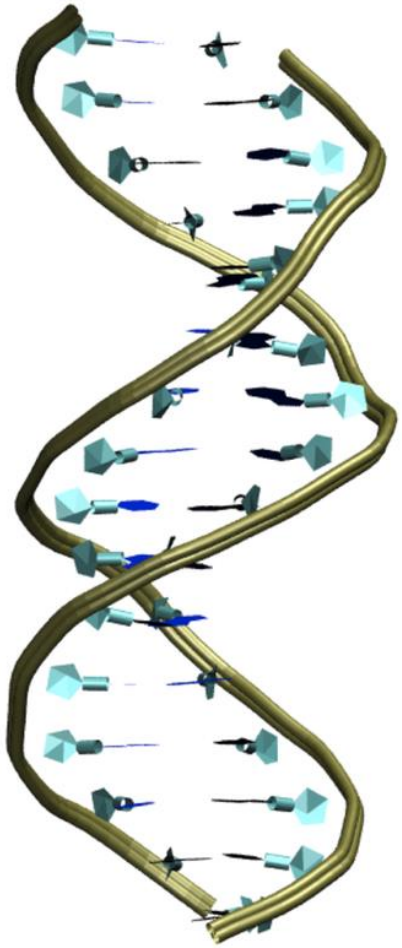


A Noy & R Golestanian, Phys Rev Lett (2012)

Flexing your genes. DNA flexibility depends on length-scale through cooperativity.

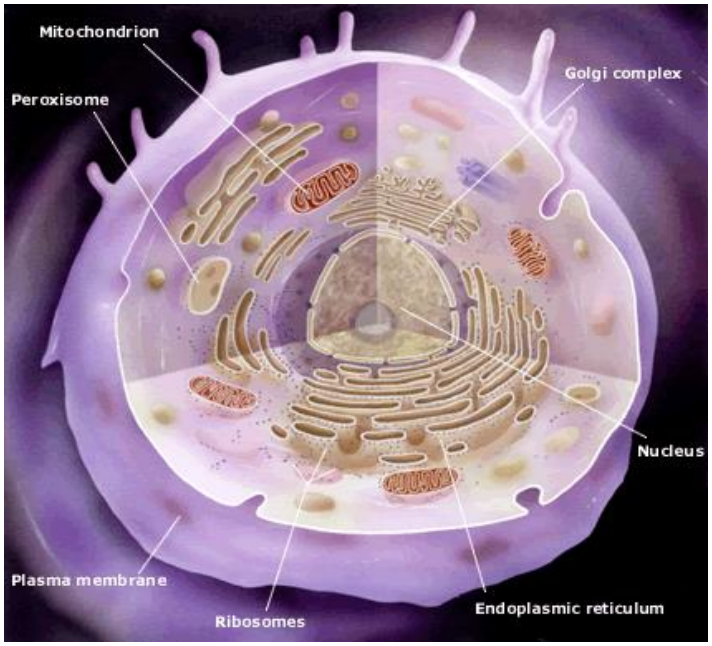
Living Matter

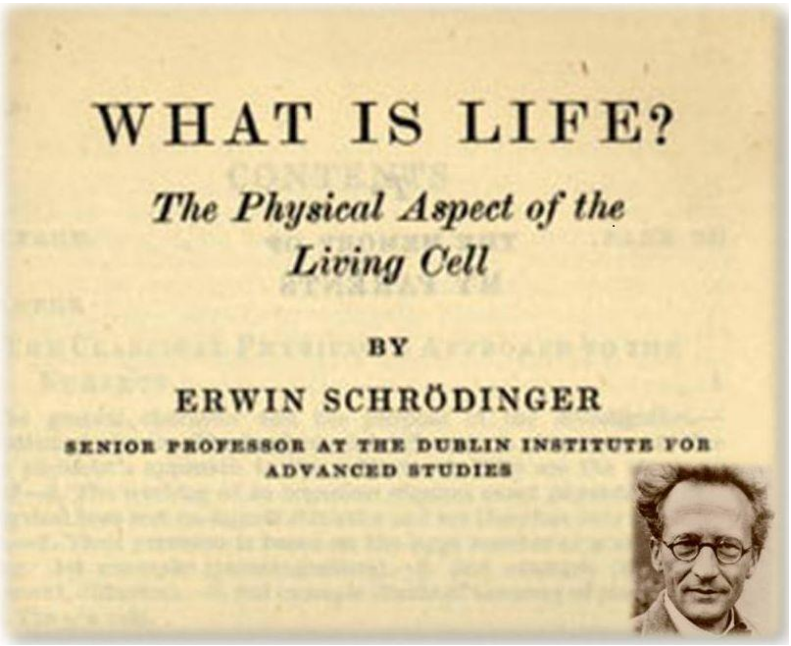
a theoretical physics perspective

Ramin Golestanian

Rudolf Peierls Centre for Theoretical Physics

Saturday Morning Theoretical Physics
21 September 2013




WHAT IS LIFE?

