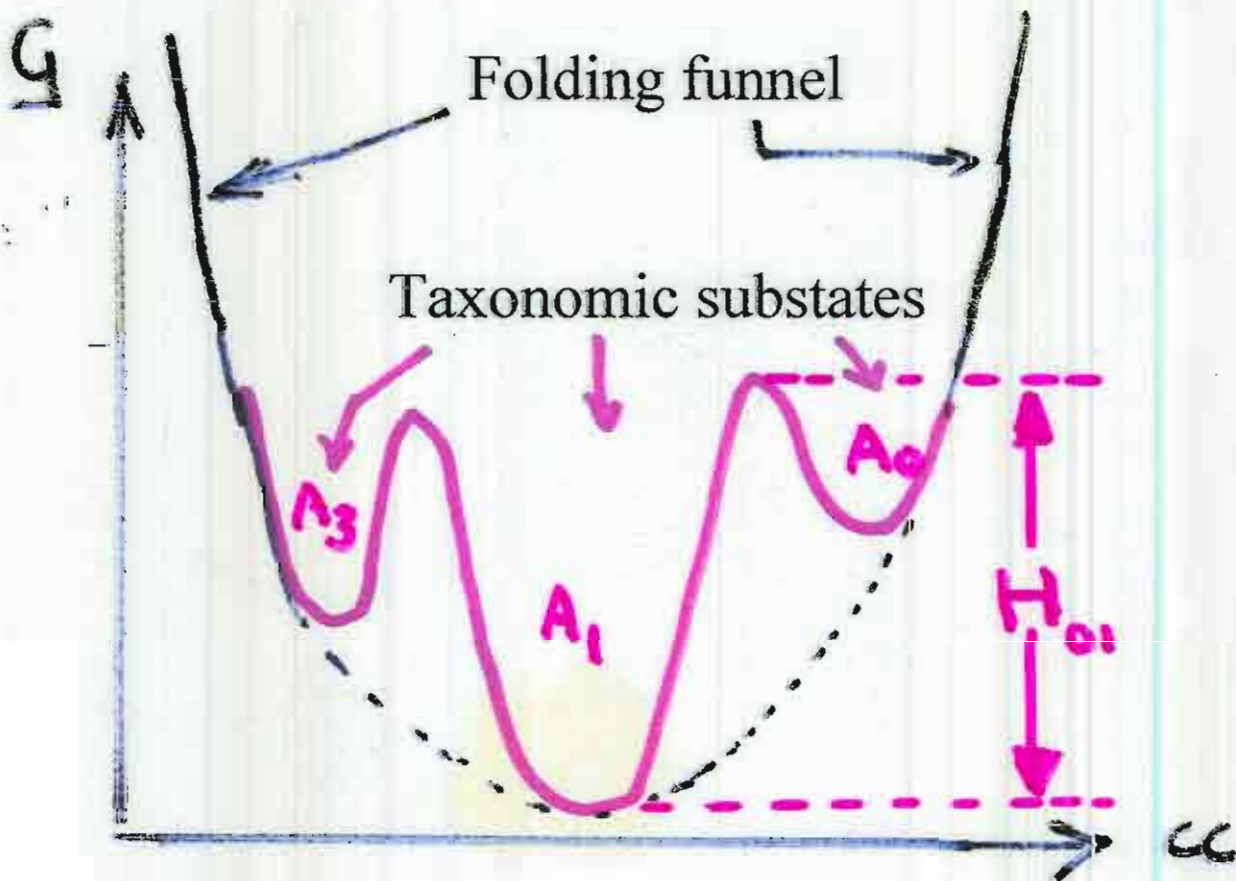


1. SUBstate: Proteins are machines, have usually more than one state. Each state split into CS.

