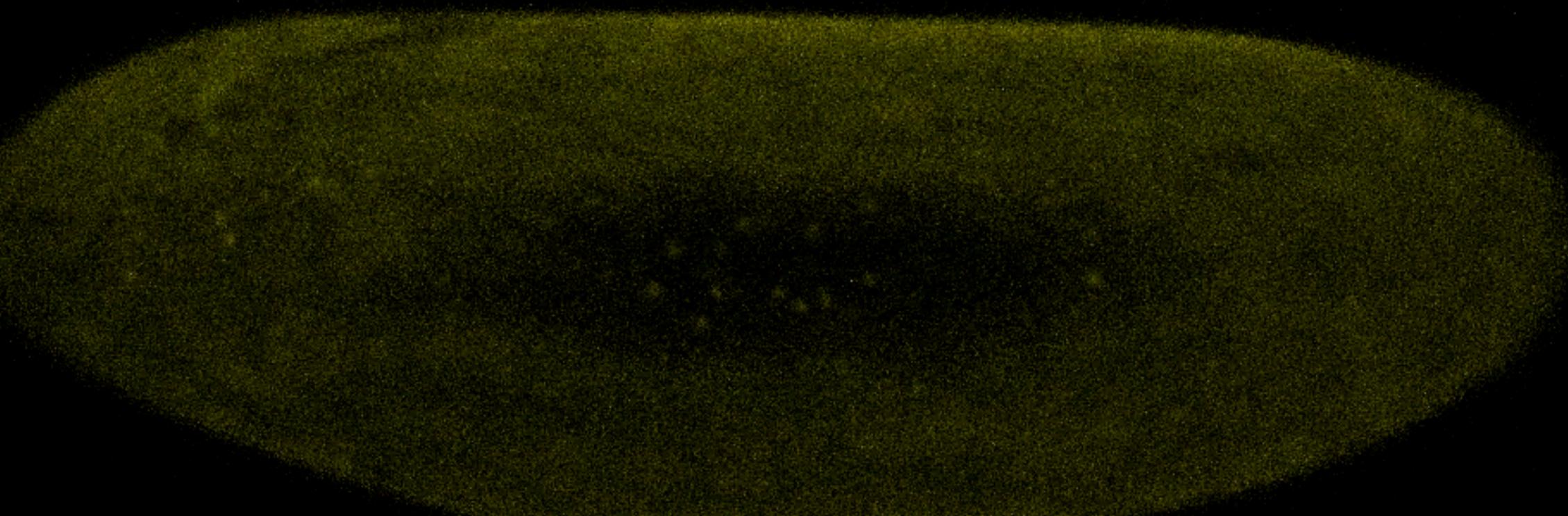


The physics of life



0 min



How much can we calculate?

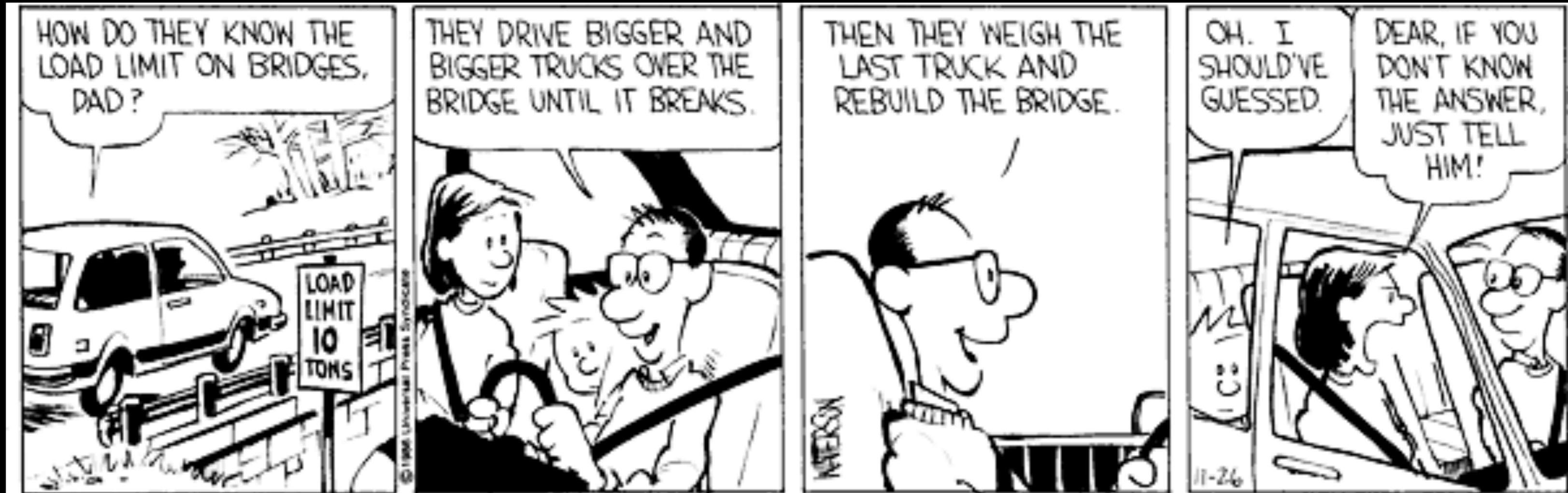
What do theoretical physicists do?