The Physical Aspect of the Living Cell

BY

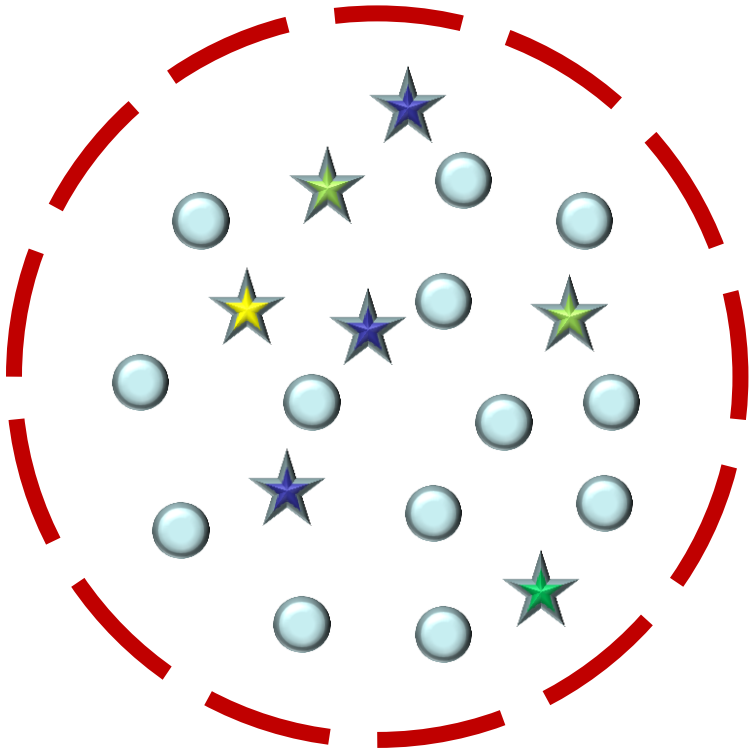
ERWIN SCHRÖDINGER

SENIOR PROFESSOR AT THE DUBLIN INSTITUTE FOR ADVANCED STUDIES

Schrödinger in 1944, after developing Quantum Mechanics:

"The large and important and very much discussed question is: How can **the events in space and time** which take place within the spatial boundary of a living organism be accounted for by physics and chemistry?"

Schrödinger's question:

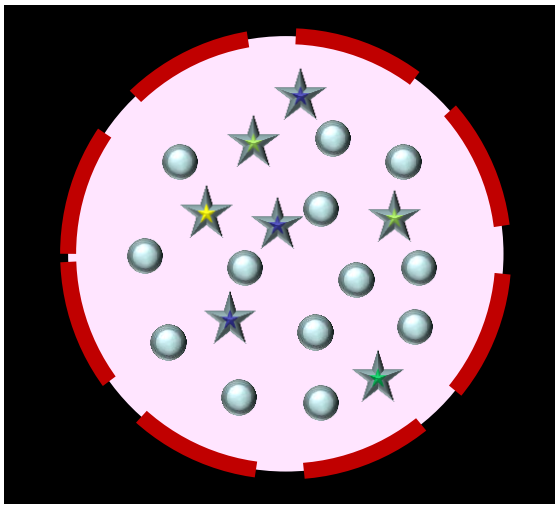


suppose we know how to make a **sack of chemicals** that contains all the ingredients of a **Living Cell**.

