Spin Glasses, Biological volution Dynamics, Cancer, and New Materials

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Dept. of Physics
Princeton University

Two parts to this crazy talk:

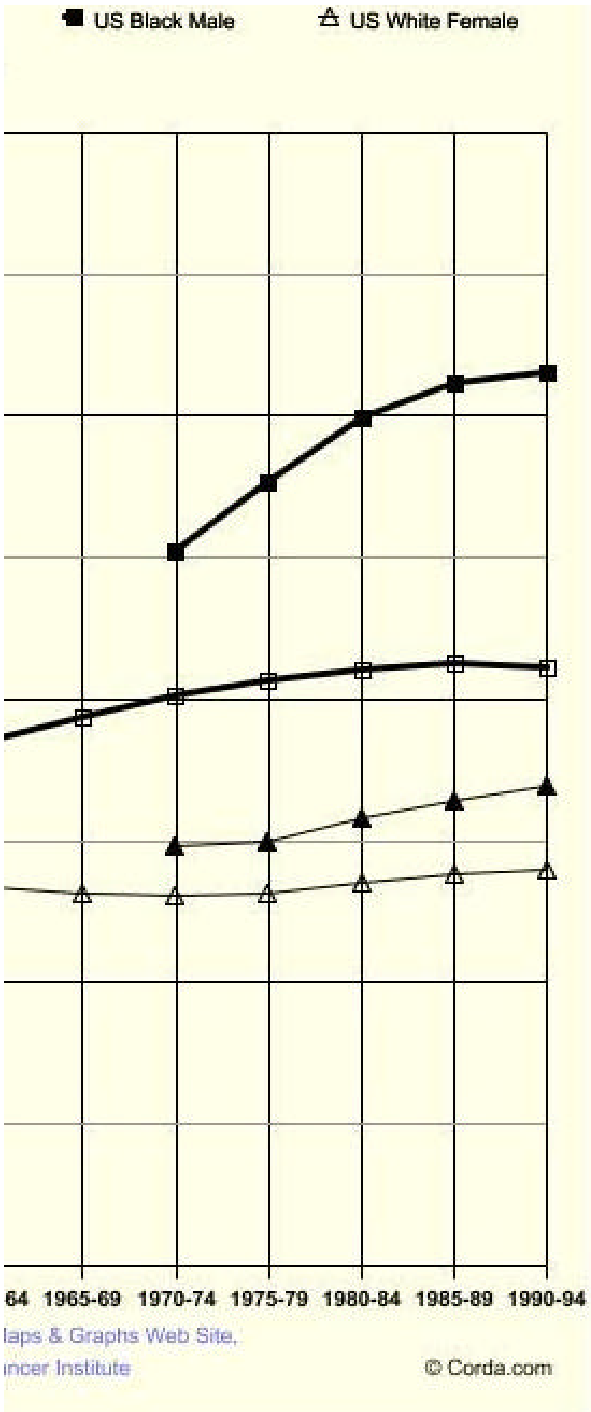
- My materials science theory can shed new light on biology, mayb

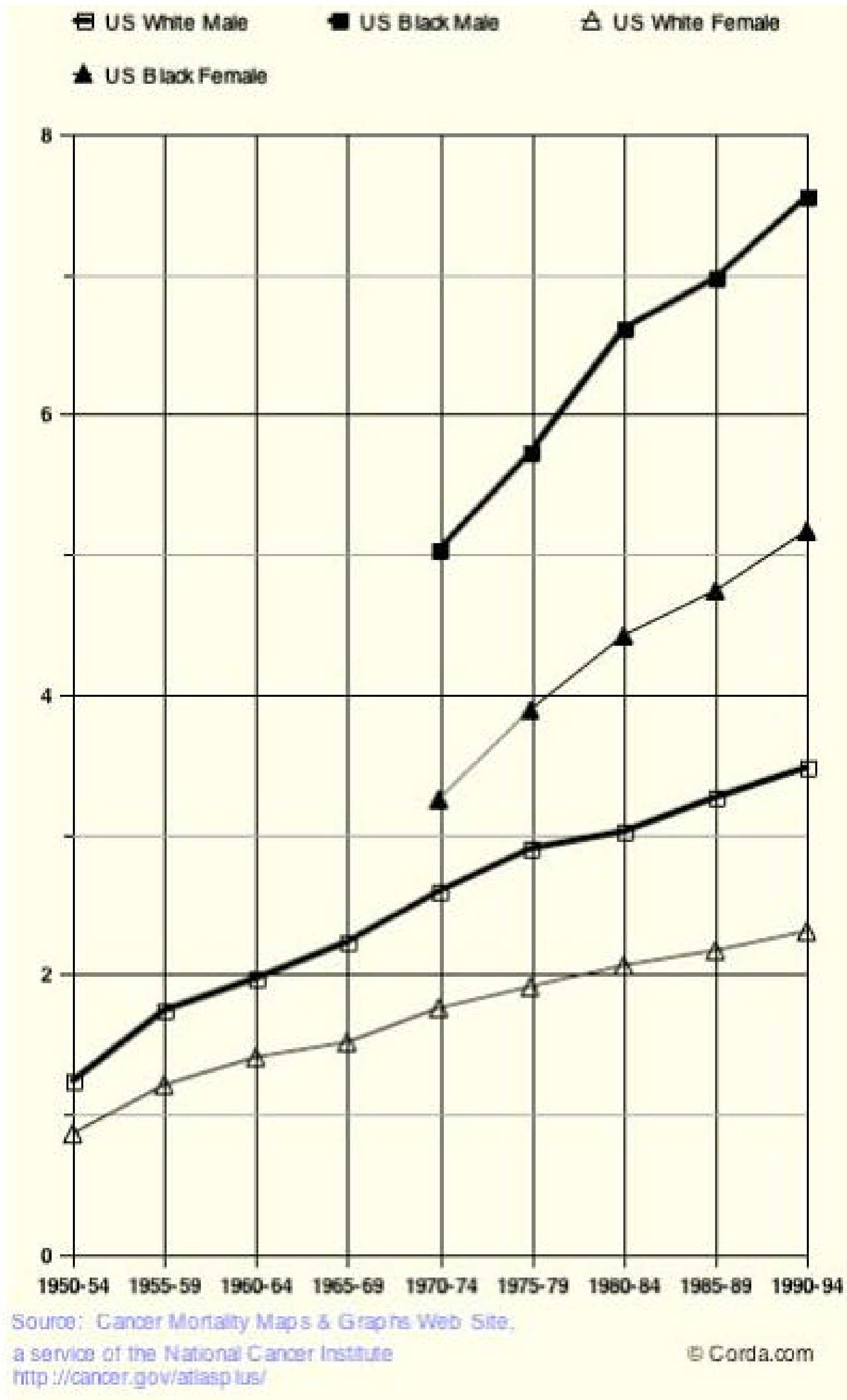
- The challenge to materials scien to create truly complex 3-D designed structures.

I. A Failed War

The National Cancer Institute (N
just finished a series of 3
Workshops
on bringing the hard physical
sciences into oncology (study o
cancer), and not in the usual wa
of building new ways to detect
cancer, but to understand cance

Why? Aren't we making fabulou


US Black Male
US White Female
64 1965-69 1970-74 1975-79 1980-84 1985-89 1990-94
laps & Graphs Web Site,
ıncer Institute
© Corda.com


US White Male
US Black Male
US White Female
US Black Female
8
6
4
2
0
1950-54 1955-59 1960-64 1965-69 1970-74 1975-79 1980-84 1985-89 1990-94
Source: Cancer Mortality Maps & Graphs Web Site,
a service of the National Cancer Institute
http://cancer.gov/atlasplus/
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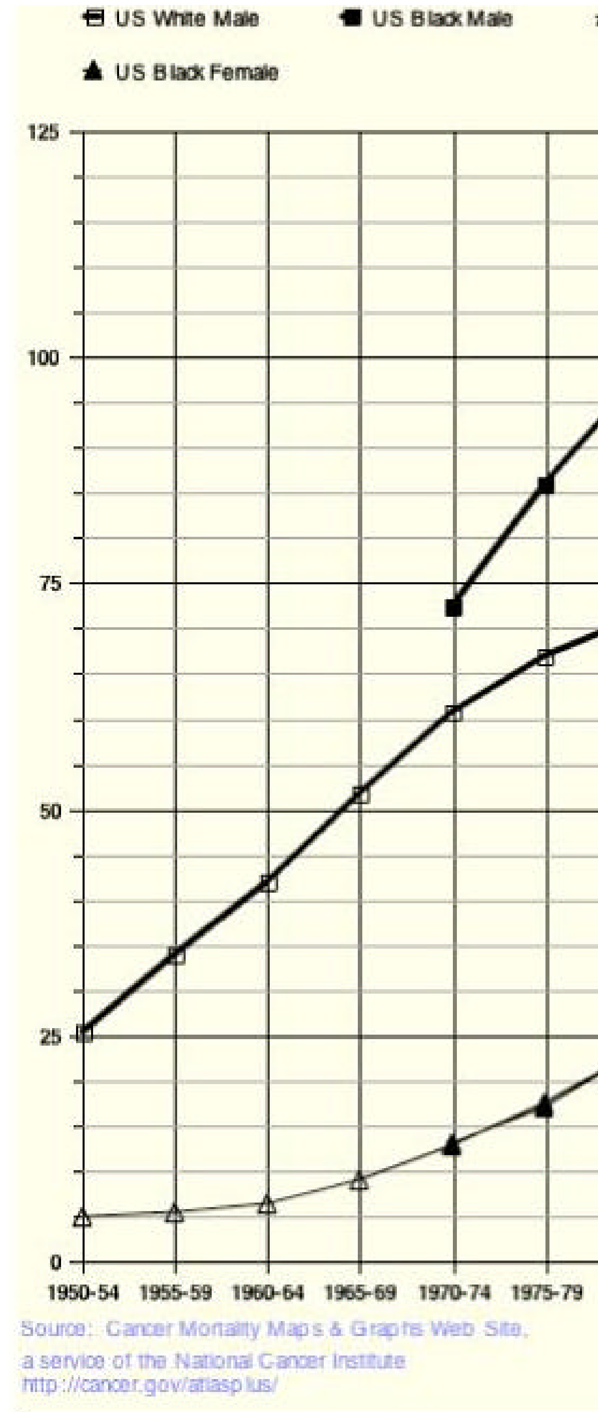
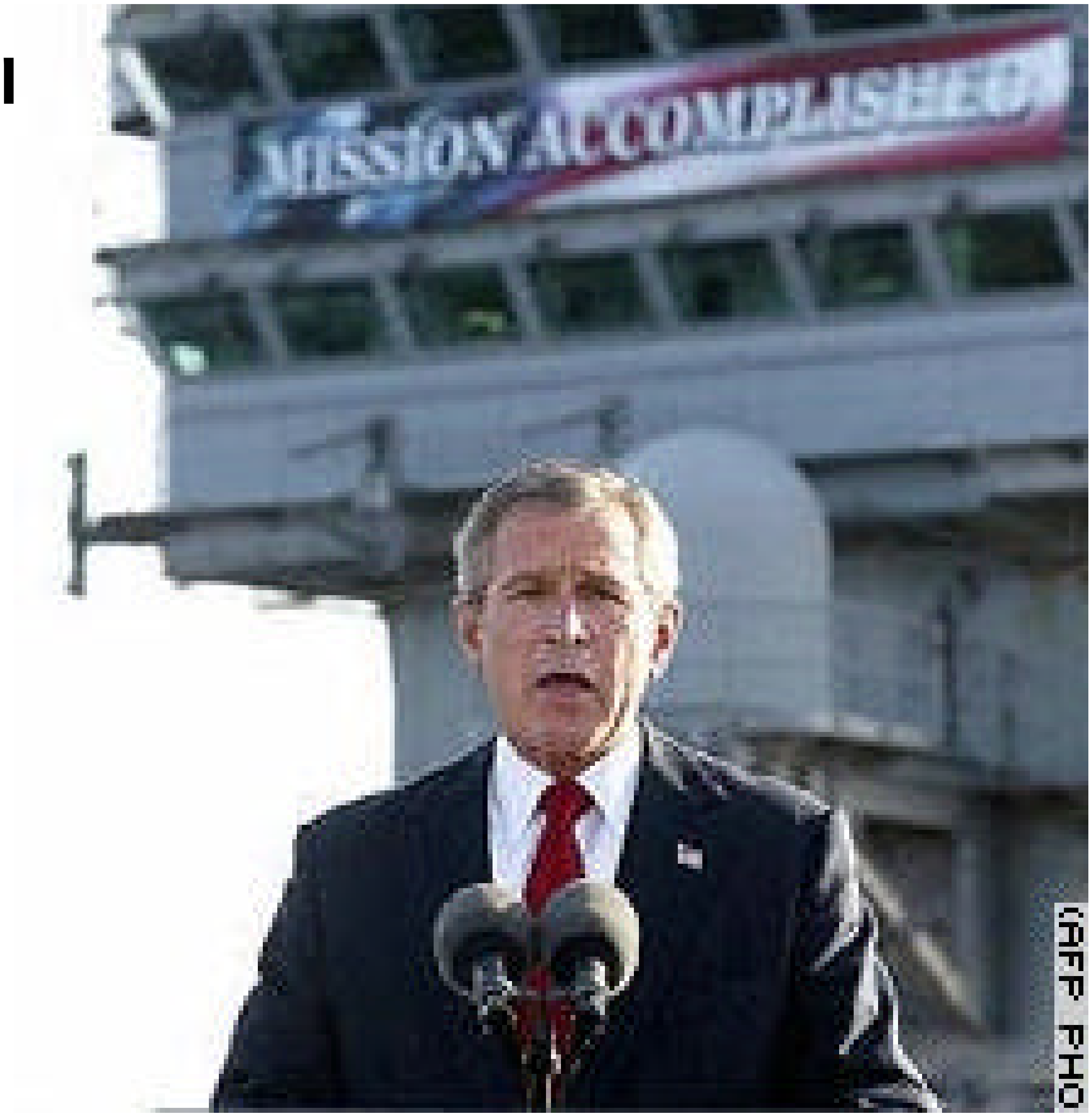

US White Male
US Black Male
US Black Female
125
100
75
50
25
0
1950-54 1955-59 1960-64 1965-69 1970-74 1975-79
Source: Cancer Mortality Maps & Graphs Web Site,
a service of the National Cancer Institute
http://cancer.gov/atlasplus/

ed by relapse after 2 years, which was fatal.
old story.

happe
y?