“La filosofia è scritta in questo grandissimo libro che continuamente ci sta aperto innanzi a gli occhi (io dico l'universo), ma non si può intendere se prima non s'impara a intender la lingua, e conoscer i caratteri, né quali è scritto. Egli è scritto in lingua matematica, e i caratteri sono triangoli, cerchi, ed altre figure geometriche, senza i quali mezzi è impossibile a intenderne umanamente parola; senza questi è un aggirarsi vanamente per un'oscuro laberinto.”

The book of Nature is written in the language of mathematics. (Galileo Galilei, 1623)

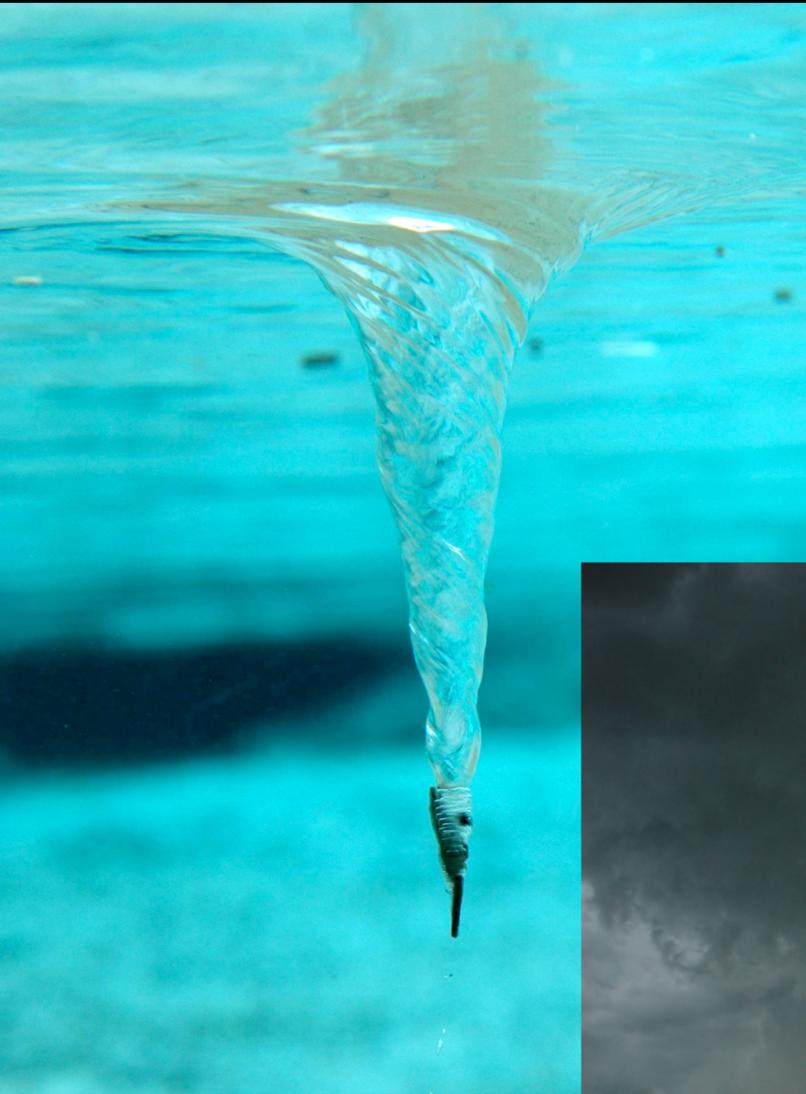


This is not a universally held view of the world.