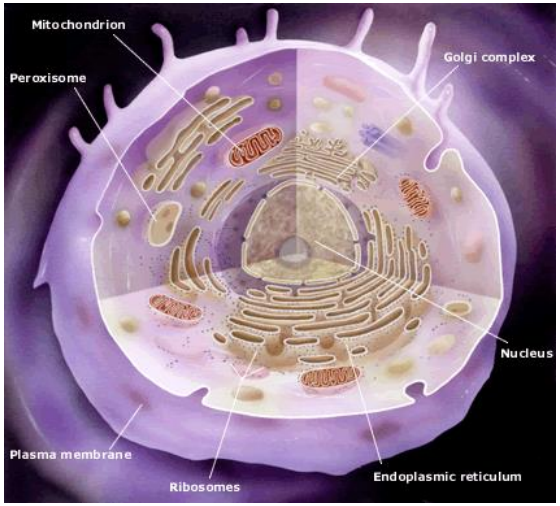
then, …

how do we go from one

to the other



sack of chemicals

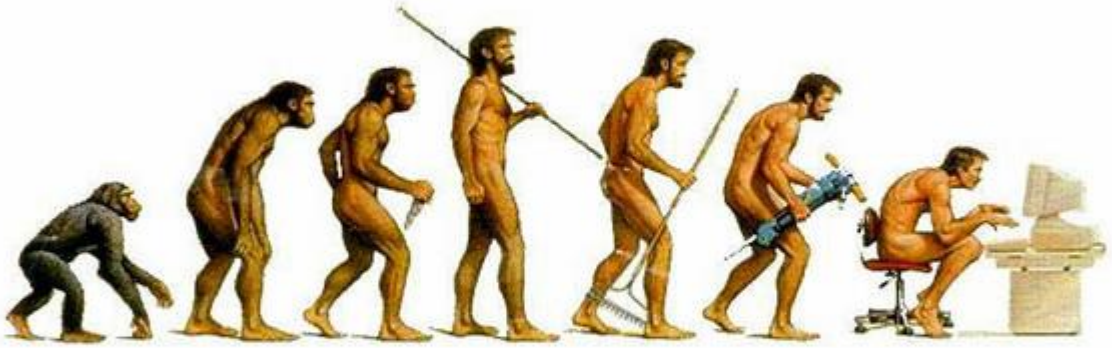


Living Cell

The most fundamental dynamical governing rule in biology is:

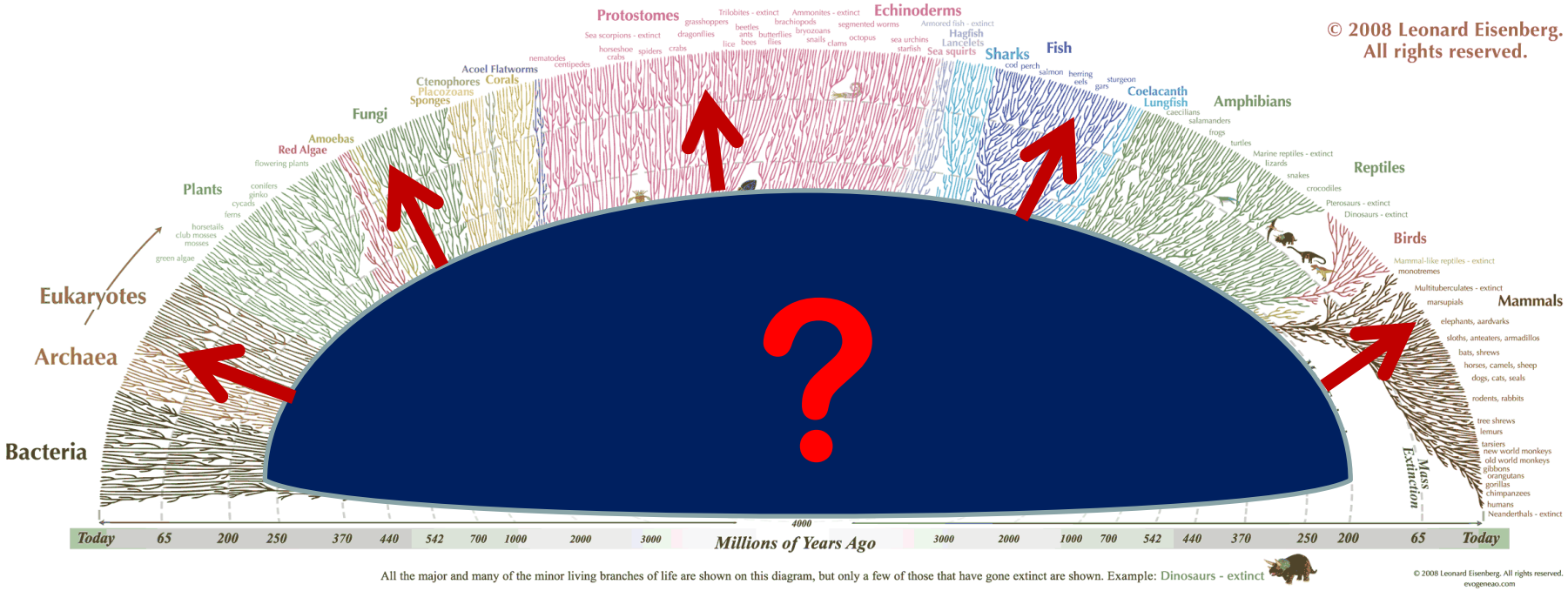
Evolution

credit: bmc.com



Can we find our answer through evolution?