Where is th

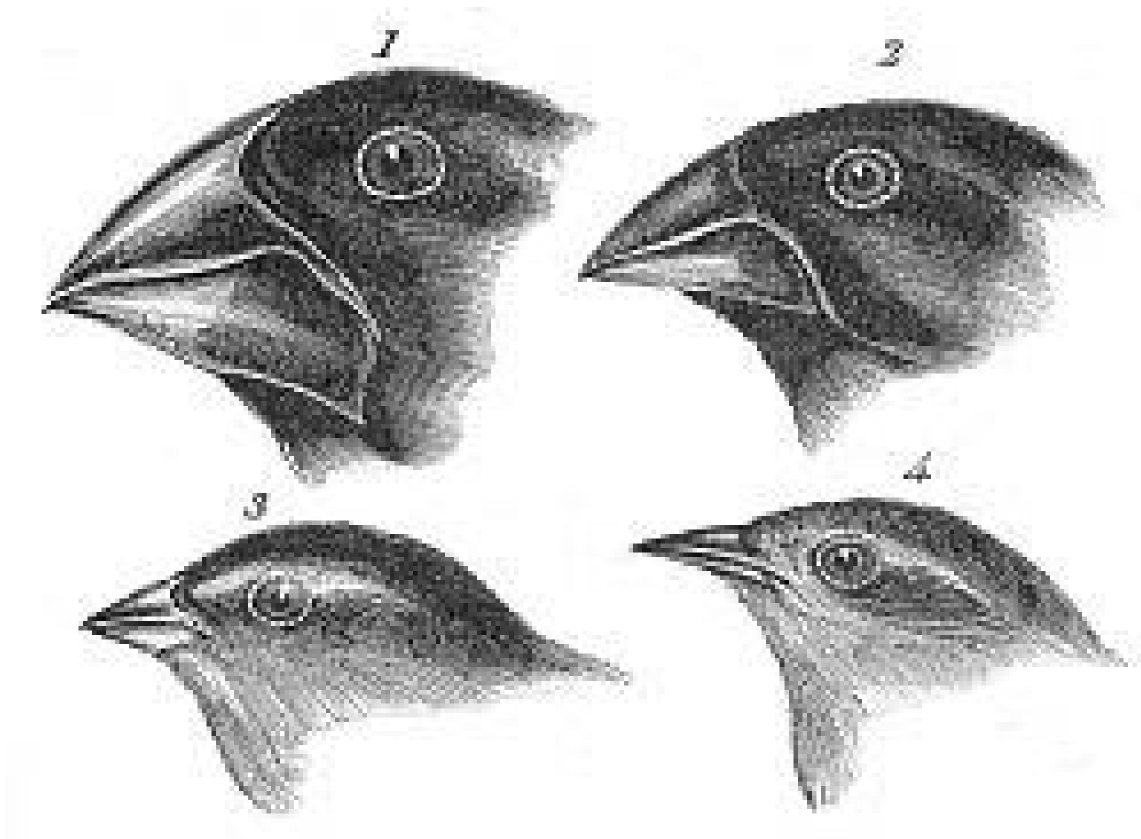
II. Darwin and Evolution: proble

and examine the mathemati
and biological foundations
evolution and natural selecti
you can soon feel yoursel
becoming dangerously clos
the ranks of excommunicat
scientists who wonder: ho
well do we really understar
the dynamics of evolutior
under stress?

This I think is one of our gr

random, point mutations explain the
ible rates of evolution observed in Nat

iverse beaks of Darwin's finches were
keys to natural selection. But, it was a
/ation.



ut Peter and Rosemary Grant
rinceton) found that there was much
ore to Darwin’s finches then even he
ought.

documented some 13 species of "Darwin's Finc
ıg:

hat is flightless

hat cohabits with
iguanas

the vampire finch
es on blood

hat is entirely
rian;

s and traced their elaborate lineage, ng them to document the changes tha dual species make, primarily to their be ction to the environment.

g prolonged drought, for instance, bea ecome longer and sharper, to reach th of seeds.

s the problem: we are talking about ands of birds, not millions. We are talk beaks that change over periods of yea of Darwin's finches and the small population size pose a severe problem for this kind of a model.

$$\Delta N = suN$$

$$u << 1$$

$$s << 1$$

ma''.

implply put, it says that the number g of
ations needed to "fix" a mutation is ab

ation of this magic number 300 is rath
but it is roughly ln(1/su).

se problem is then optimizing (fixing)
: now we are talking about 300,000
ations. That's too long.

d evolution on his little islands.
y?

nk 2 things are at work:

ess drives evolution (and stress
es cancer) in a non-linear way.

all heterogenous populations driv
lution (and drives the evolution of

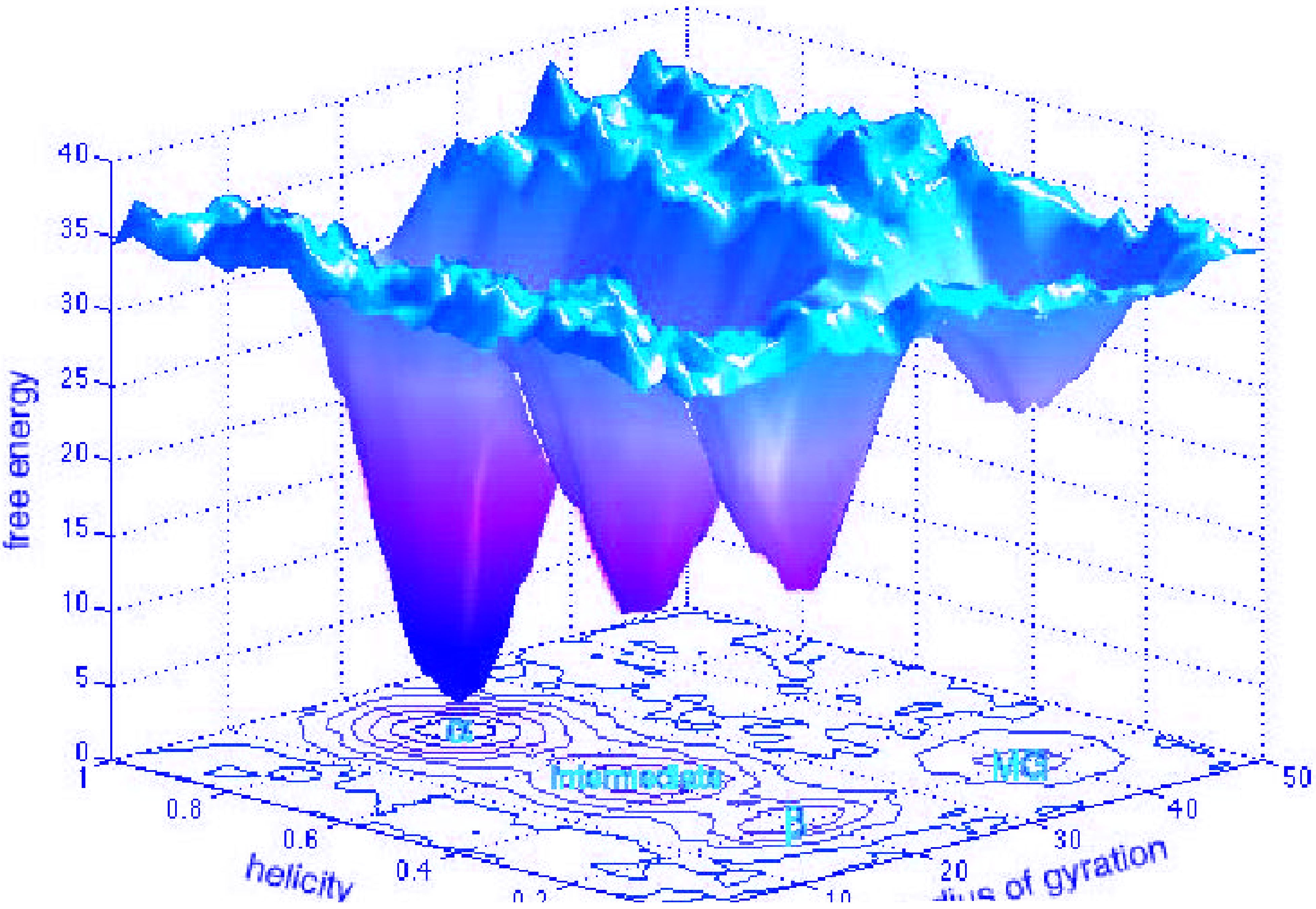
. Proteins, Energy landscapes ar
bin glasses.

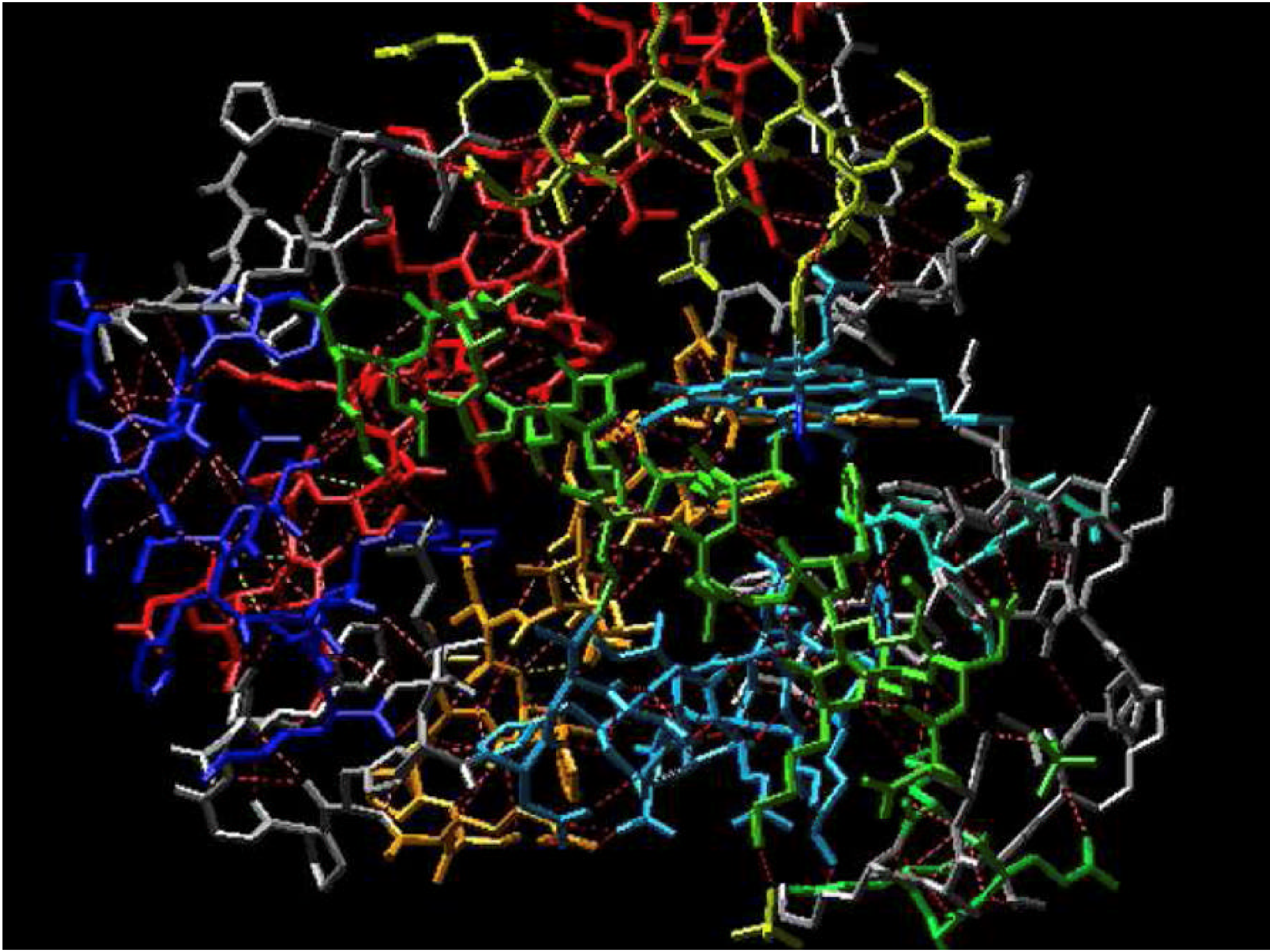
hings happen:

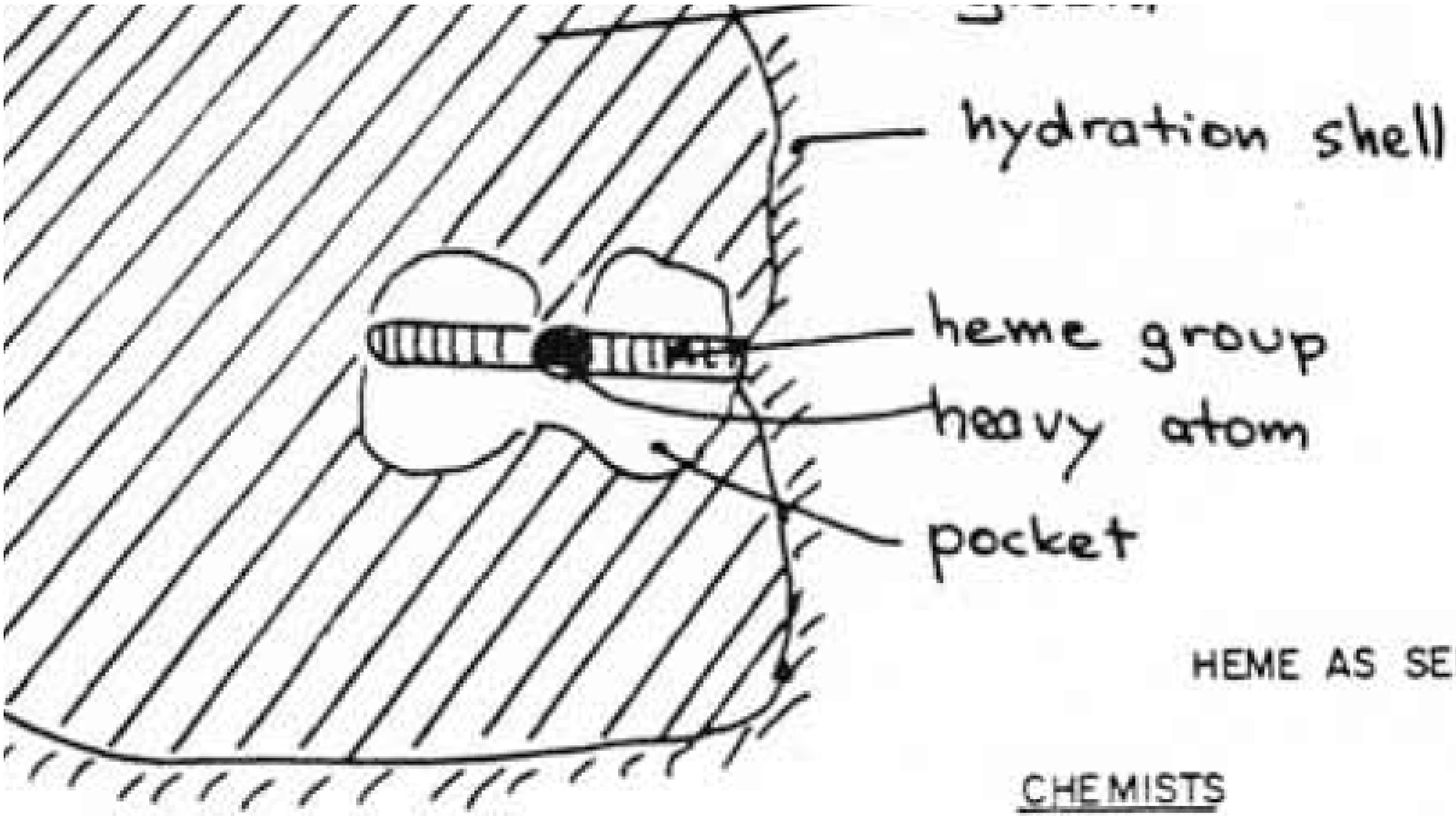
system freezes into a distribution of s
e is no one protein conformation, but a
y landscape of them.

the frozen distribution of states the
onse function" of the system is a pow
an exponential.