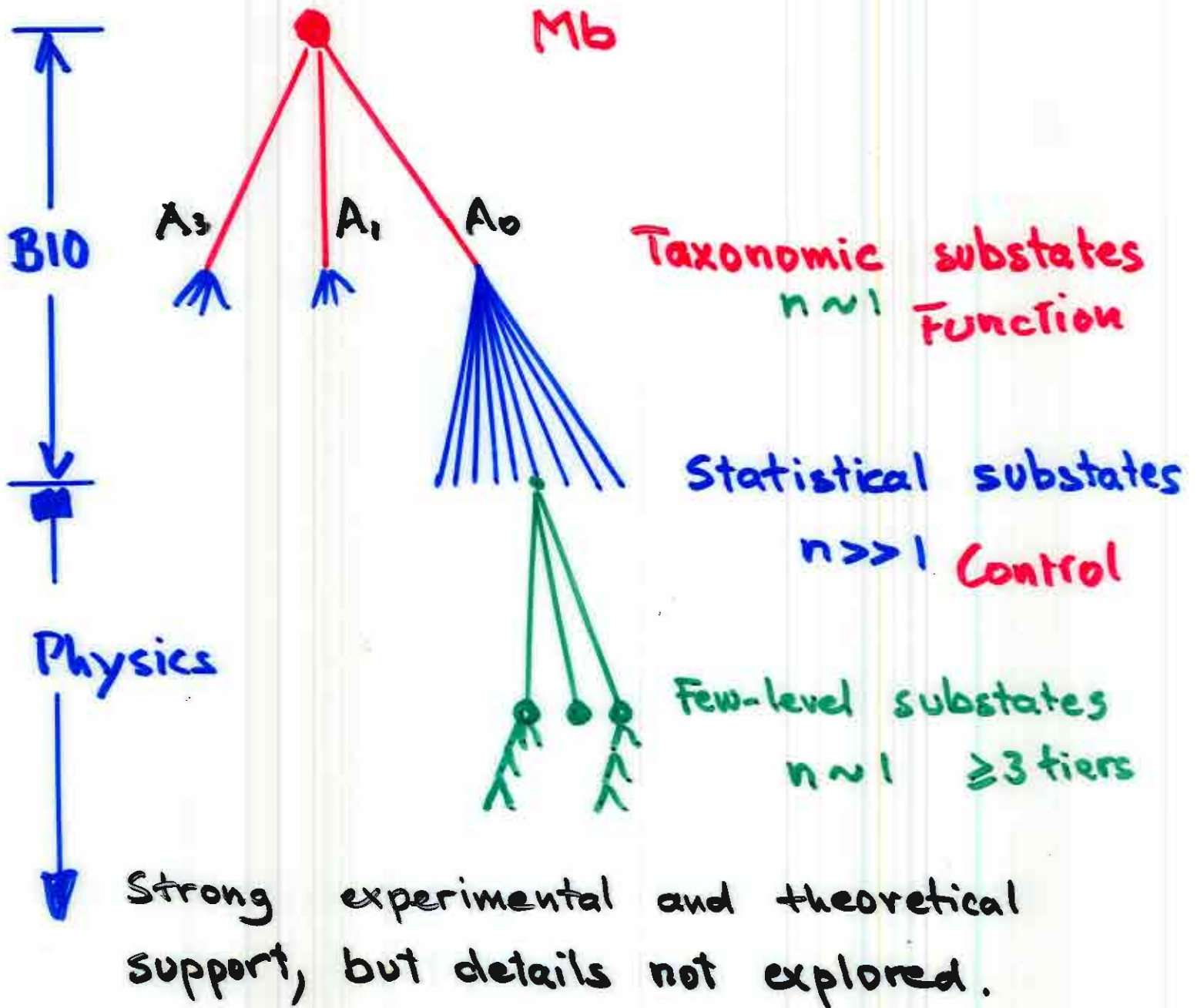
2. GLASTEMP. $T > T_g$: fluctuations.
 $T < T_g$: CS frozen \rightarrow distributions!!