Darwinian Evolution and the Arrow of Time

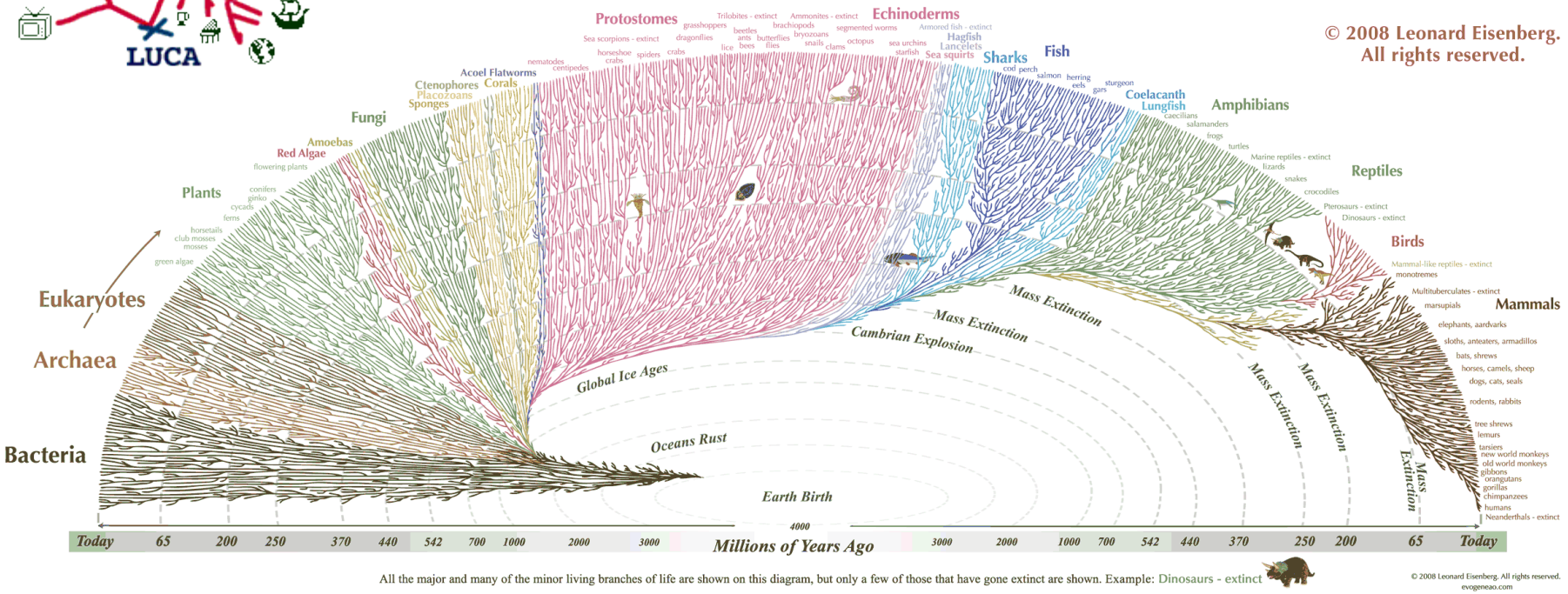


evolution has helped us understand diversity

but we cannot extrapolate back in time to find out

how things started in the first place …

Last Universal Common Ancestor (LUCA)



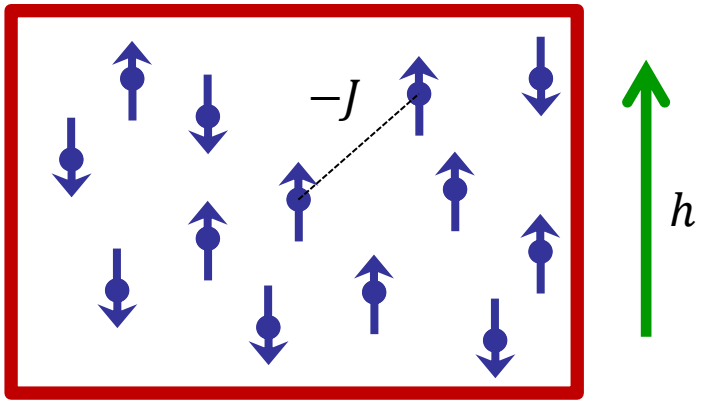
the first living cell was the same as any living cell!