e groundwork for rough landscape mo

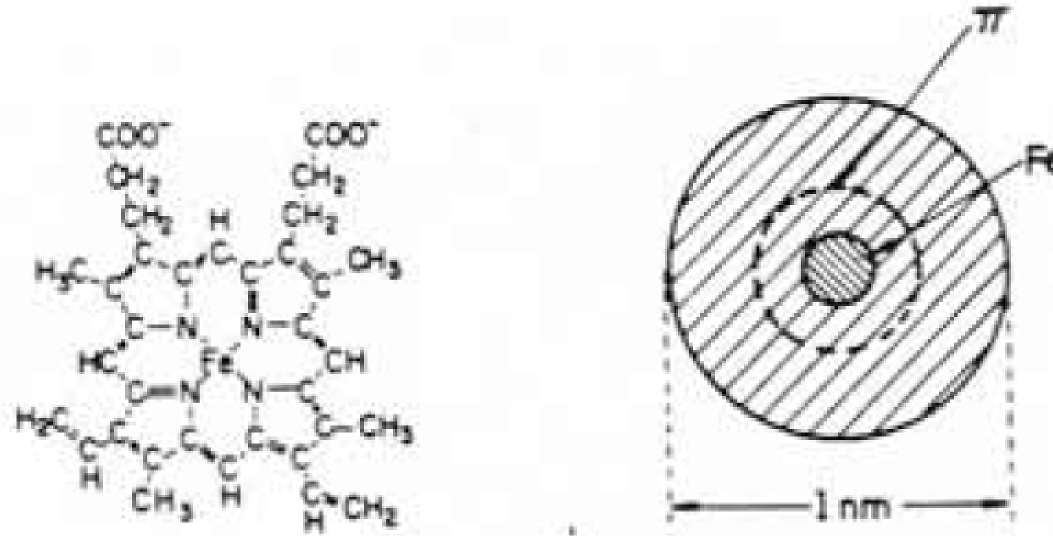






HEME AS SEEN BY

CHEMISTS PHYSICISTS

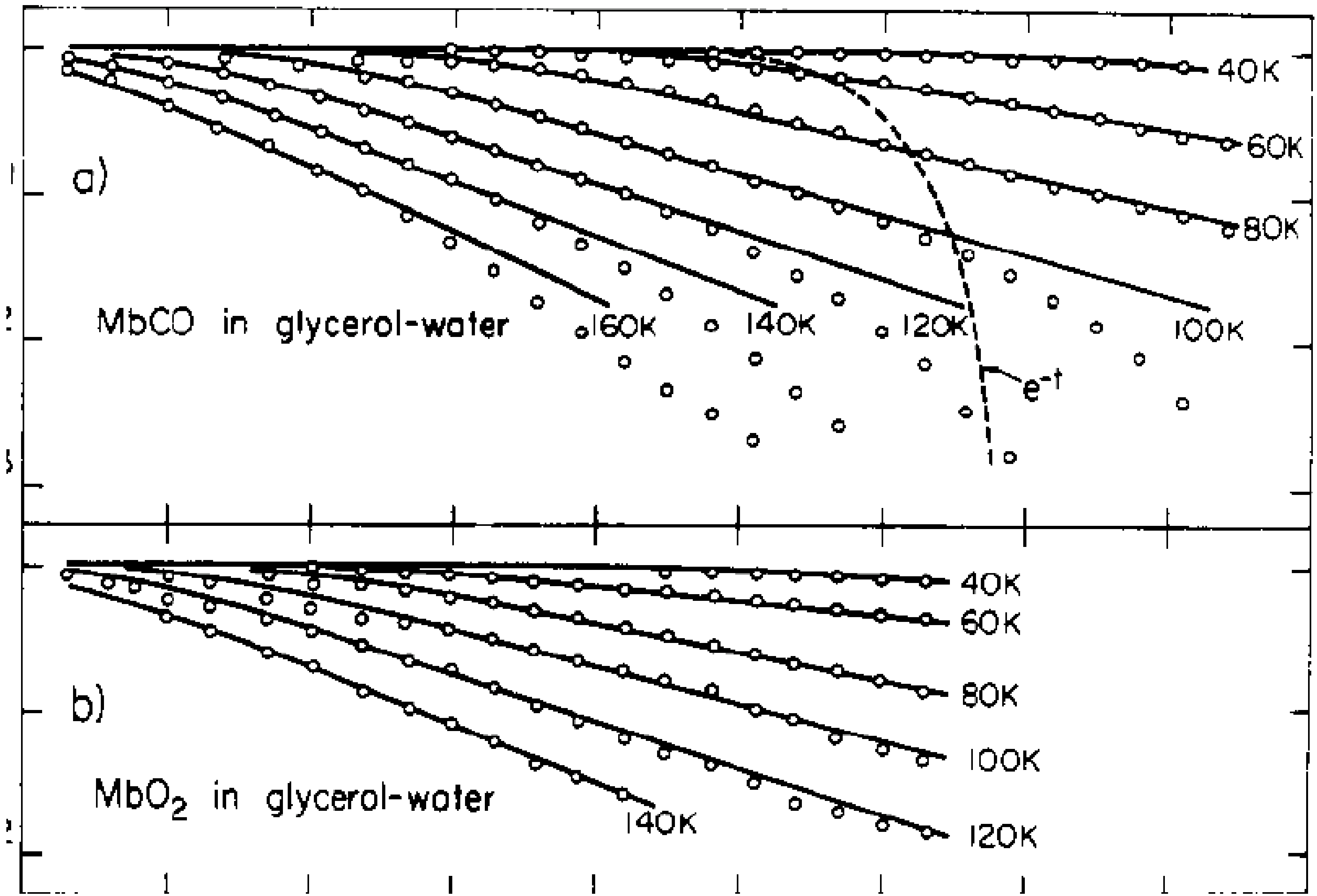


$$\frac{N}{lt} = -R(T)N[CO] \sim -k(T)N$$

$$N(t,T) = N_o \exp[-k(T)t]$$

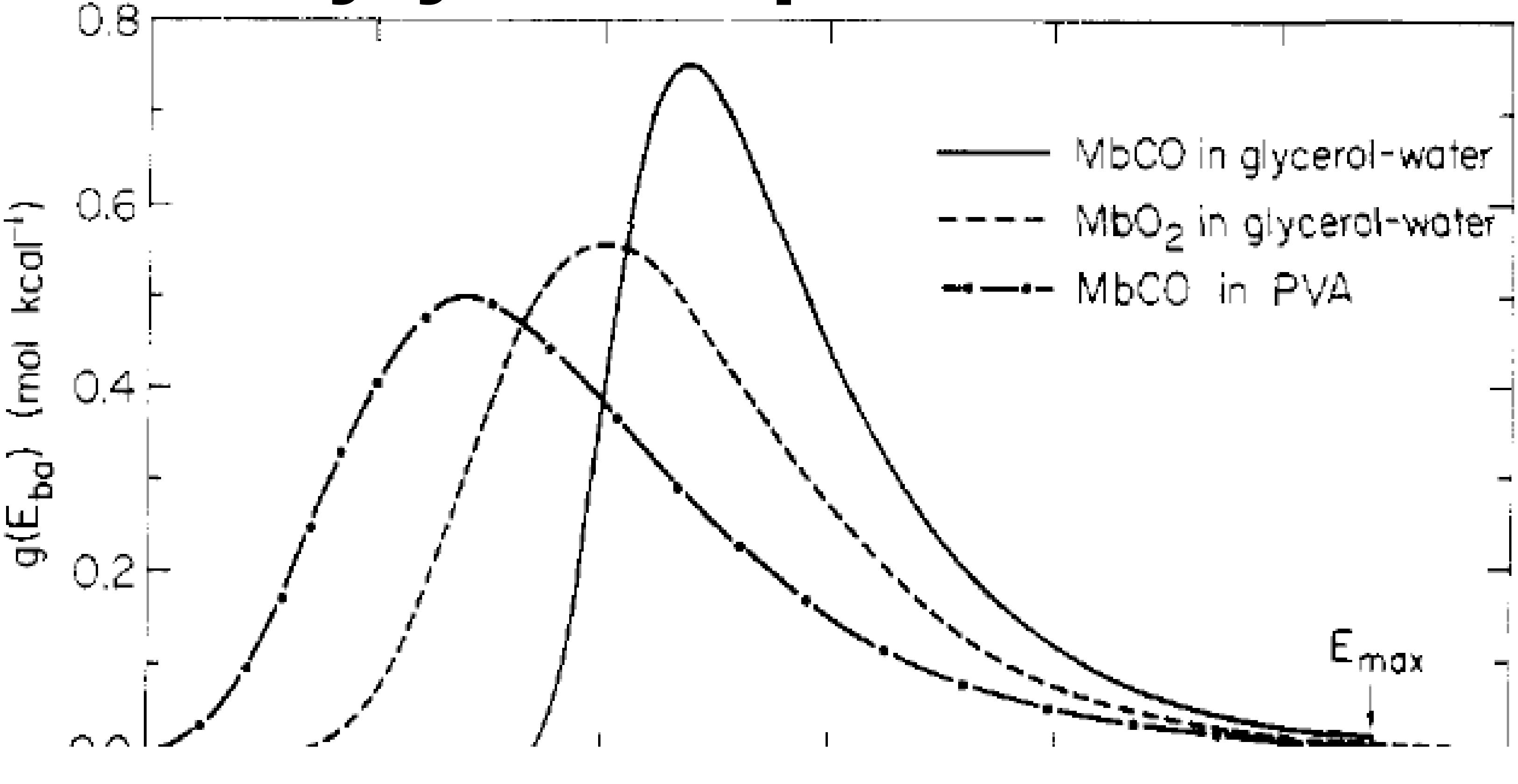
$$k(T) \sim [CO]R \exp[-H_{ba}/k_B T]$$

state rather than water baths as de-



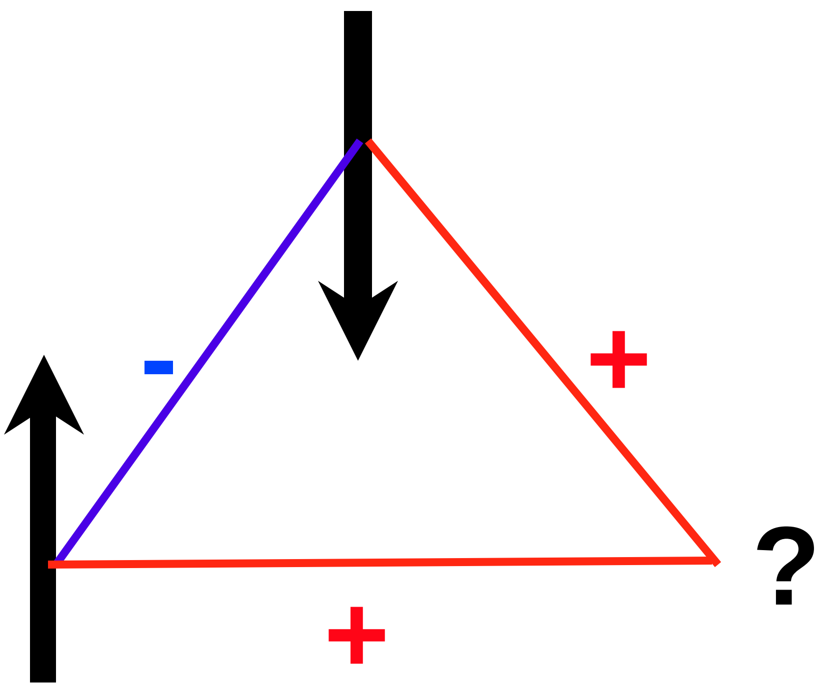
Jo

roteins have a distribution of conform
s, it turns out that the probability distr
:ion (pdf) of the activation energies, g(
otation, must be an exponential in H_{ba}
ematically yield a power law in the tail



is the origin of these probability distributions?

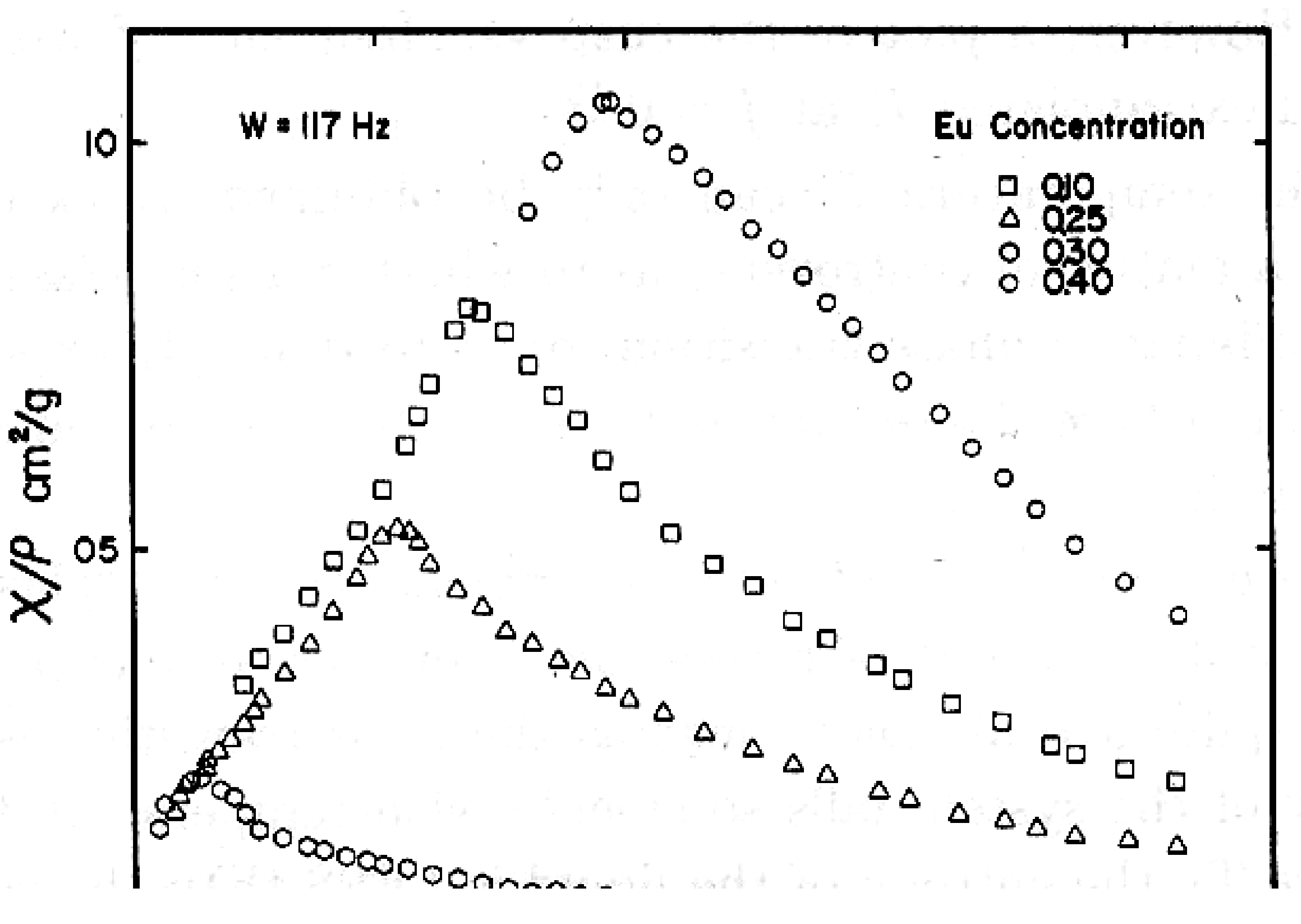
n glass is a system of coupled spin
rustrated interactions.



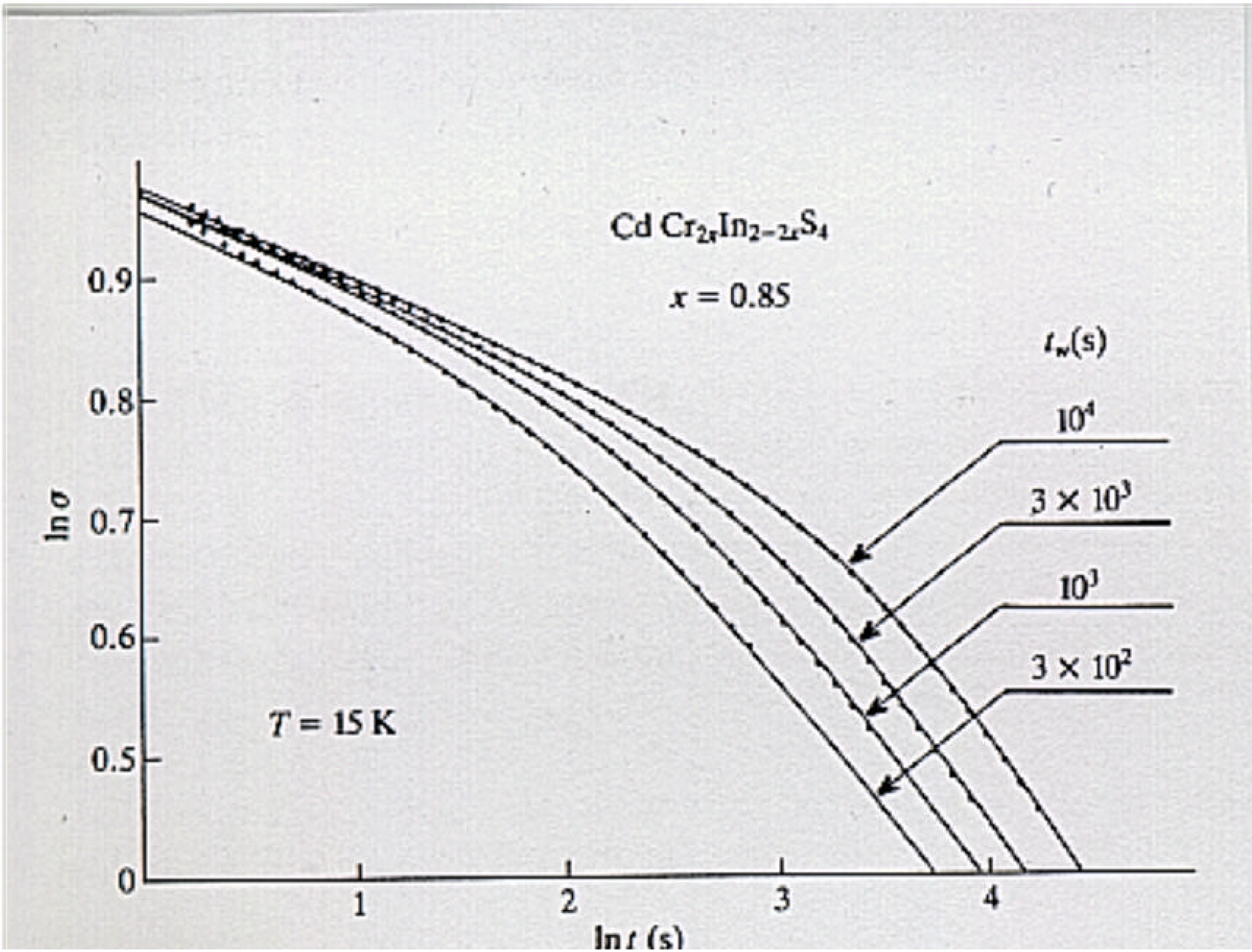
$$H = \Sigma_{i,j} J_{ij} S_i S_j + B$$

lytically even for simplest systems):

pin system has a freezing point, like
:ein.



...ective spin "metapopulations": energy landscape.



en spin metapopulations.

$$d_{\sigma,\sigma'} = \Sigma_i |\sigma_i - \sigma'_i|$$

$$\sigma = 1, 1, 0, 1, 0, 1$$
$$\sigma' = 1, 0, 1, 1, 0, 0$$

$$d_{\sigma,\sigma'} = 3$$

Ultrametricity for physicists

R. Rammal

Centre de Recherches sur les Très Basses Températures, Centre National de la Recherche Scientifique, BP 166 X, 38042 Grenoble-Cédex, France

G. Toulouse

Ecole Supérieure de Physique et Chimie Industrielles, 10 rue Vauquelin, 75231 Paris, France

M. A. Virasoro

Dipartimento di Fisica, Universita di Roma I, I-00185 Roma, Italy

$$d_{A,C} < d_{A,B} + d_{B,C}$$

le inequality, can be used for minimizing pat
HKUST building labyrinths)

or spin space populations, “stronger”
lity:

$$d_{A,C} \leq Max[d_{A,B}, d_{B,C}]$$

$$\sigma_B = 1, 1, 0, 0, 0, 0, 0$$

$$\sigma_C = 1, 0, 0, 0, 0, 0, 0$$

|:

$$d_{AB} = 5, d_{BC} = 6, d_{AC} < 11$$

se

':

$$d_{AC} \leq Max[5, 6] = 6$$

::

$$d_{AC} = 6$$

.