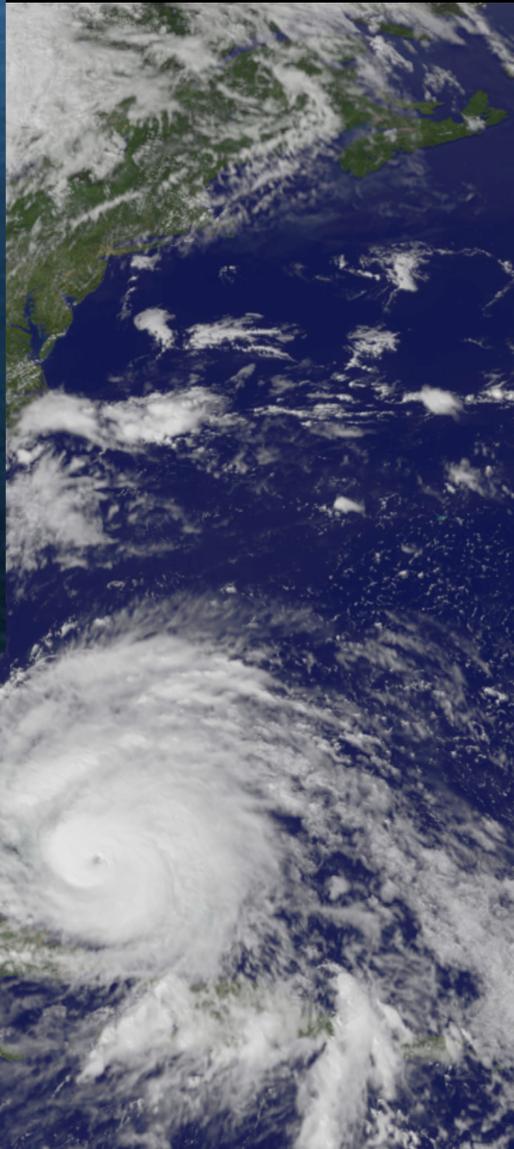
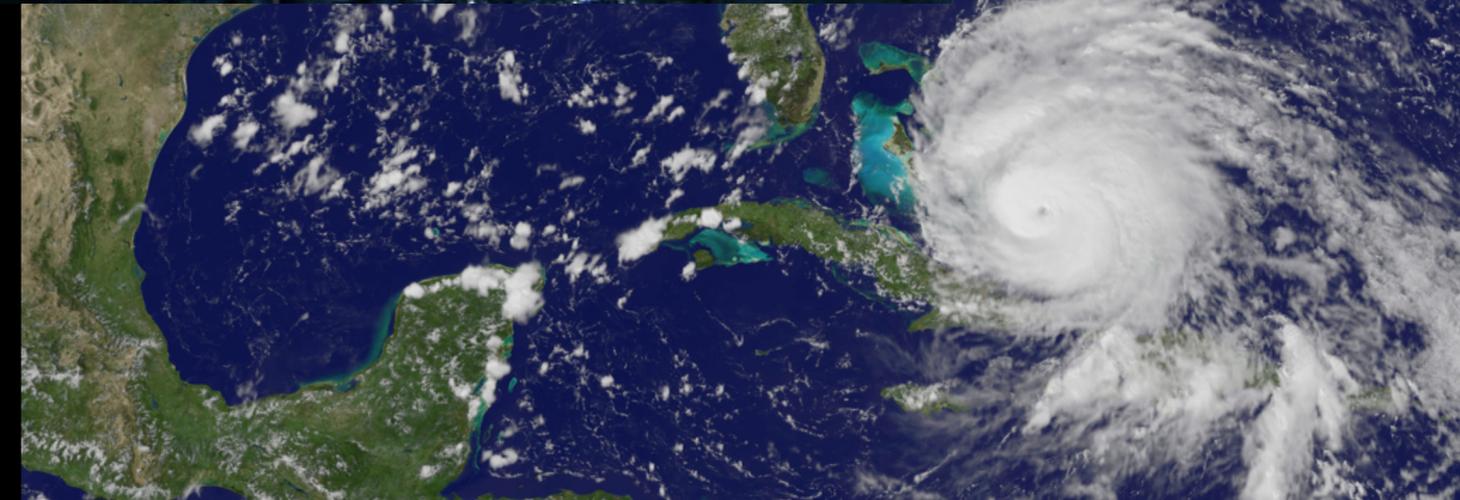


(see also Mayr on biology vs. astronomy!)

Why should we believe in (relatively) simple, universal mathematical descriptions?