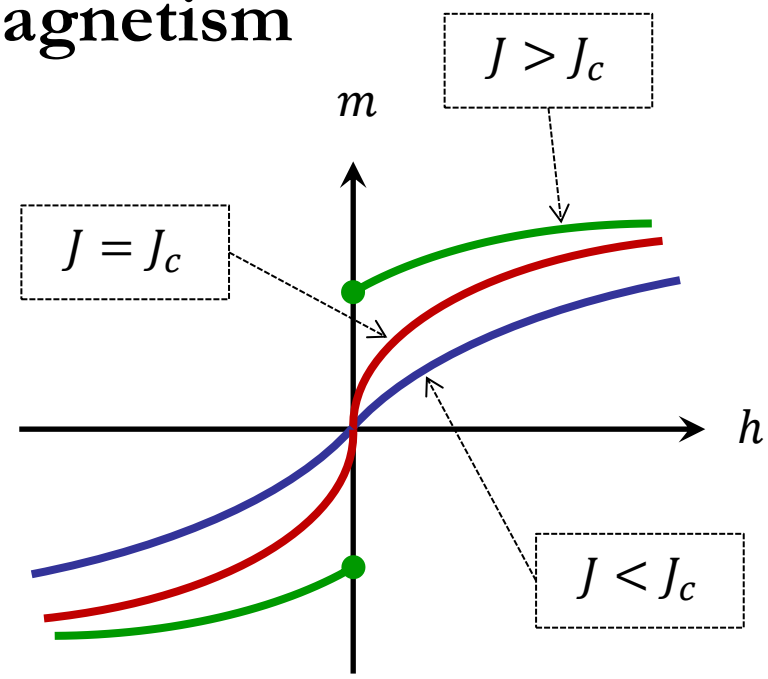
► LIFE as a collective emergent behaviour?

… something physicists might be able to help with …

Example from previous success stories in physics:

paramagnetism → ferromagnetism





the Ising model [exact solution: Onsager (1944)]

► **spontaneous symmetry breaking**

Understanding Emergence

What are the generic features?

- no discernible signature of the collective emergent property in the microscopic elements
- sharp onset, macroscopic transition, sensitive response (critical point)
- we need to compromise on some details to be able to reach across length scales: use of *minimal* models

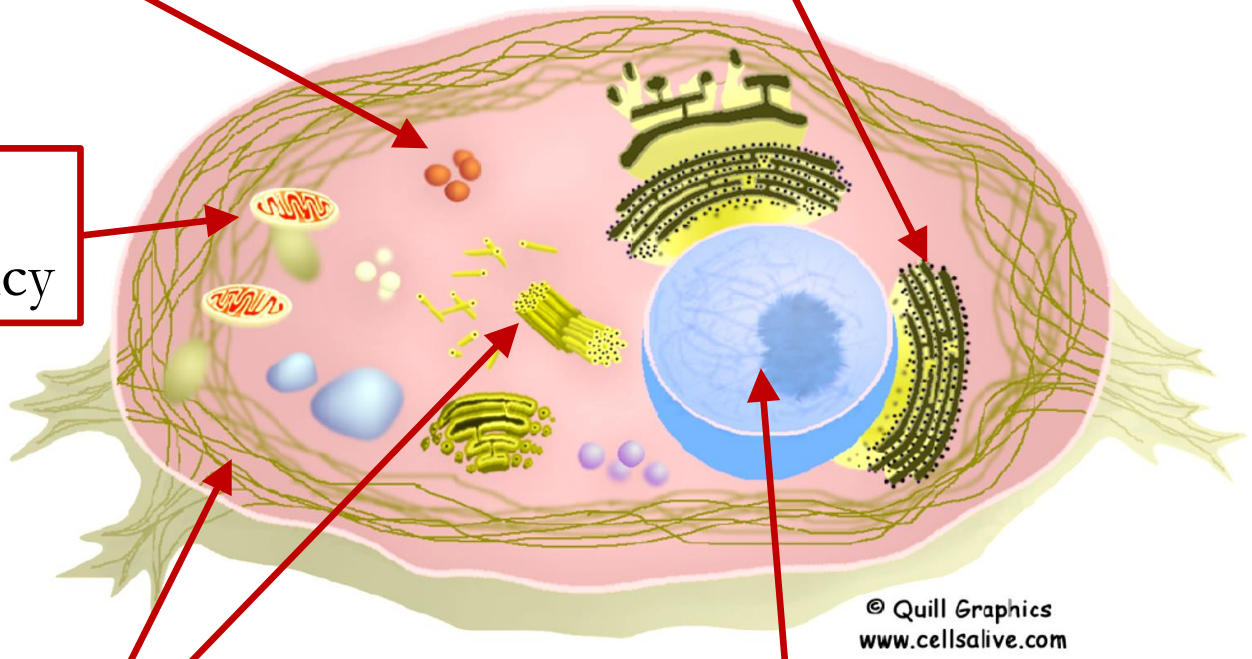
► **can we do something like this for biology?**

The Living CELL

materials factory: making the functional agents

materials transport: raw material in, waste out

energy factory:
providing the currency



dynamical scaffold: keeping in shape

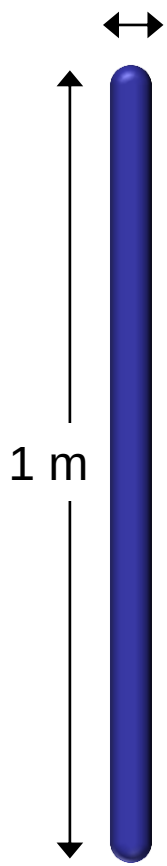
information storage: code of life

What do we observe in a Living Cell?