ORGANIZATION OF THE EL

Experiments show that the EL of proteins is organized hierarchically into a number of tiers. In other words there are valleys within valleys. . . For the present discussion, only the top three are considered. For myoglobin (Mb), the folding funnel leads into (at least) three “taxonomic substates” :



THE EL : HIERARCHY

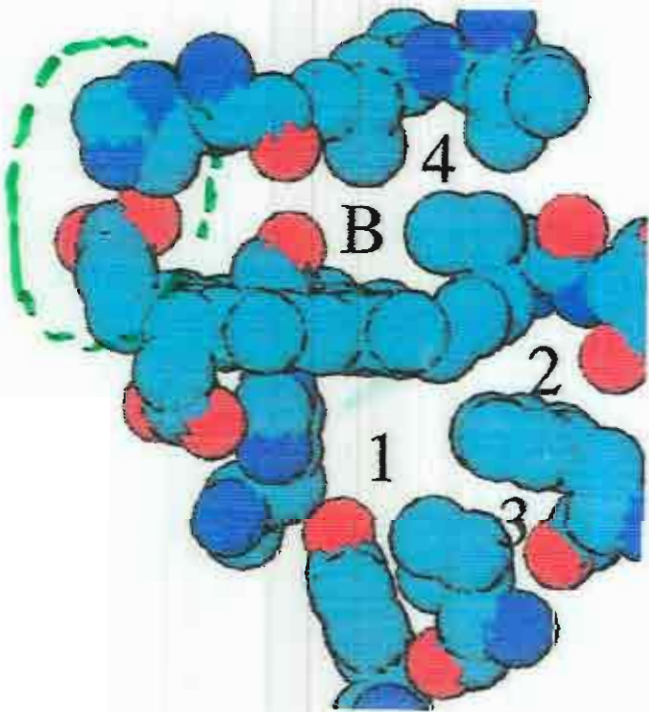


TAXONOMIC SUBSTATES

"Small" structural differences.

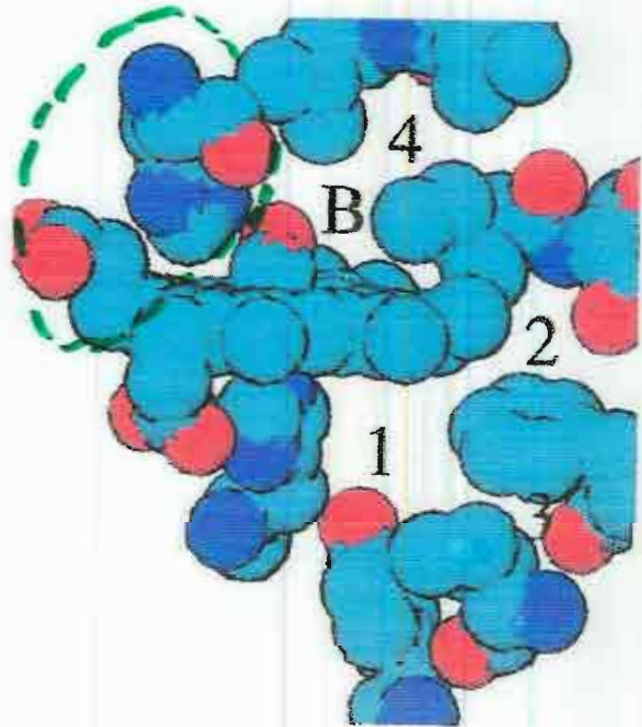
→ Large functional differences.

"NO" catalysis
↓



A₀MbCO

O₂ storage
↓



A₁MbCO

THE EL : QUESTIONS

Hierarchical organization

Dynamics

Connection to structure

Connection to function.

Understanding only at a primitive state.

Bohr atom state?

Use myoglobin as standard protein. Results are, however, more general.