<http://www.efluids.com>
<http://www.treehugger.com>
<http://www.vintechology.com>
<http://earthobservatory.nasa.gov>



J. Physiol. (1952) 117, 500-544

A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

BY A. L. HODGKIN AND A. F. HUXLEY

From the Physiological Laboratory, University of Cambridge

$$I = C_M \frac{dV}{dt} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_l (V - V_l),$$

$$I = \frac{\alpha}{2R_2} \frac{\partial^2 V}{\partial x^2},$$

$$\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n,$$

$$\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m,$$

$$\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h,$$

$$\alpha_n = 0.01 (V + 10) / \left(\exp \frac{V + 10}{10} - 1 \right),$$

$$\beta_n = 0.125 \exp (V/80),$$

$$\alpha_m = 0.1 (V + 25) / \left(\exp \frac{V + 25}{10} - 1 \right),$$

$$\beta_m = 4 \exp (V/18),$$

$$\alpha_h = 0.07 \exp (V/20),$$

$$\beta_h = 1 / \left(\exp \frac{V + 30}{10} + 1 \right).$$

20 parameters



Theory of Superconductivity*

J. BARDEEN, L. N. COOPER,† AND J. R. SCHRIEFFER‡
Department of Physics, University of Illinois, Urbana, Illinois

(Received July 8, 1957)

Although our calculations are based on a rather idealized model, they give a reasonably good account of the equilibrium properties of superconductors. When the parameters of the theory are determined empirically, we find that we get agreement with observed specific heats and penetration depths to within the order of 10%. Only the critical temperature involves the superconducting phase; the other two parameters required (density of states and average velocity at the Fermi surface) are determined from the normal phase. This quantitative agreement, as well as the fact that we can account for the main features of superconductivity is convincing evidence that our model is essentially correct.

essentially 0 parameters



What do we do about all the parameters?

~~1. Give up, biology really is just complicated.~~

2. Nature has selected mechanisms in which parameters don't matter: functions are "robust."

3. The parameters chosen by Nature are special.

Before we dig in, let me emphasize that I didn't come to these views alone.*

Collaborators and Mentors

MJ Berry II (Princeton)
CG Callan, Jr (Princeton)
A Cavagna (Sapienza, University of Rome)
AJ Doupe (UC San Francisco)
I Giardina (Sapienza, University of Rome)
RF Goldstein (Claremont Colleges)
AM Leifer (Princeton)
R Koberle (University of Sao Paulo)
ER Lewis (UC Berkeley)
SA Kivelson (Stanford)
SG Lisberger (Duke)
JN Onuchic (Rice)
WG Owen (UC Berkeley)
FC Pereira (Google)
RR de Ruyter van Steveninck (Indiana University)
WS Ryu (University of Toronto)
AL Schweitzer (UC San Diego)
JW Shaevitz (Princeton)
DW Tank (Princeton)
NTishby (Hebrew University)
EF Wieschaus (Princeton)
A Zee (KITP, UC Santa Barbara)

Postdoctoral Fellows

GS Atwal (Cold Spring Harbor Laboratory)
GJ Berman (Emory University)
AF Bitbol (Universite Pierre et Marie Curie)
S Bradde (Physical Review)
N Brenner (Technion)
M Castellana (Institut Curie)
LJ Colwell (Cambridge University)
AL Fairhall (University of Washington)
O Marre (Institut de la Vision, Paris)
T Mora (Ecole Normale Superieure, Paris)
LC Osborne (Duke University)
SE Palmer (The University of Chicago)
K Rajan (Mount Sinai School of Medicine)
E Schneidman (Weizmann Institute)
K Sen (Boston University)
S Setayeshgar (Indiana University)
TO Sharpee (Salk Institute)
N Slonim (IBM Haifa)
GJ Stephens (VU Amsterdam & OIST)
SP Strong (retired from DE Shaw)
S Still (University of Hawaii)
AM Walczak (Ecole Normale Superieure, Paris)

Undergraduates

B Agüera y Arcas (Google)
T Broderick (MIT)
E Lee (Cornell)
K Moortgat (Mohr Davidov)
Mariela Petkova (Harvard)