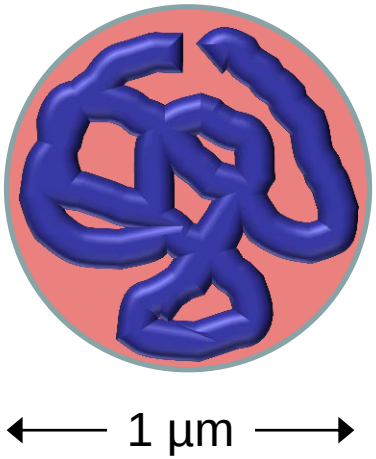
- hierarchical *spatial* and *temporal* organisation
- *robustness* and precision despite *stochasticity*
- high flux of *material* (small molecules) and *energy*
- *economy:* multi-purpose building blocks, recycling
- *crowded* yet *agile* environment

► **how can we understand these physically?**

e.g. The Wonders of DNA Storage



$$V(\text{left}) = 1\ \text{m} \times (1\ \text{nm})^2 = (1\ \mu\text{m})^3 = V(\text{right})$$

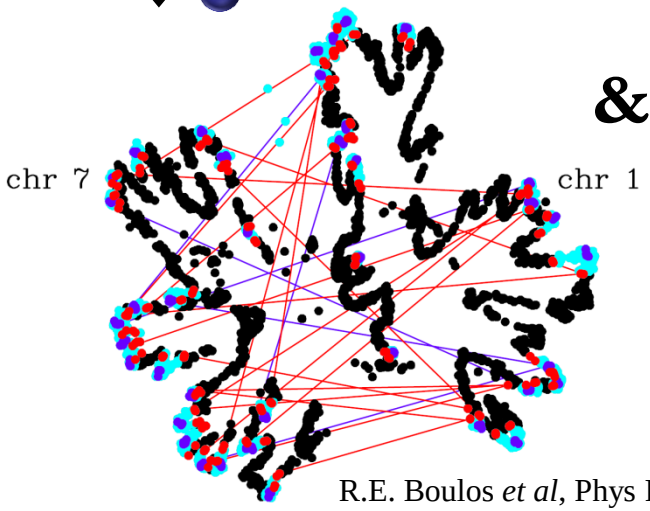


DNA is close-packed!

… yet dynamically accessed

with high precision

& without access to higher dimensions!

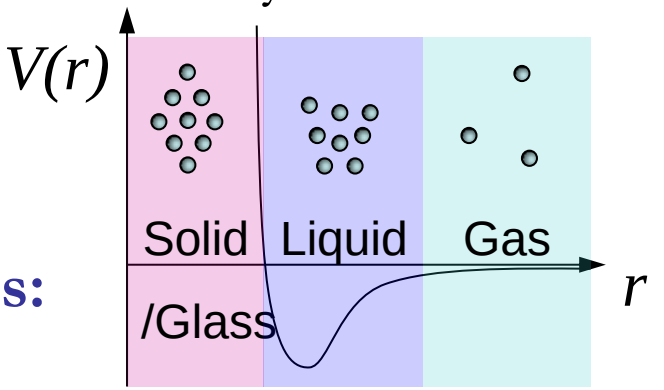


► **DNA is hierarchically structured**

R.E. Boulos *et al*, Phys Rev Lett **111**, 118102 (2013)

Equilibrium Statistical Physics tells us:

- interactions determine the phase behaviour of the system
- phase separation and sensitive response



Within EQUILIBIUM, we have problems:

- stable phases are *macroscopic*; cannot have spatial microstructure
- once triggered, it goes all the way; can't have a temporal structure
- sensitive response only for macroscopic systems
- we expect jamming/glassiness in a close-packed system

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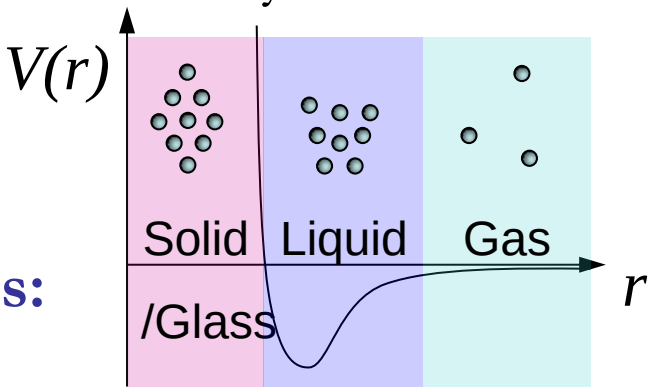

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Conclusion: EQUILIBIUM is DEAD.