ısider a sphere of radius R which tains all spin populations whose ɪual distance is less then R.

n: Any other sphere must be either tained within R or be disjoint from ou can't share populations ween different spheres.

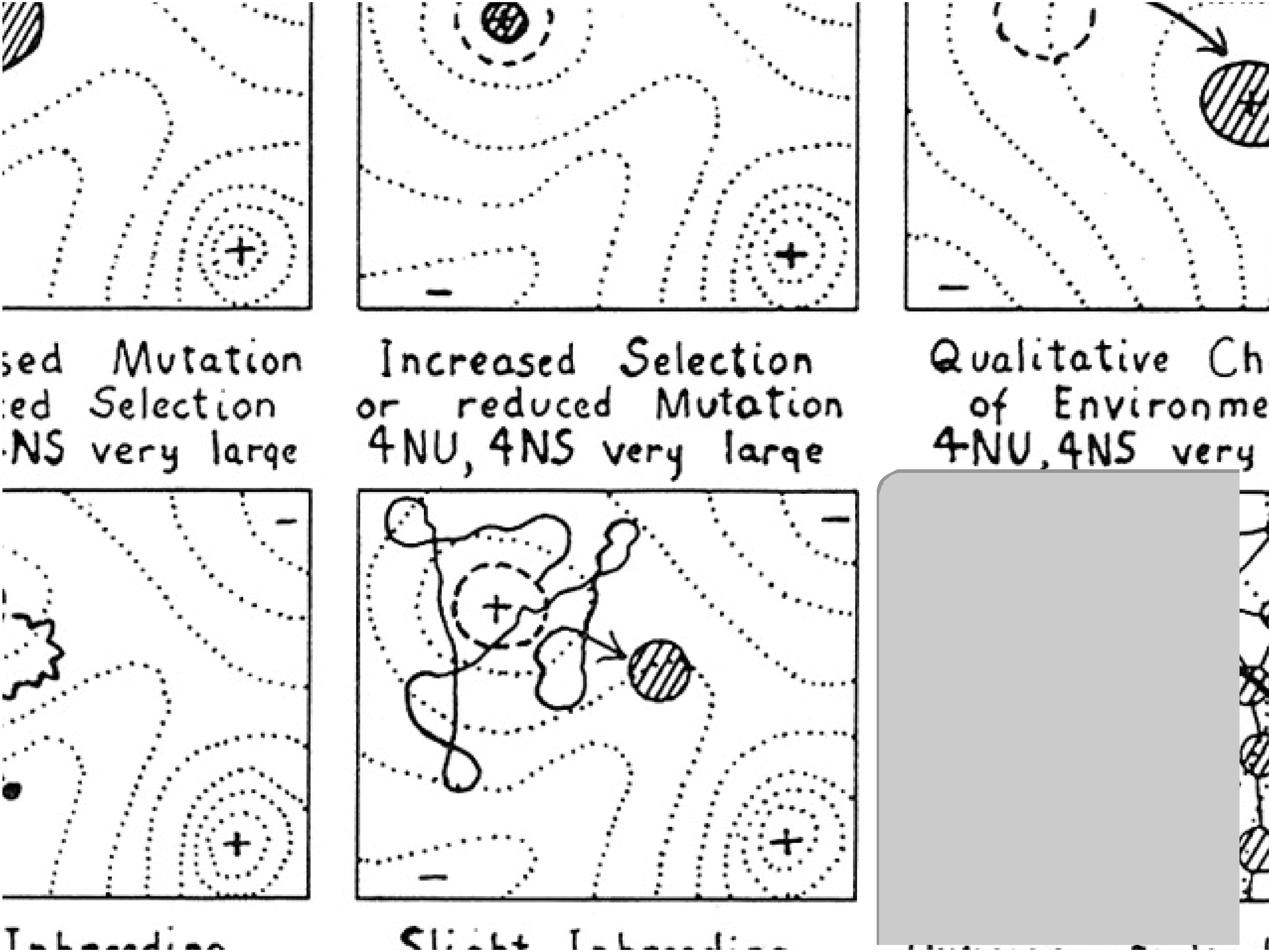
s, you have speciation in spin-

'. Fitness landscapes and spin asses.

scape by a metapopulation is ally a subject of physics interest.

general field is called spin-glass ics, and it is about the flow of rmation".

hird Workshop that the NCI sored was called "Coding, Decod sfer and Translation of informatio er.


sed Mutation
ed Selection
NS very large
Increased Selection
or reduced Mutation
4NU, 4NS very large
Qualitative Ch
of Environme
4NU, 4NS very

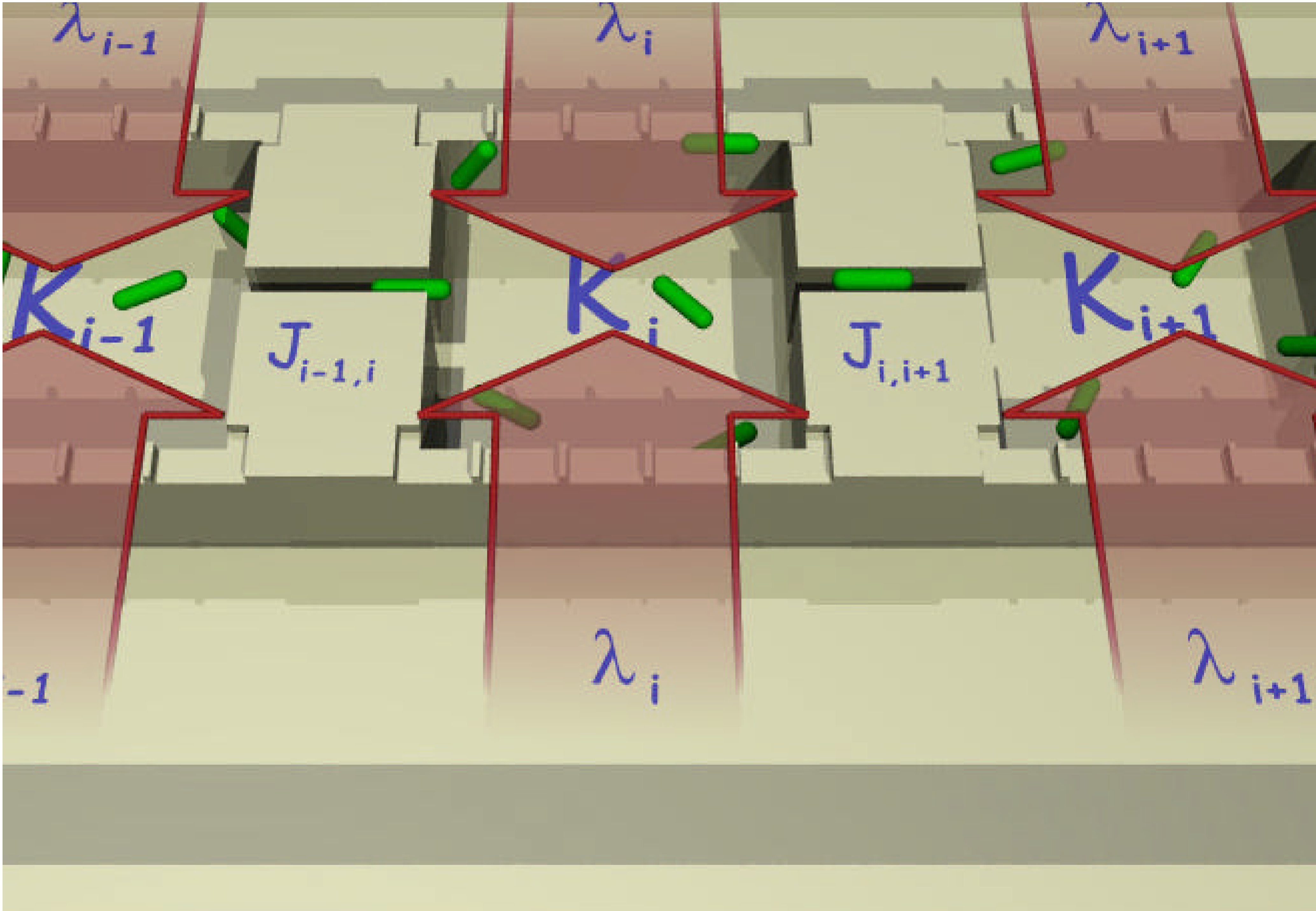
ocal number of individuals with a "qua
:ies" genome homology i.

"interbreeding" between quasi-specie
j, which you can also view of genomic
rangements on a metascale (not SNPs)

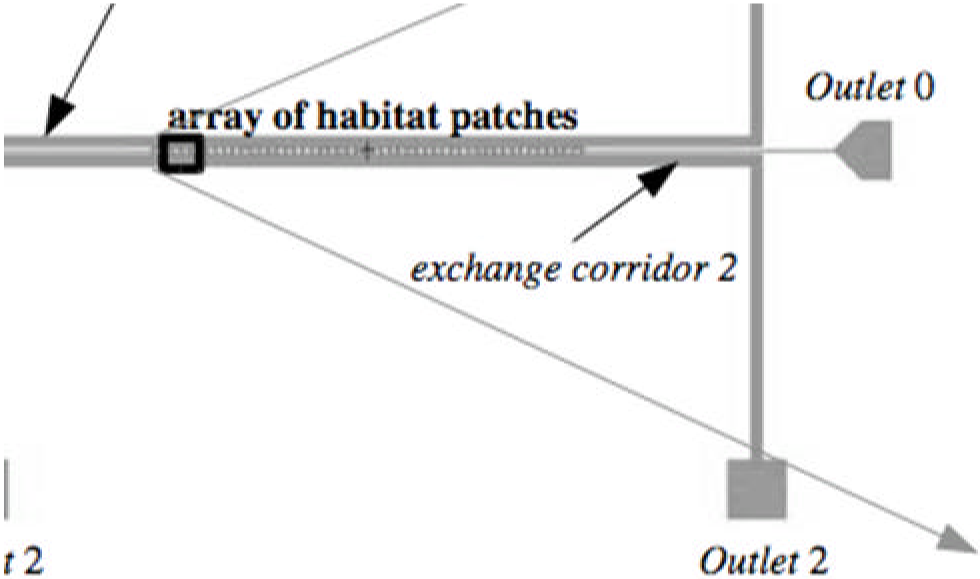
oenvironment is the local fitness arou
quasi-species. In the valley: stress.

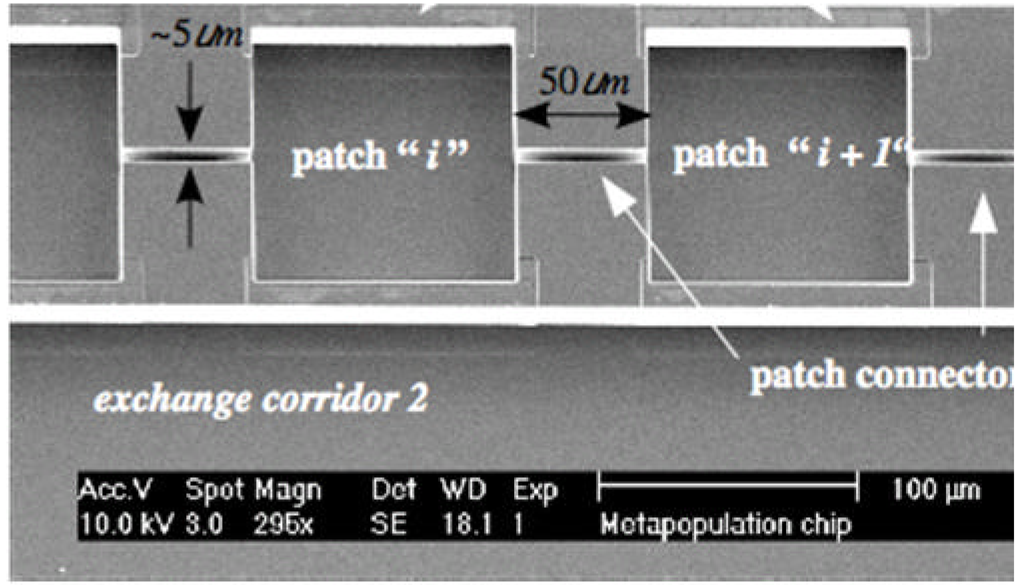
ugged field of this character, selection
carry the species to the nearest peak, b
may be innumerable other peaks which
but which are separated by "valleys."

roblem of evolution as I see it is that of
anism by which the species may contin
s way from lower to higher peaks in suc
n order that this may occur, there must
trial and error mechanism on a grand s
the species may explore the region