PhD Students

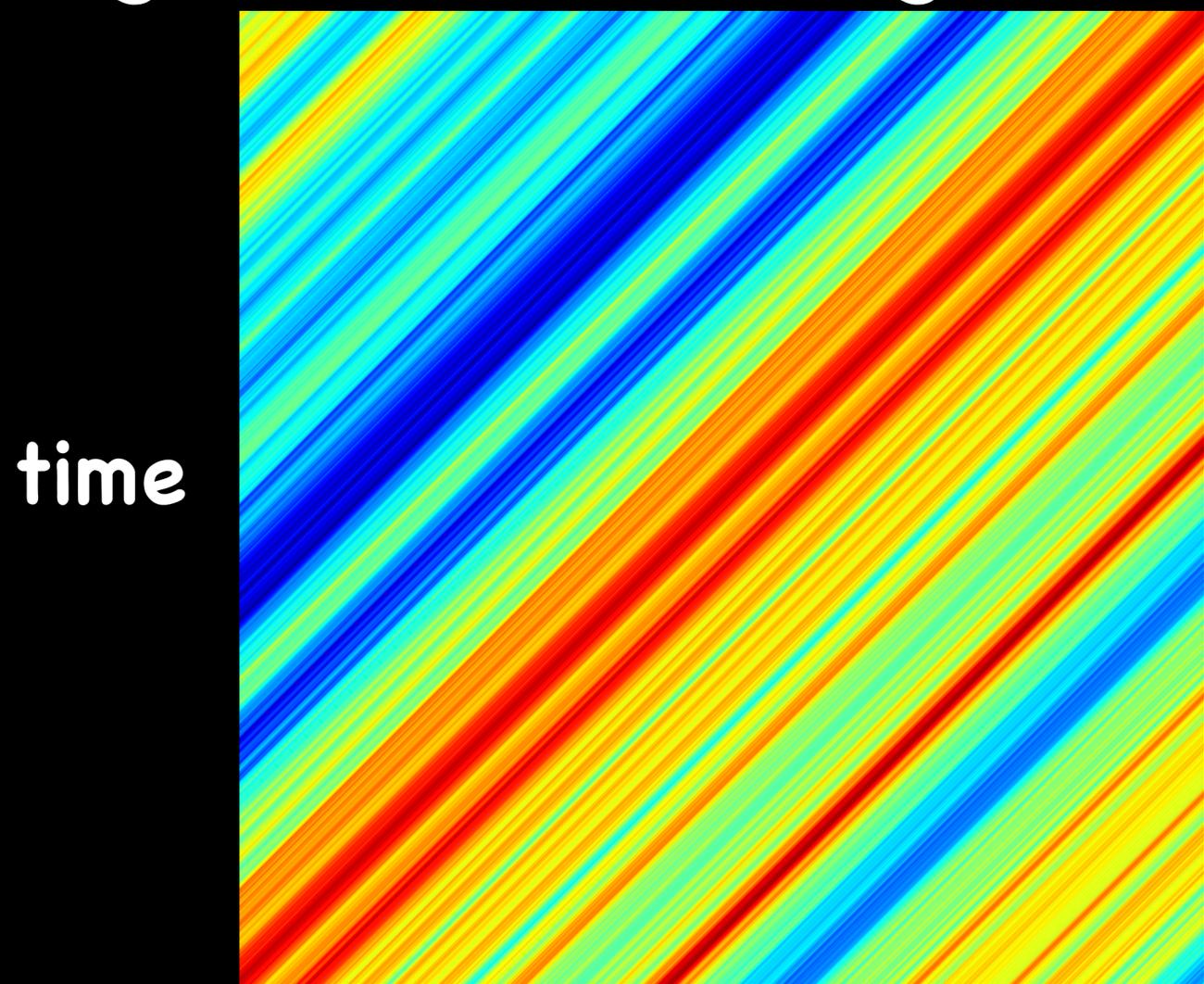
V Alba (Northwestern)
D Amodei (Stanford)
F Azhar (Johns Hopkins)
JH Bak (KIAS)
S Bruder (Webalo)
WJ Bruno (LANL)
X Chen
DV Chigirev (I2BF Capital)
MC Crair (Yale)
M DeWeese (UC Berkeley)
JO Dubuis (BCG)
T Gregor (Princeton)
D Krotov (IAS)
L Kruglyak (UCLA/HHMI)
L McGough
L Meshulam
M Potters (Capital Fund Management)
I Nemenman (Emory University)
F Rieke (University of Washington/HHMI)
DL Ruderman (USC)
S Skourtis (University of Cyprus)
S Smirnakis (Baylor)
ND Socci (Sloan-Kettering)
M Tikhonov (Harvard)
SF Taylor
G Tkacik (IST Austria)
D Warland (UC Davis)