► **it seems that we need to bring in "magic" …**

Living Matter is ACTIVE

Biological systems go non-equilibrium via "agents"

- **mechanical:** exert local forces **[motor proteins]**
- **chemical:** catalyze chemical reactions **[enzymes]**

What are the consequences?

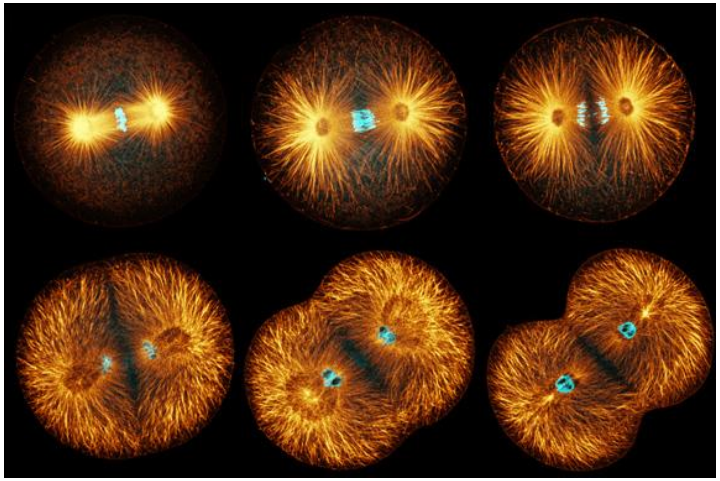
- enforcing and maintaining gradients
- liquefying or disentangling the jammed/glassy structures
- instabilities, patterns, and dynamic order

► **… the new field of Active (Soft) Matter**

Mechanical Activity

credit: George von Dassow

Mitotic Spindle:



Reconstituted cell extracts:

T. Sanchez *et al*, Nature **491**, 431 (2012)

keep things dynamic, yet, in control

► **intrinsic selection of LENGTH scale?**

What do enzymes do?

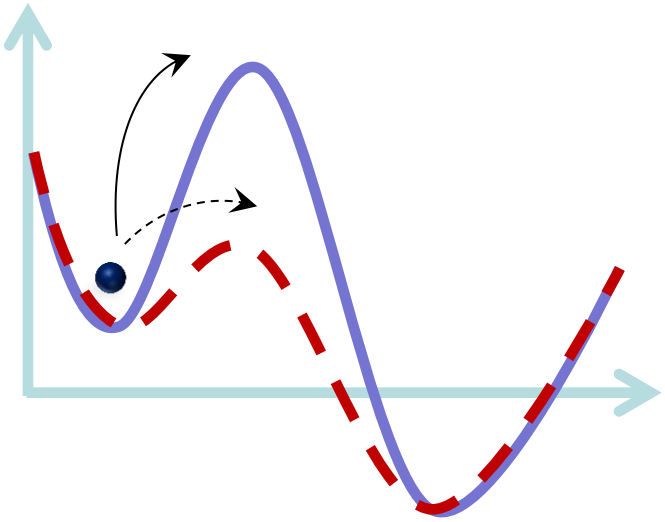
- chemical reaction from an initial higher energy state to a final lower energy state, with a large energy barrier;

… this will not happen …

- enzyme comes along and lowers the barrier;

… the reaction happens, ONLY where the enzyme is …

- enzymes are made following prescriptions stored in DNA code



► **nonlinear catalytic reaction**

► **driving non-equilibrium at the right place/time**

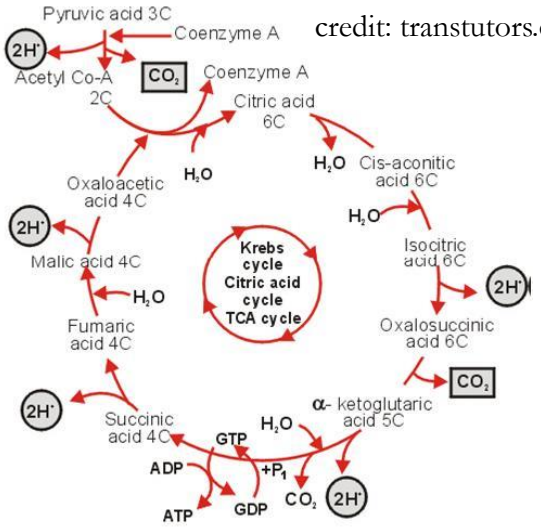
Reaction Cycles

What else?