LOCAL SUBSTATES

6338 *J. Phys. Chem. B*, Vol. 101, No. 33, 1997

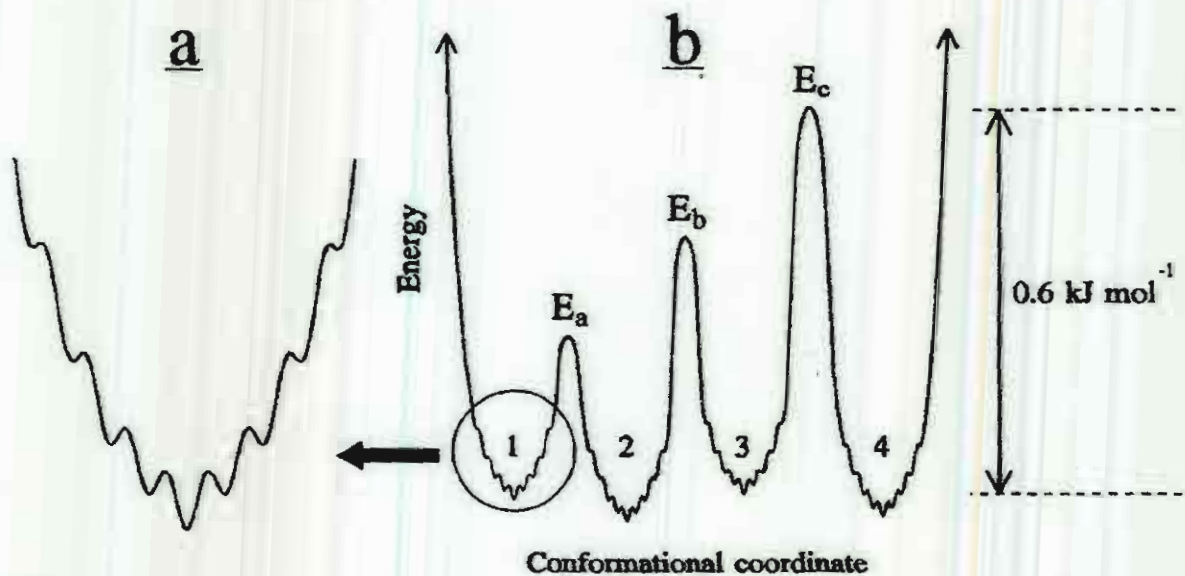


Figure 10. Schematic representation of the energy landscape of myoglobin in the region up to 1 kJ mol⁻¹ based on the results presented.

Spectral hole burning

Thoru Leeson, Wiersma, ...