***But all the nonsense is my fault.**

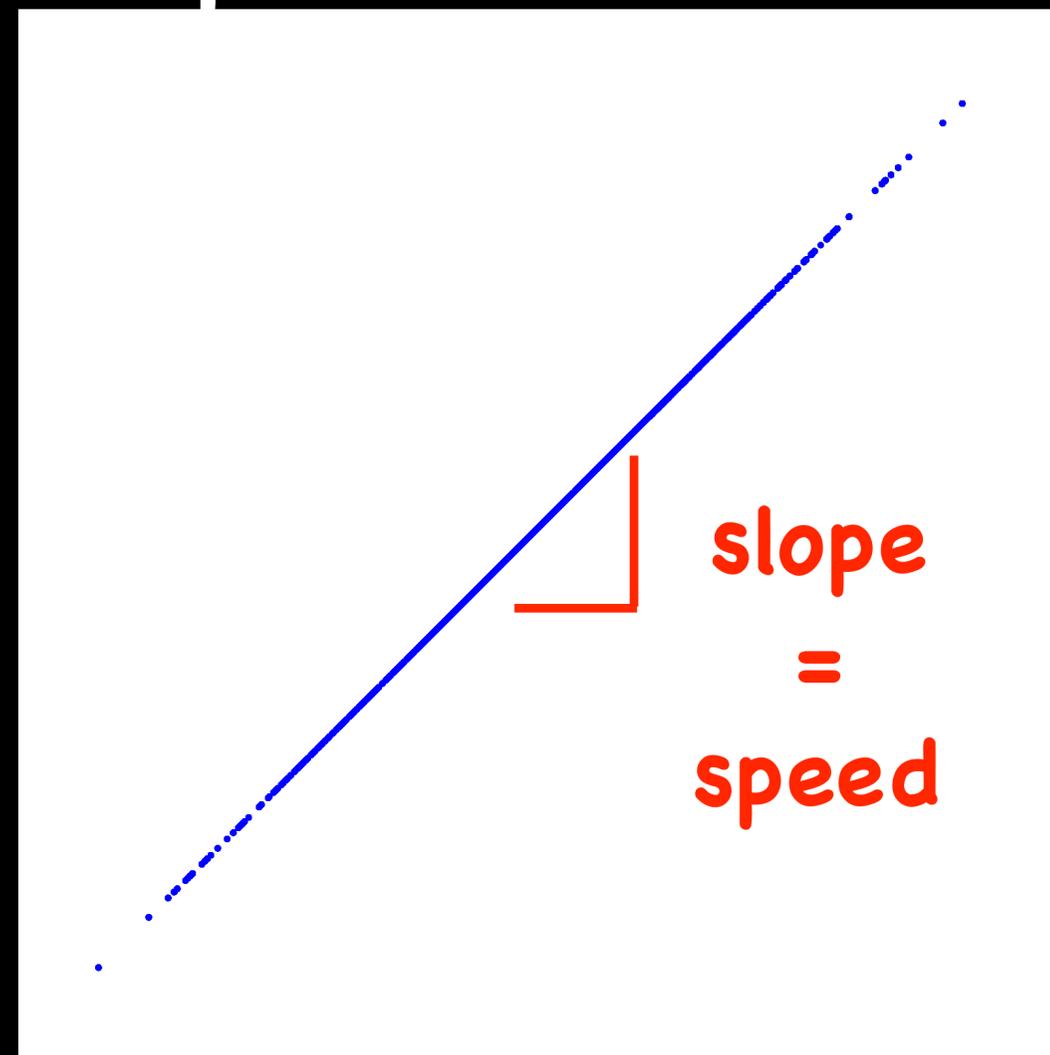
Example: How do we use our vision to estimate the speed of a moving object, or our own speed?

Imagine taking a slice through an image, and following it in time ...

Detect the lines:
compute differences.