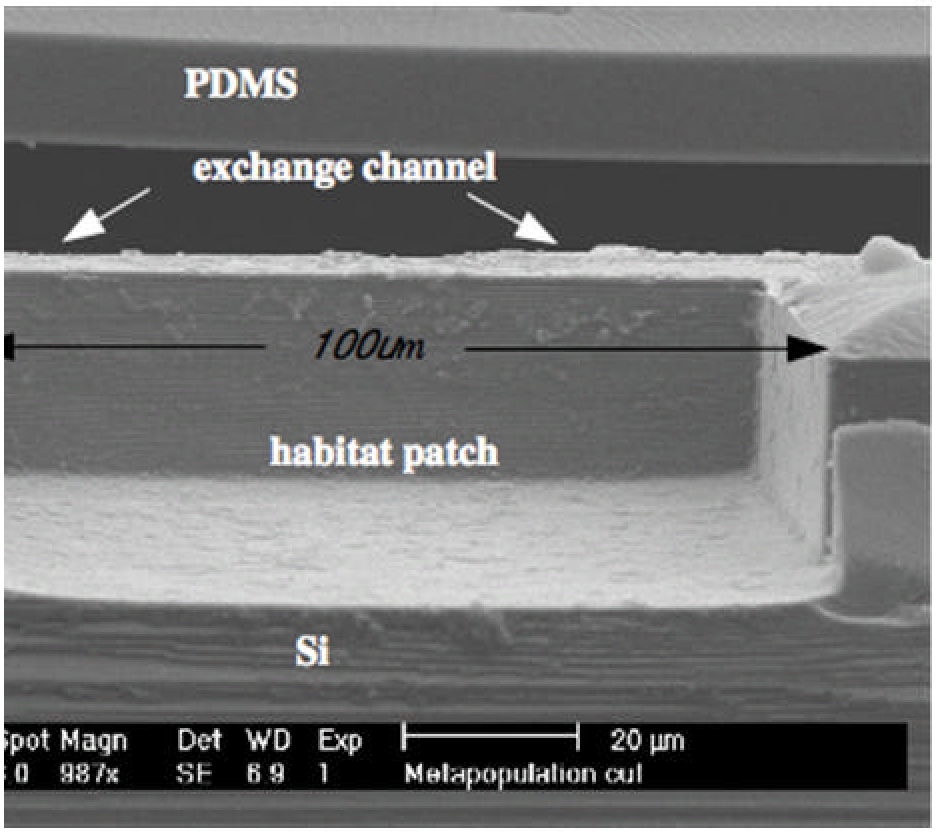


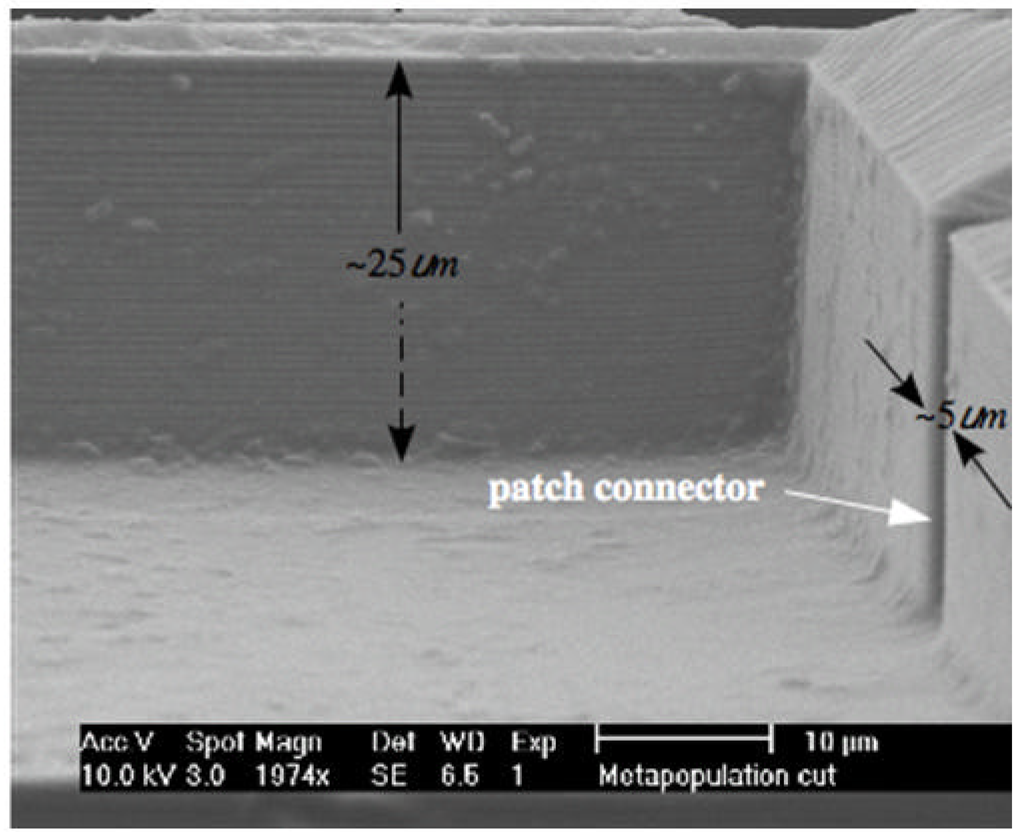
an design fitness landscapes mic

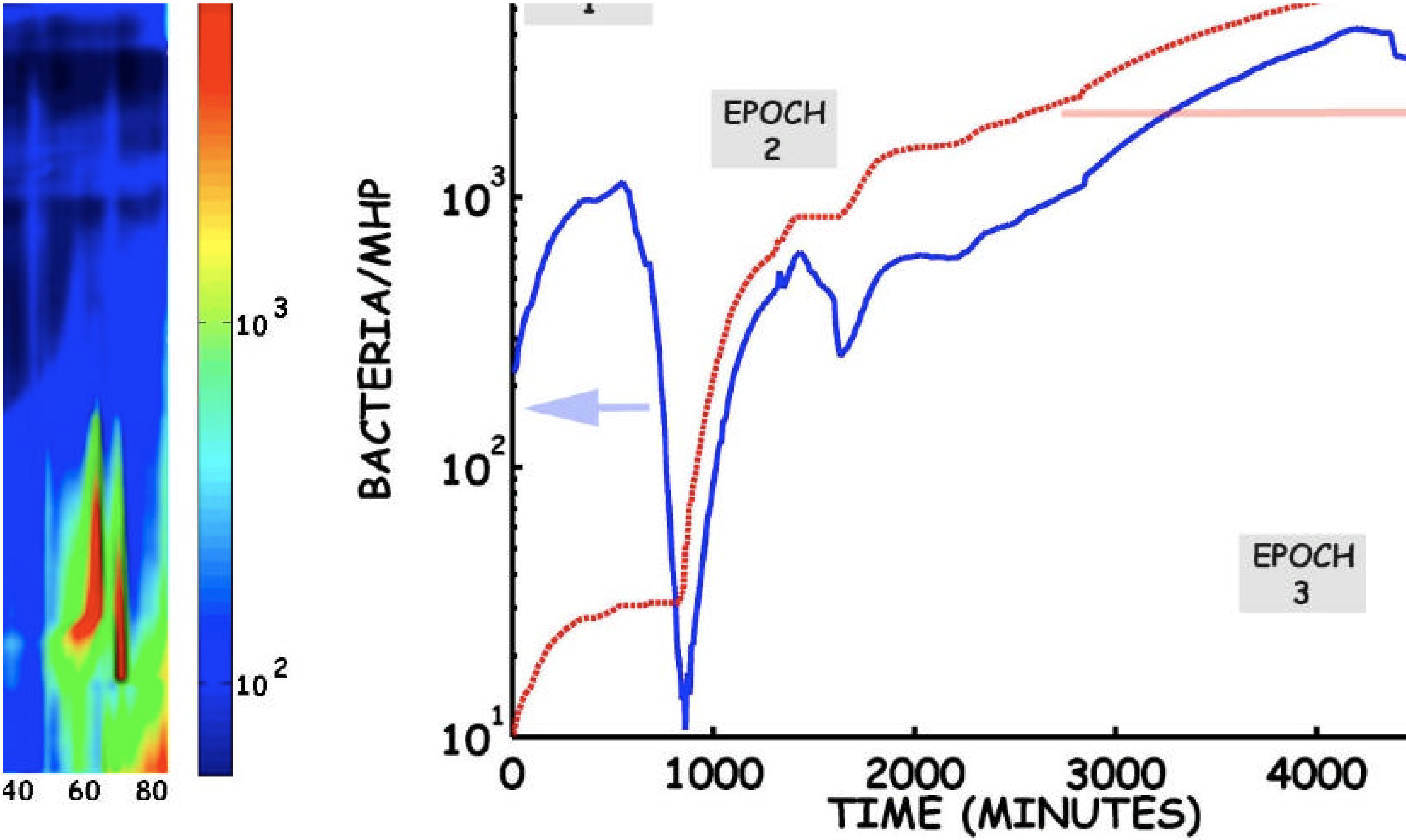

array of habitat patches
Outlet 0
exchange corridor 2
t 2
Outlet 2


~5 um
50 um
patch "i"
patch "i + 1"
exchange corridor 2
patch connector
Acc.V Spot Magn Det WD Exp 100 µm
10.0 kV 3.0 295x SE 18.1 1 Metapopulation chip

(C) **(D)**


PDMS
exchange channel
100um
habitat patch
Si
Spot Magn Det WD Exp 20 µm
987x SE 6.9 1 Metapopulation cut


~25 um
~5 um
patch connector
Acc.V Spot Magn Det WD Exp 10 µm
10.0 kV 3.0 1974x SE 6.5 1 Metapopulation cut



a “learned” to grow more slowly and exploit stres
bitats. In this sense we see the evolution of resi

population sizes in microhabitats in evolution dynamics.

ective advantage s to “fix” (dominate)
lation of N individuals?

$$< t > \sim \frac{1}{s} ln(N)$$

s, the larger the population, the longer
to fix a mutation. Large populations b
ion rates, and is connected to the pow
s.

evolution can proceed more rapidly if
up a population N into sub-population
abers, and let them interbreed at rate r

$$\langle t \rangle \sim \frac{1}{s}\ln(N)$$

s is a very strange and important resul
ays that the combinatorics (entropy!) o
ogenous genome gives rise to slower
f a trait with increasing populations siz

different then, say, radioactive decay, w
mean lifetime for 1/2 the atoms to deca
independent of the number of atoms.

e we can define distances and aps amongst genomes using encing and mapping, evolution mics has become quantitative. It ’t with Darwin.

ution on a fitness landscape thus mes a biased random walk proble e the distance between genomes easured, with mutations acting as

V. Cancer and spin glasses: the delicate balance between rapid evolution, freezing, and melting

bution of the little metapopulation
that move evolution forward rapid
Wright called:

trial and error mechanism on a
d scale by which the species m
ore the region surrounding the
l portion of the field which it
pies."

e selection s is "too small, you
imulate
may bad mutations and the popu
s a "mutational meltdown".

k of the Royal Families of Europe
ce Charles.

s, you need a finite selection pres

ntain a stable small population

e metapopulation size n is too sma
y local maxima in local fitness you
a “complexity catastrophe”
fman) and the system is stuck in
glass frozen state even at finite
erature:

distance <d> to local maximum g
g(n), so always near local maximu

catastrophic genomic delocalizat

ke that expression because it sou
ke quantum mechanics).

omic delocalization means that th
xist no stable solutions to populat
quations, no quasi-species, and th
ystems wanders through sequenc
pace.

occurs at ar u^* 1reshold u* g

$$\frac{\quad}{n^*} \sim 1$$

is an important result;

iere is an analogy between phase sitions in physics and genomic ibilities in genomics. u* = melting ɔerature.

iere is “danger” in too small a

e is a dual purpose to stress (= tion):

ss drives natural selection and tion. No stress, no evolution.