Protein states and proteinquakes

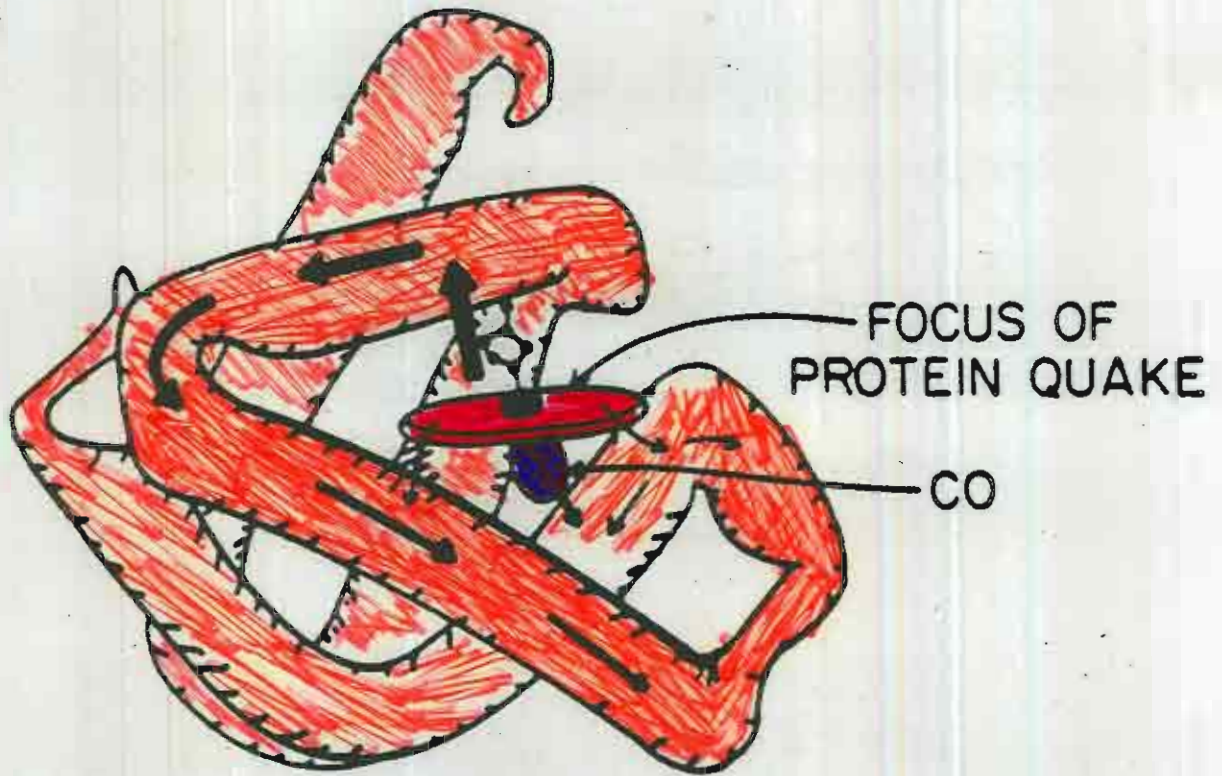