- *material economy*: the reverse reaction is also contemplated; using other appropriate enzymes

… cyclic nonlinear catalytic reaction…

- ubiquitous reaction cycles, such as the Krebs Cycle
- robustness **[limit cycles]**
- frequency selection **[intrinsic clock]**
- spatial patterns **[intrinsic ruler]**



credit: transtutors.com

►nonlinearity could lead to: stability, robustness, selection of TIME and LENGTH scales

So, from the point of view of

Condensed Matter Physics

Living Matter is

an emergent collective phase of active soft matter that maintains dynamic yet robust non-equilibrium conditions in the form of information-controlled chemical and mechanical activity, via proteins and other agents.

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Condensed Matter Physics

Living Matter is

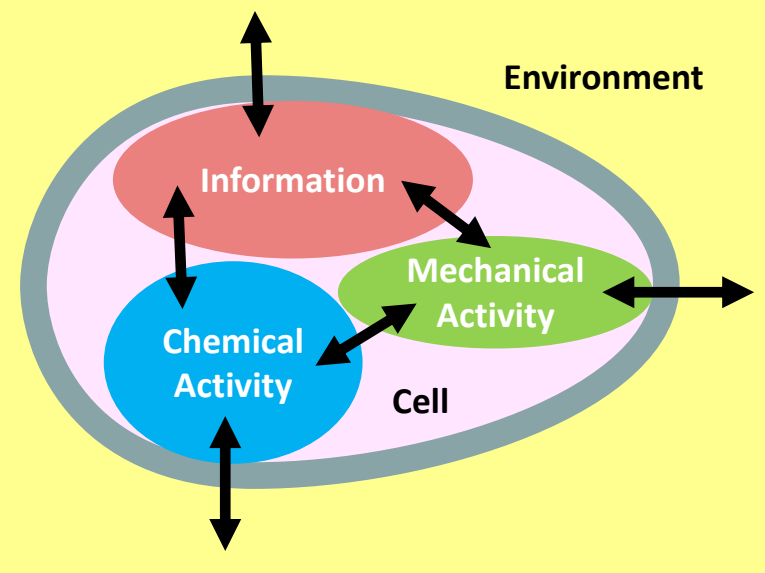
an emergent collective phase of active soft matter that maintains dynamic yet robust non-equilibrium conditions in the form of information-controlled chemical and mechanical activity, via proteins and other agents.

► does this mean we have all the theoretical tools we need to study Living Matter in this context?

► the answer is NO! There is a PROBLEM

The Other Hierarchy Problem

REGULATION that goes up and down the hierarchy involving a multitude of time and length scales



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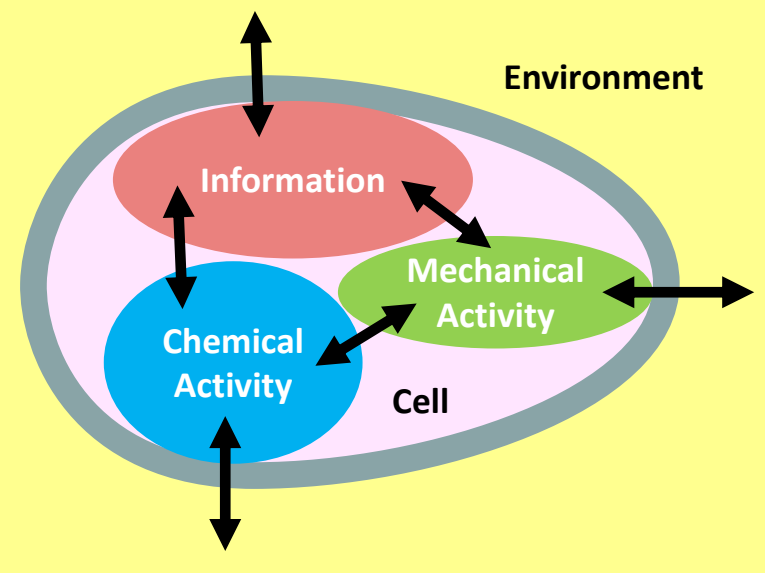

… we do not have experience with this in physics …

- **this will keep us busy for quite a few years**
- **we'll keep you posted on the progress …**

A growing bacterial colony that calculates its collective shape

credit: Eshel Ben-Jacob