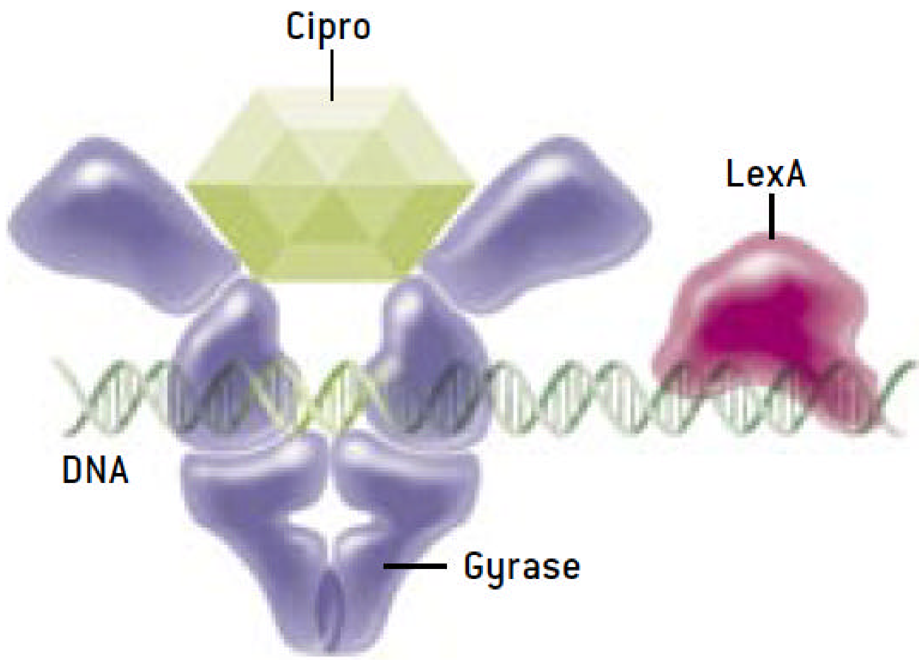
ss causes mutations, and change

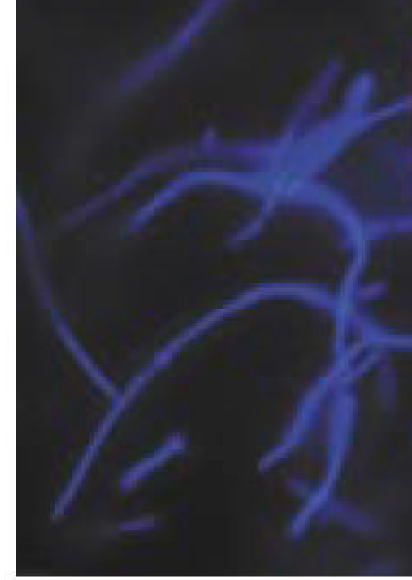
eased stress = increased mutatior

nutations in *Escherichia coli* bacteria can undermine the effectiveness
acin (cipro), an antibiotic that is increasingly being prescribed by physicians.

tion

harms bacteria
an enzyme
e and preventing
ioning properly

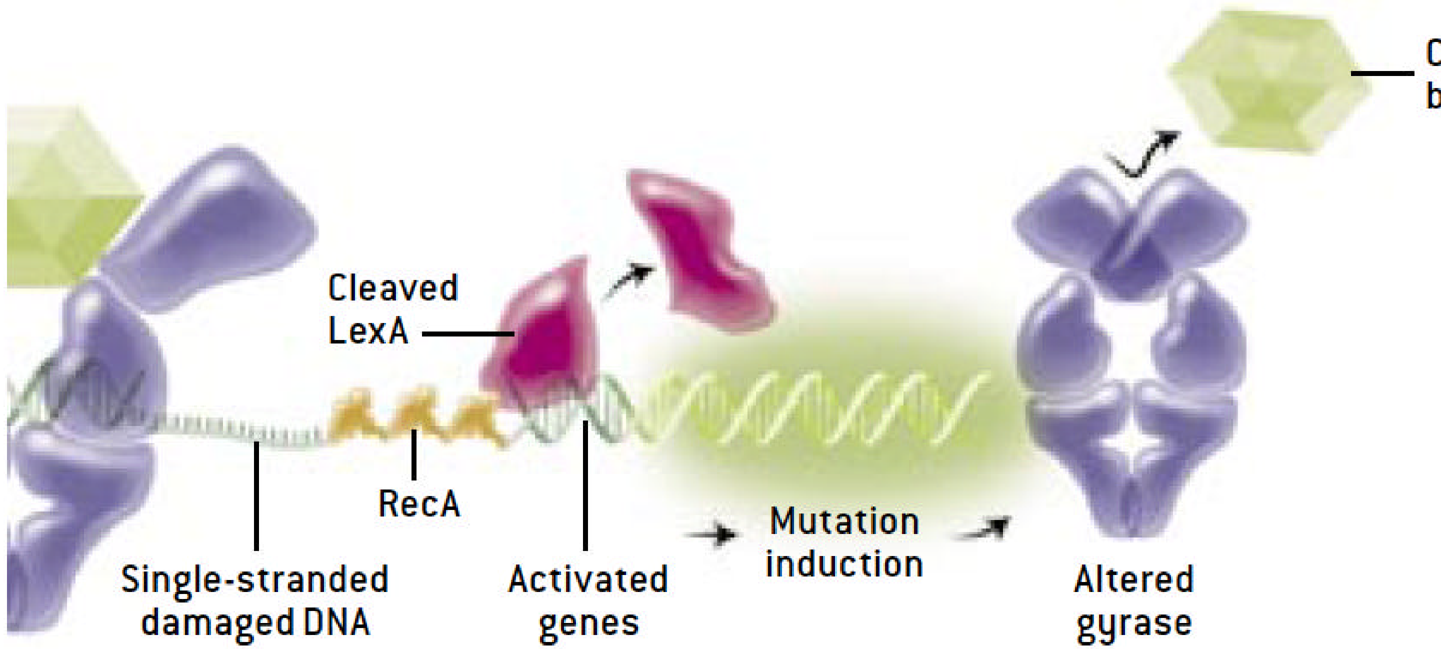




DNA of *E. coli* (*shown a*
cannot replicate when
exposed to cipro.

stance Arises

s initiated when *E. coli* responds by
ingle-stranded DNA. Individual
another protein, RecA, then line
and attach to the single-stranded
cilitates cleavage of a regulatory
. This change frees a set of
ressed genes to induce mutations
he mutations end up blocking
ng to gyrase, thereby preventing
n working



ly, stress drives individuals within
nisms to cheat, to defect, to gain
fitness at the expense of others.

is the province of Game Theory,
t really has no analogy that I am
e of to physical systems, but may
ucially
rtant in biology.

is why biology may be deeper in

The Prisoner's Dilemma Matrix

	Silent	Defect
Silent	-2, -2	-10, 0
Defect	0, -10	-5, -5

Optimal Solution

Nash Equilibrium

he role of deliberate mutational diversi
/all Wright's "trial and error mechanisr
grand scale") is to accelerate evolutio

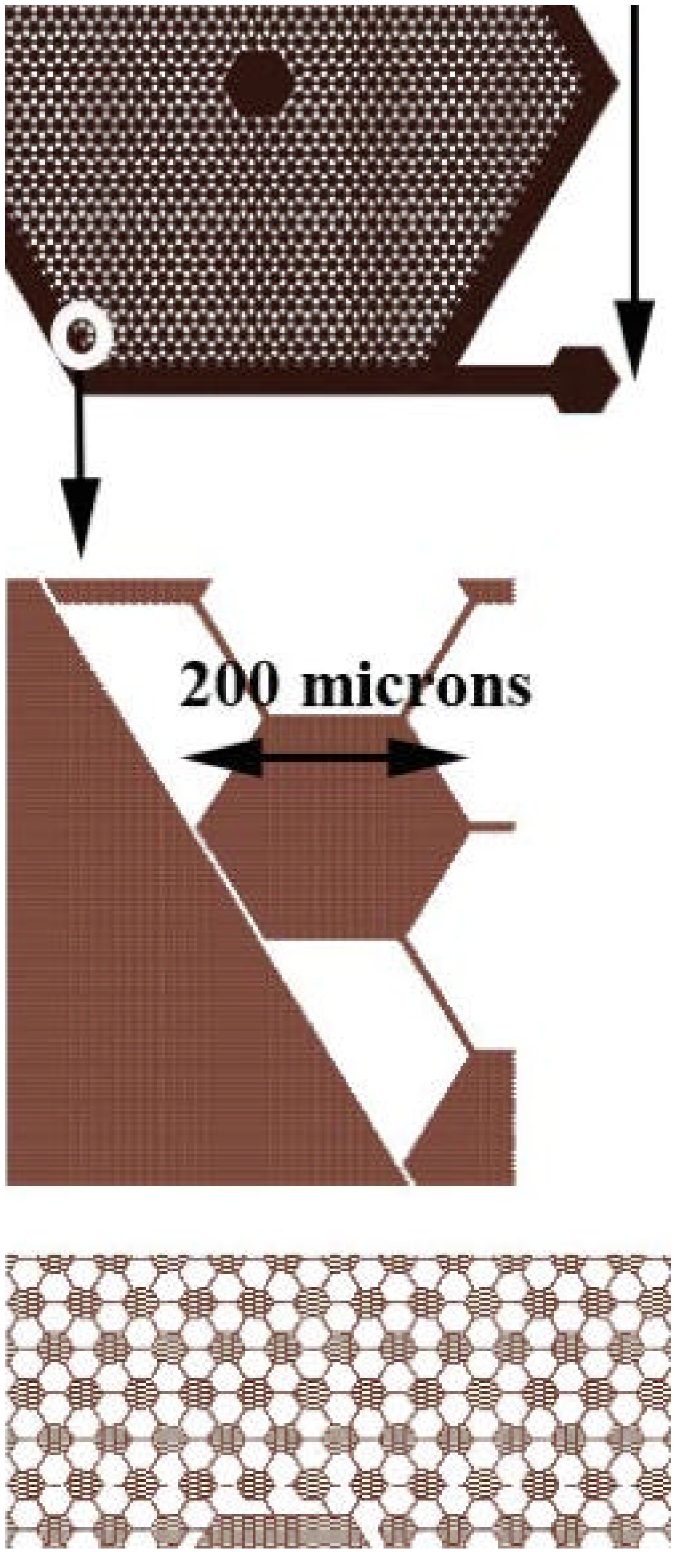
›ossible that the germline
›oductive/stem cell) genomic diversity
ıisms is generated deliberately in rapi
/ing organisms....and that cancer is a
ssary byproduct of rapid evolution wh
ot be removed because of the fundam
bilitv of the individuals to cheat in a

rice of high evolution rates of course
r: the heterogenous genomes and
sale genomic rearrangements neces
oid evolution means that occasionall
n will lose control, and that’s OK at t
es level, just bad for you.

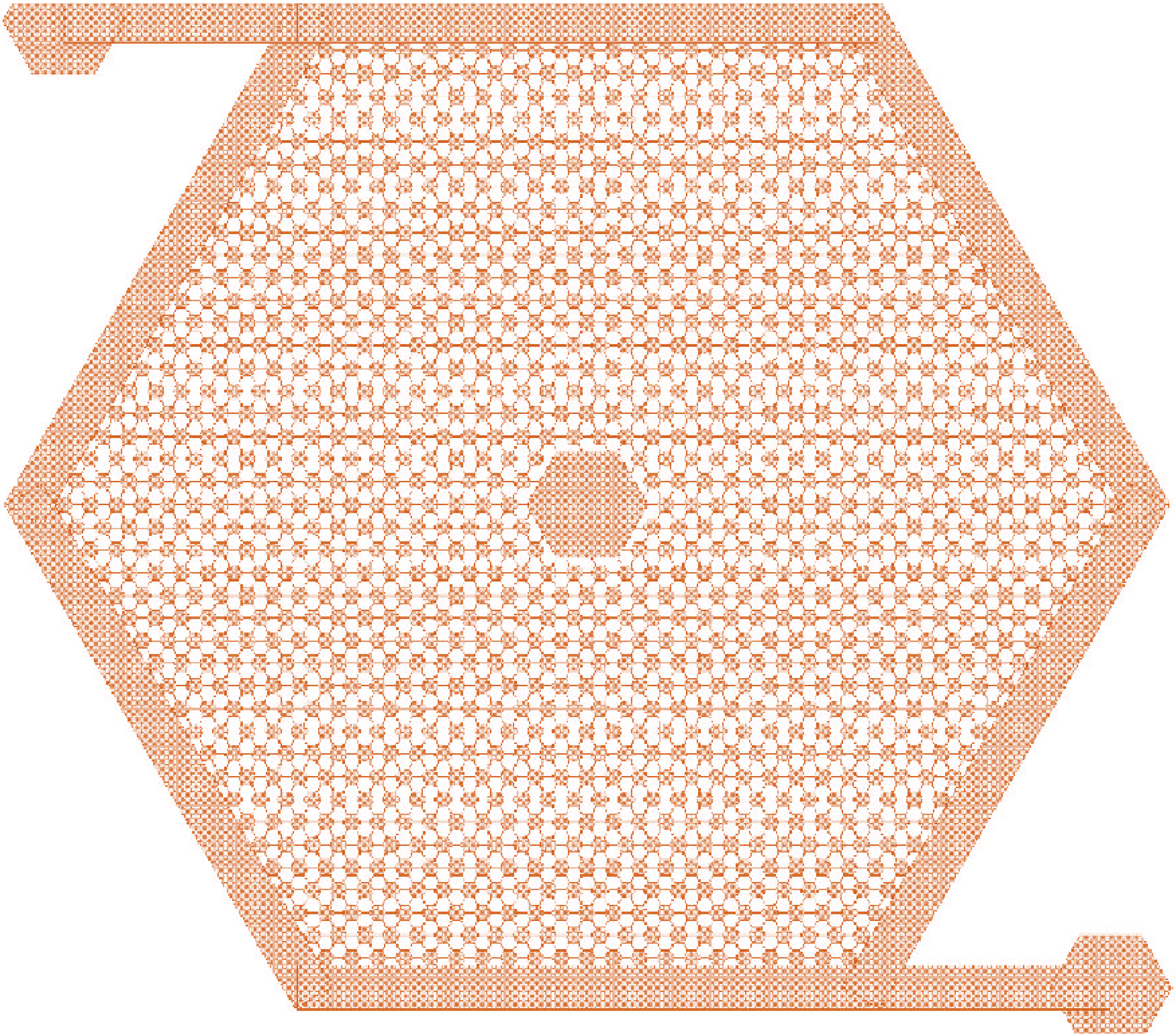
ıus, cancer IS necessary for high .tes of evolution and is not a sease.