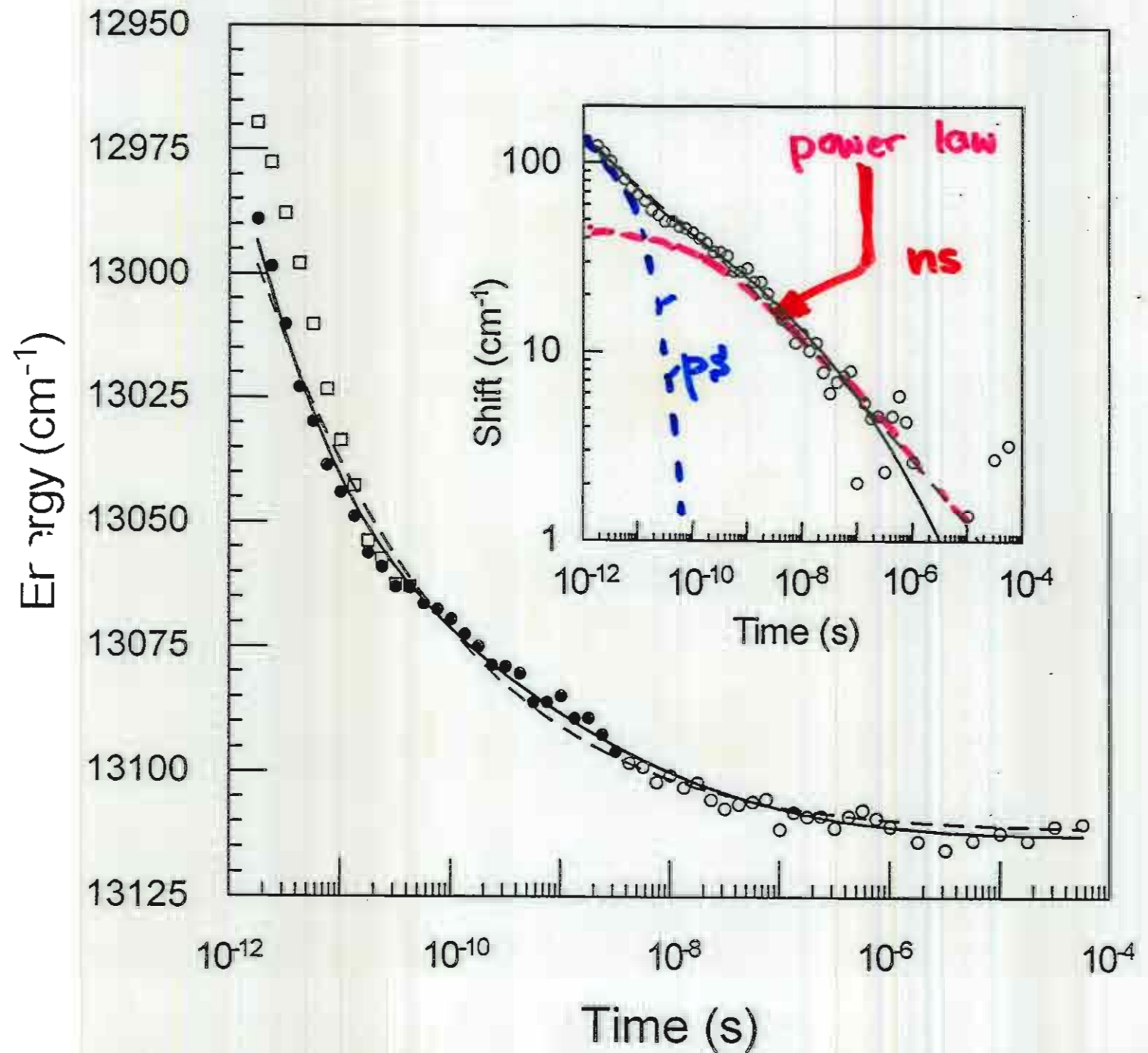