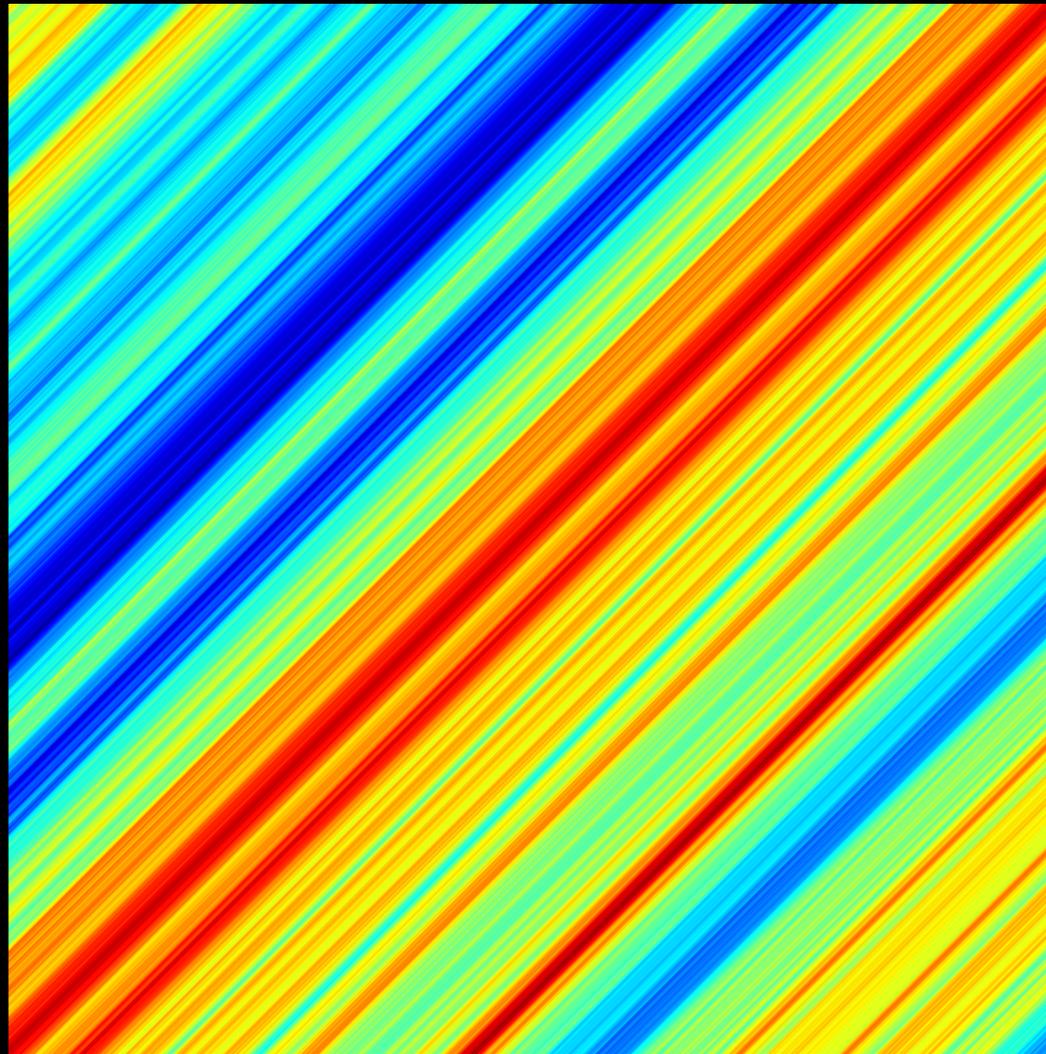


difference from
one moment
to the next

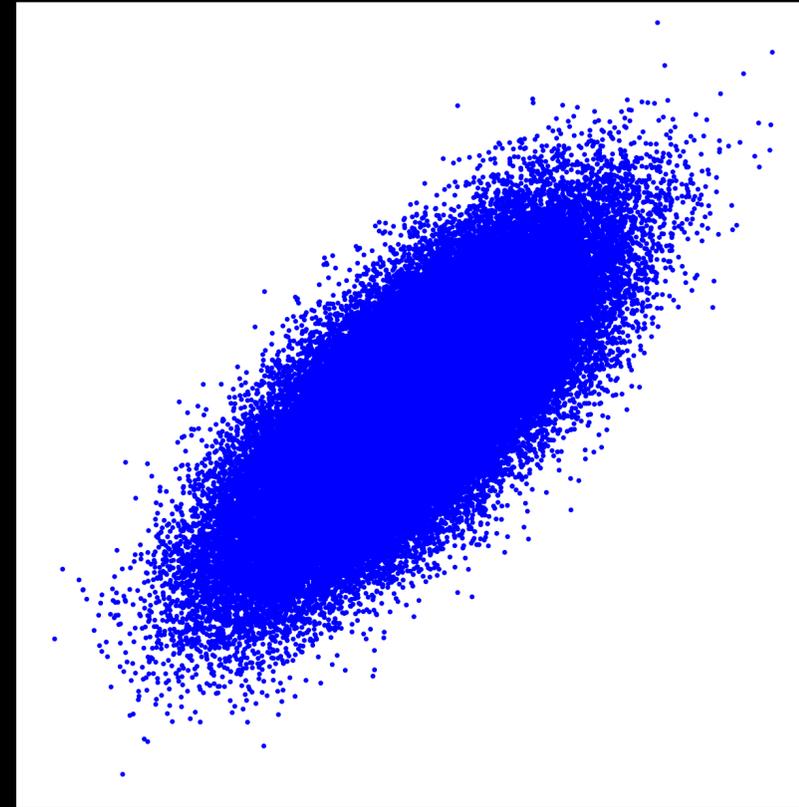


difference between neighboring pixels

But if our image of the world is a little noisy ...



taking differences
makes a mess!