ıink of it as Windows Vista.

VI. New Materials to Build New Ecologies in Biology



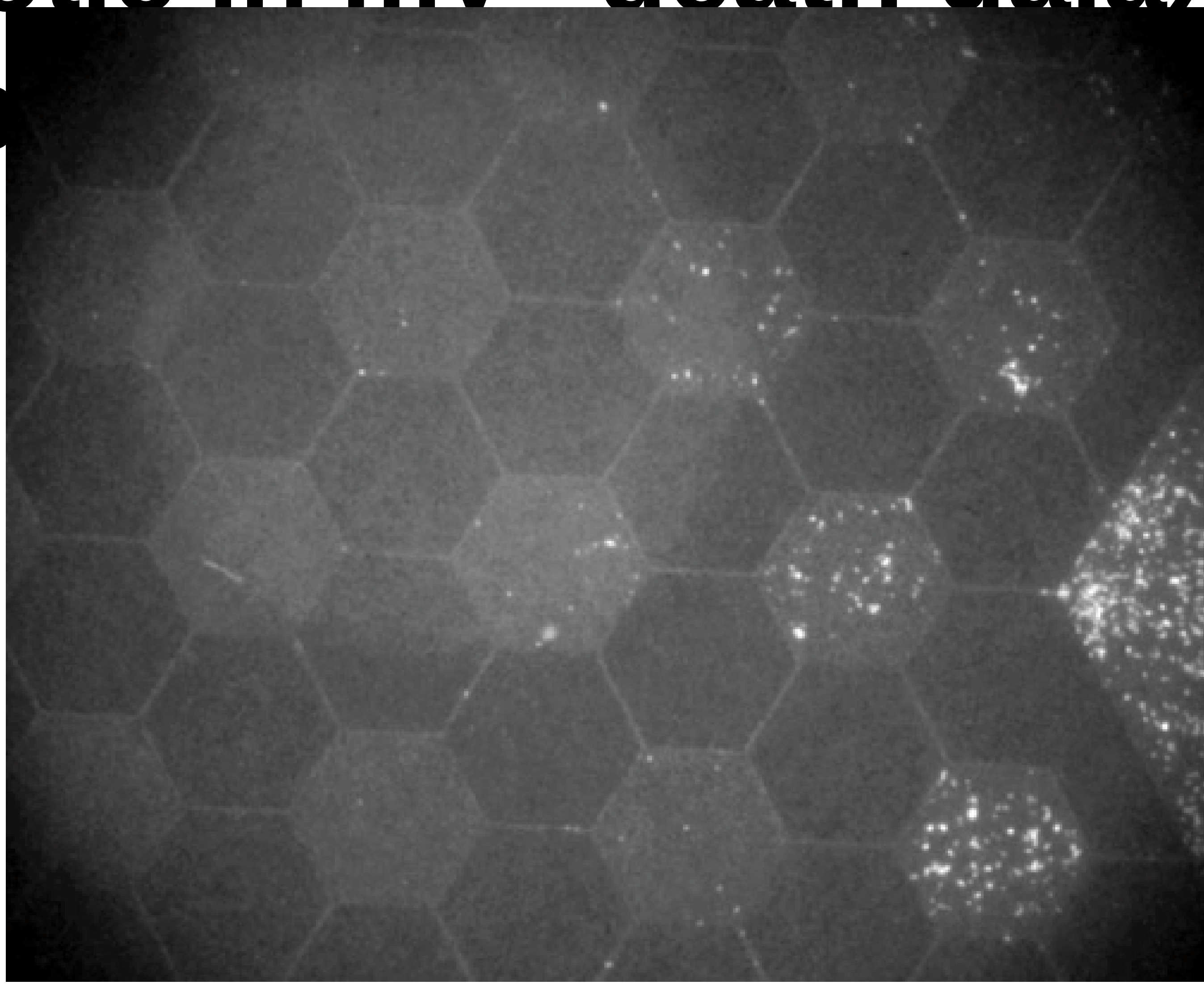
The “death galaxy”
my design for a
physics-based-eco
which will show all
features of what w
doing wrong in car
therapy.



Chemical coupling is through (10 micron polymer barrier.

'

rapidly evolve bacterial resistanc
tibiotic in my "death galaxy" usin
of b   science
cs?

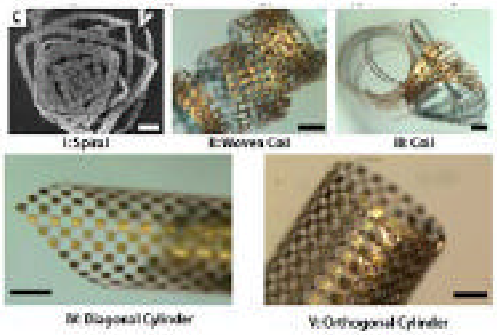


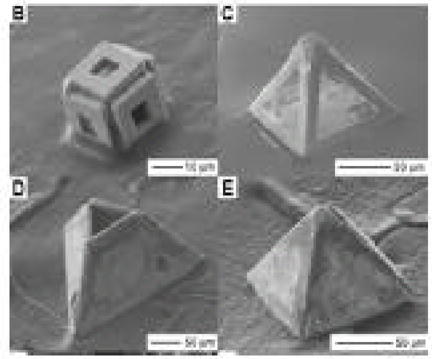
t this is just 2-D! We need to build
nplex 3-D ecologies to really emu
ual biological ecologies.

f-assembly of micropatterned 3-D
uctures is not something I do, but
ers are doing.

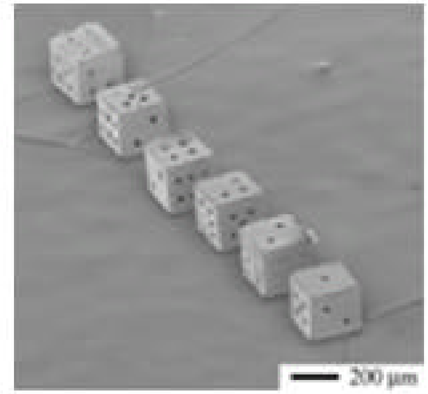
vis Garcias, Johns Hopkins

numbers
an be highly
ost effective)

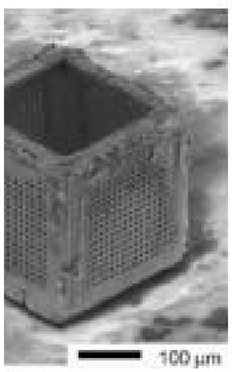


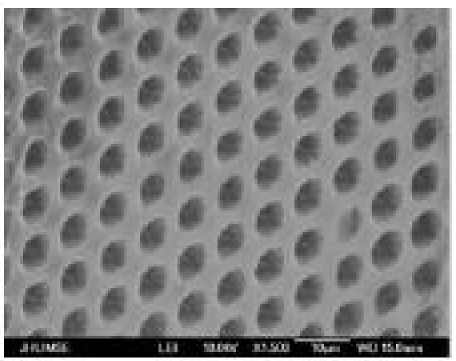


Variety of complex 3D structures; spirals, coils, polyhedra

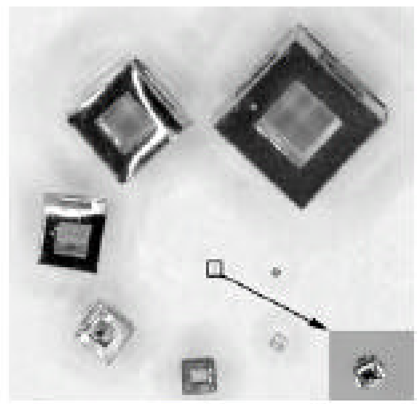


Lithographic patterning in 3D
(3D patterning demonstrated with line widths down to 15 nm)

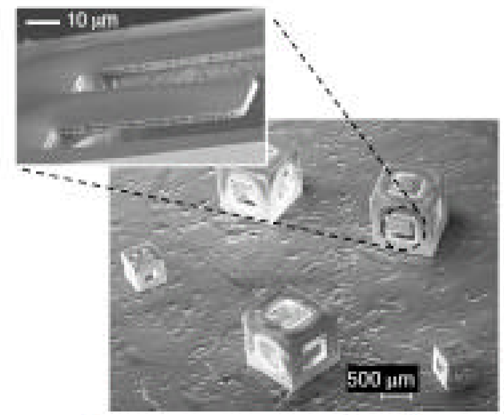




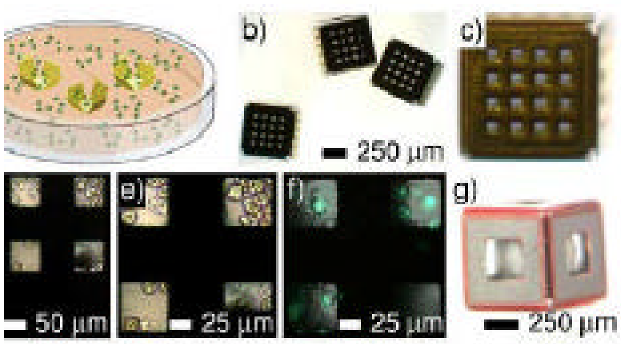
lled monodisperse 3D porosity
cro -nanoscale pores demonstrated on some or all faces)

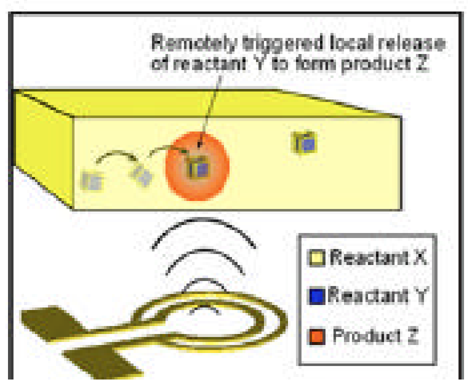


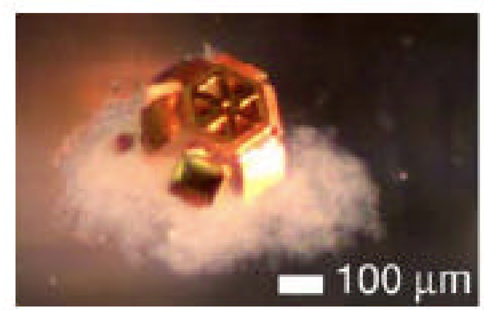
Containers with sizes ranging from 100 nm to 2 mm

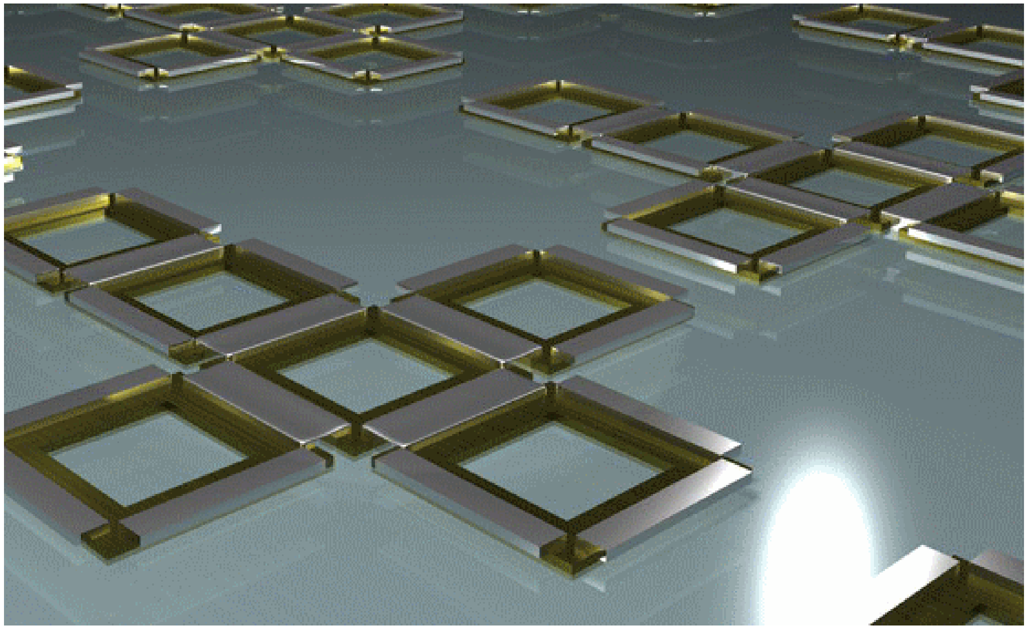


3-axis sensors / electron









QuickTime™ and a
MPEG-4 Video decompressor
are needed to see this picture.

Materials science will be driven by biological questions and we will earn how to design 3-D construction of extremely comple shapes with defined purposes.

At some point, we may begin to rival Nature in her fantastic design of “one-off” complex structures.


Thanks!!!