FIG. 1. Proteinquake. Binding or dissociation of a ligand at the heme iron causes a proteinquake.

Myoglobin. (binds O_2 , CO, ...)

PROTEIN QUAKE



Anfinrud et al.

Shift of a spectral line.

LOCAL (TLS) SUBSTATES

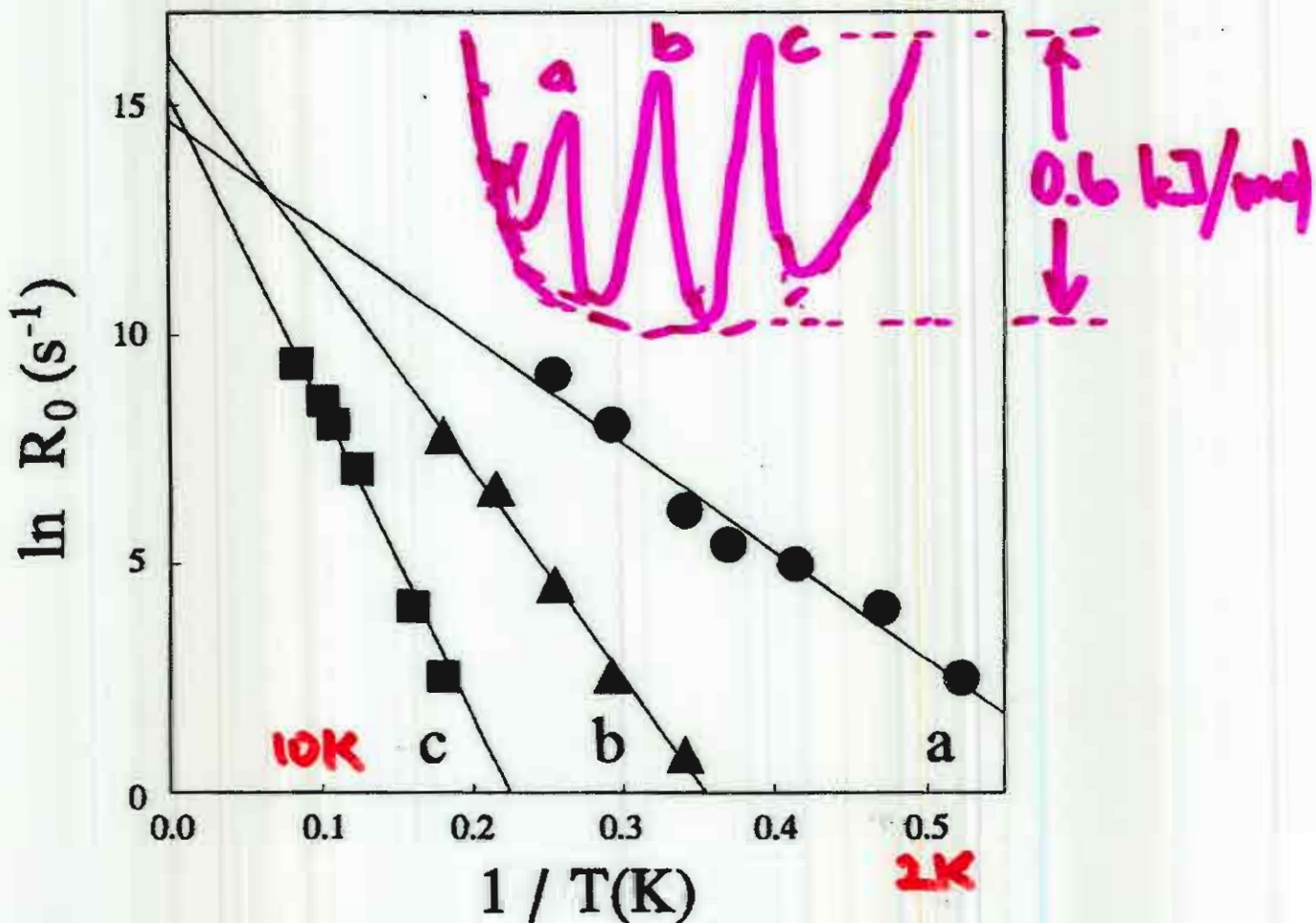


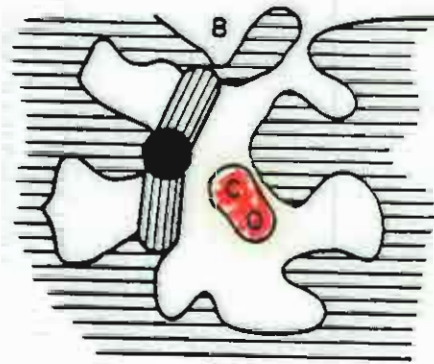
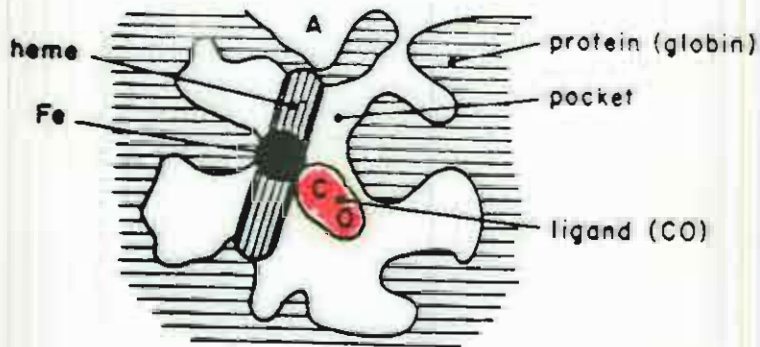
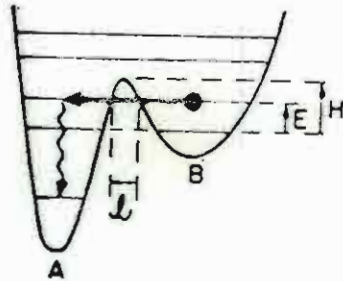
Figure 5. Temperature dependence of the fluctuation rates, R_0 , corresponding to the centers of the rate distributions obtained from fits of line broadening data on Zn-mb as shown in Figures 4 and 6. The solid lines are fits to an Arrhenius law.

THORN LEESEON

WIERSMA.

FRIEDRICH.

REACTION I



A
↑
B

Expect : Exponential Binding