



Institute of Theoretical Physics
São Paulo State University

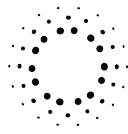
Precision and Emergence in the Physics of Biological Systems

IV Journeys Into Theoretical Physics
Prof. William BIALEK
July 6-12, 2019
Níckolas de Aguiar ALVES

Precision and Emergence in the Physics of Biological Systems

IV Journeys Into Theoretical Physics

Professor: William BIALEK, Princeton University
Notes by: Níckolas de Aguiar ALVES
Level: Undergraduate
Period: July 6-12, 2019



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Precision and Emergence in the Physics of Biological Systems

William Bialek - Princeton University

Biology \neq Physics: recent

Rayleigh: how do we perceive sound?

How do we know where it comes from

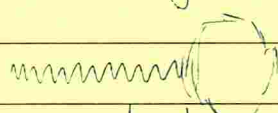
By ~~small~~ frequency small wavelength

↳ "acoustic shadow"

↳ higher volume in one ear

Nicholas Alvar
IFUSP

alvar.nicholas@usp.br
2019



low
volume

high
volume

w.bialek@princeton.edu

Small frequency: large wavelength

↳ only phase differences

↳ we are phase deaf, and thus can't hear where large wavelengths come from

For a physicist: Biology is interesting, but very messy

↳ though biologists act like this is intrinsic, nowadays there is a huge gamma of topics that can be treated with the same organization as in Physics

This talk: precision and emergence

although Bio is messy and sloppy, biological systems are extremely precise

↳ we can see individual photons



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↳ the properties of cells emerge from lots of molecules, the properties of which emerge from lots of parts, and etc

life is more than the sum of the parts,
life is not a molecule


↳ known from physics
↳ Stat Mech

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Diagrams

Precision: eelocation measures 10ns of difference
 we can perceive μ s of difference between our ears
 molecule counting
 higher level examples
 "measure" the velocity of movement of something being seen

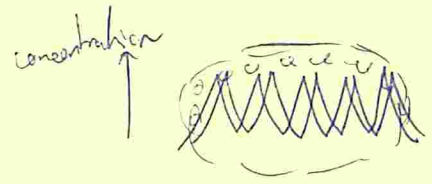
Precision

 caterpillar
 → segments with approx same size
 How does the animal does it?

Fruit-fly → breeds fast, good to experiment

egg → larva in 1 day
 concentration of certain molecules

measured after 3h



blueprints for the segments

↳ cousin embryos & no genetic effects

Phys: how much do the peaks vary from embryo to embryo? → 8×10^{-3} size of embryo

Periodic pattern

Turing: perhaps it comes from random + symmetry?

↳ Nope, for the mother breaks the symmetry at the beginning

messenger RNA
 is put at the head-to-be

Concentration.

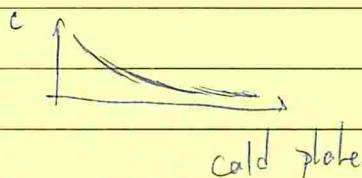
$$\partial_t c = D \nabla^2 c - \frac{c}{\tau}$$

$$\rightarrow D \frac{\partial c}{\partial x} \Big|_{x_0} = 2 \text{ (source)}$$

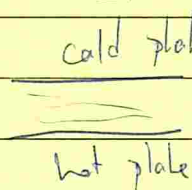
$$c(x, t \rightarrow \infty) \approx c_0 e^{-x/\lambda}, \quad \lambda = \sqrt{D\tau}$$

Measure the concentration.

develop antibodies to the molecule, anti fluorescence. Pick the egg, cook slowly, make holes and add antibodies. Measure fluorescence



Fluids:



Small gradient: conduction

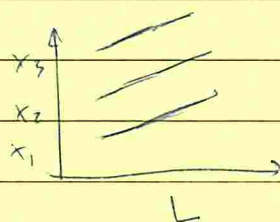
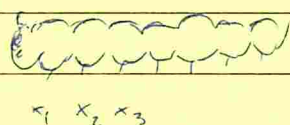
Big gradient: periodic convection

perhaps wrong arrow, but that's the idea

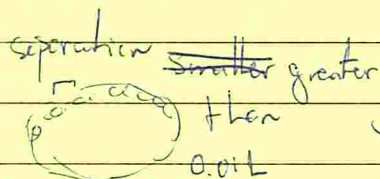
~~~~~

↳ Not the case for Bio → symmetry broken at start

Different sized embryos: always the same number of stripes, even if another could be put in



we don't know



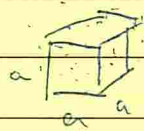
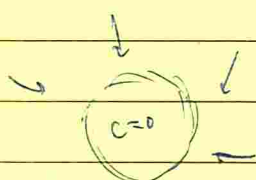
each molecule knows where it is

Difference in concentration needed to make a difference 10%

↳ how can different embryos look the same?

↳ bio systems can be precise to that point

What's the smallest Δc you can measure?



$$\bar{n} = c a^3$$

$$\delta n \sim \sqrt{\bar{n}}$$

$$\frac{\delta c}{c} \sim \frac{1}{\sqrt{c a^3}} \frac{1}{\sqrt{4/\pi c}} \sim \frac{1}{\sqrt{D a c \pi}}$$

$$v_c \sim \frac{c}{a}$$

$$\int d\mathbf{x} \nabla c \cdot \mathbf{D} \sim \frac{c a^2}{a}$$

$$\sim D c a$$

wait  $\pi_c$  for molecules to exchange and get a new sample

$$\delta \pi_c \sim a^2$$




Bialek

Regulating "gene expression"

protein  $D \sim \mu\text{m}^2/\text{s}$

$a \sim 3\text{nm}$

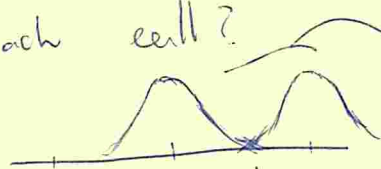
$$c \sim \text{nM} = 10^{-9} \frac{6 \cdot 10^{23}}{L}$$

$$\sim 0.6 \frac{1}{\mu\text{m}^3}$$

$$Dac \sim \frac{1}{300} \text{Hz} \sim \frac{1}{5} \text{min}$$

$\frac{dc}{c} \sim 1 \sim$  we are missing something (I've skipped somethings)

Where is each cell?



actually,  
you might be a bit confused

there is also a correlation between the distributions that seems to make out for the conclusion

$$x \in [0, L], \quad p(x) = \frac{1}{L}$$

$$y = x + \xi, \quad \langle \xi^2 \rangle = \sigma^2$$

$$I(y \rightarrow x) = \log \left( \frac{L}{\sigma} \frac{1}{\sqrt{2\pi e}} \right)$$

the problem

In Physics, we take small deviations seriously

Emergence

i) proteins  
polymer of aminoacids

$aa_1, aa_2, \dots, aa_n$



sequence of aminoacids

protein  
folding  
problem

for random cases, we would get glass when cooling down  
then proteins are organised, and thus they don't look glassy physically

usual folding problem

$$P(\vec{x} | \{s_i^a\}) = e^{-\beta E(\vec{x}, \{s_i^a\})}$$

structure  $\leftrightarrow$  sequence

but  $P(\{s_i^a\} | \vec{x})$ ?

what are the sequences compatible with the structure?



$$(S_i^\alpha) \# p \sim e^{\sum_{\alpha} h_i^\alpha S_i^\alpha}$$

if we pick some models on the computer and build the proteins, we have problems

$$(S_i^\alpha S_j^\beta)$$

the changes we make must be compatible

$$p \sim \exp\left(\sum_{\alpha} h_i^\alpha S_i^\alpha + \frac{1}{2} \sum_{\alpha, \beta} S_i^\alpha S_j^\beta\right)$$

there is correlation

interaction term

Bio: every detail matters

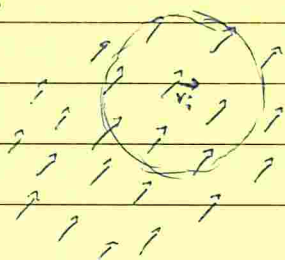
↓  
false, we can manipulate and experiment

✓  
actually, it is somewhere in the middle

Phys: details shouldn't matter

↓  
false, sometimes things go very wrong

is) Flock of birds



$$p(\{\vec{v}_i\})?$$

Guess: birds must be trying to make their velocities similar to their neighbors  $\rightarrow$  local interactions

$$Q = \frac{1}{N} \sum_i \left( \vec{v}_i - \frac{1}{n_i} \sum_{j \in n_i} \vec{v}_j \right)^2 \quad |N_i| = n_i$$

$$\bar{v} = \frac{1}{N} \sum_i |\vec{v}_i|, \quad \bar{v}^2 = \frac{1}{N} \sum_i |\vec{v}_i|^2$$



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$$p \sim \frac{1}{Z} \exp\left(-\lambda_1 \sum (v_i - \frac{1}{N} \sum v_i)^2 - \lambda_2 \sum |v_i| - \lambda_3 \sum |v_i^c|\right)$$

Draw a distribution, compute properties and compare

continuous

↳ correlation functions

Direction: spontaneous symmetry breaking with local interactions

Amplitude: no symmetry