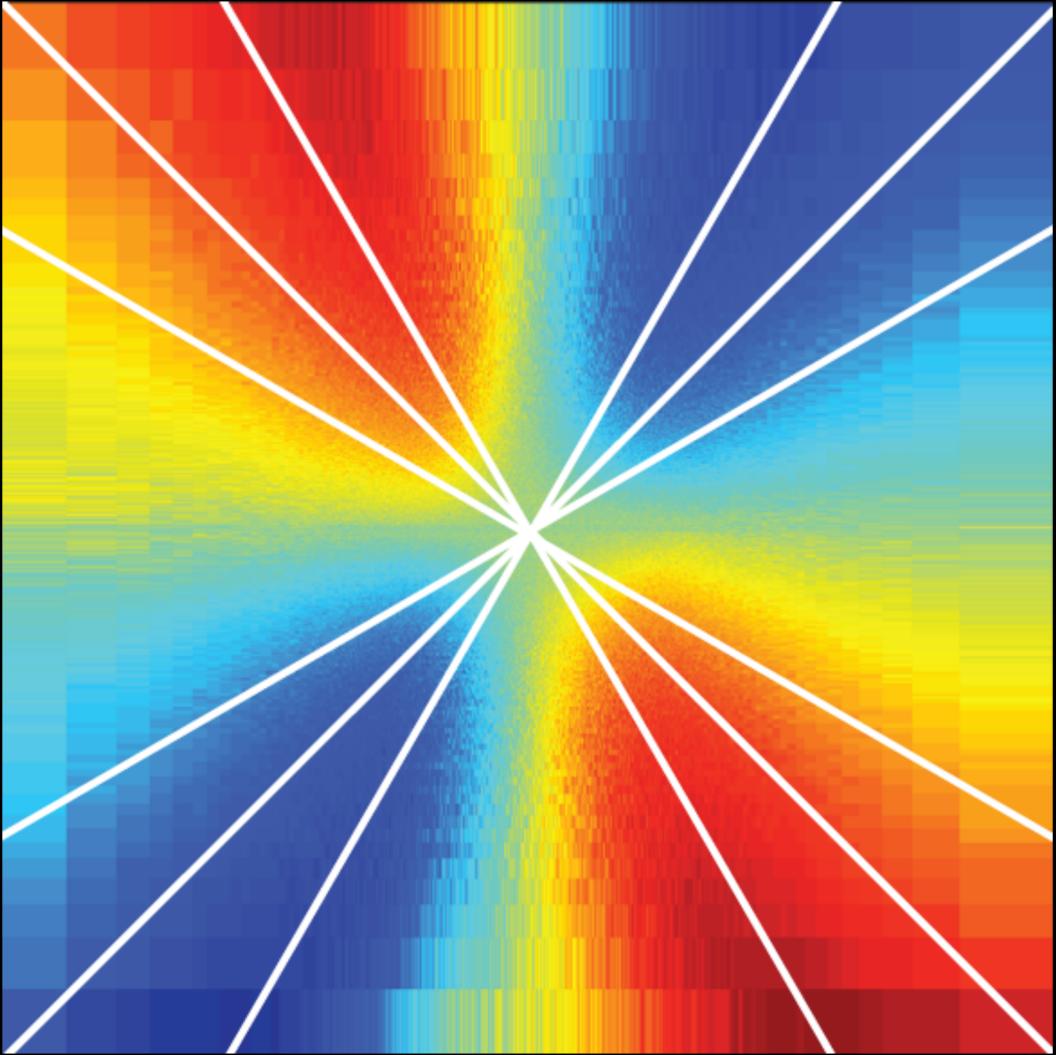
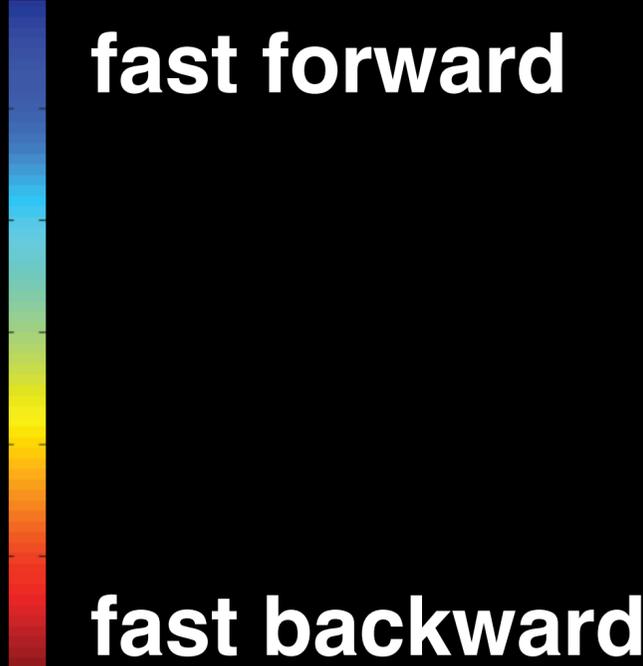
Noise sets a limit to the accuracy
of motion perception.
Real brains approach this limit.

Crucially, the "best" estimate always is a compromise between systematic and random errors.

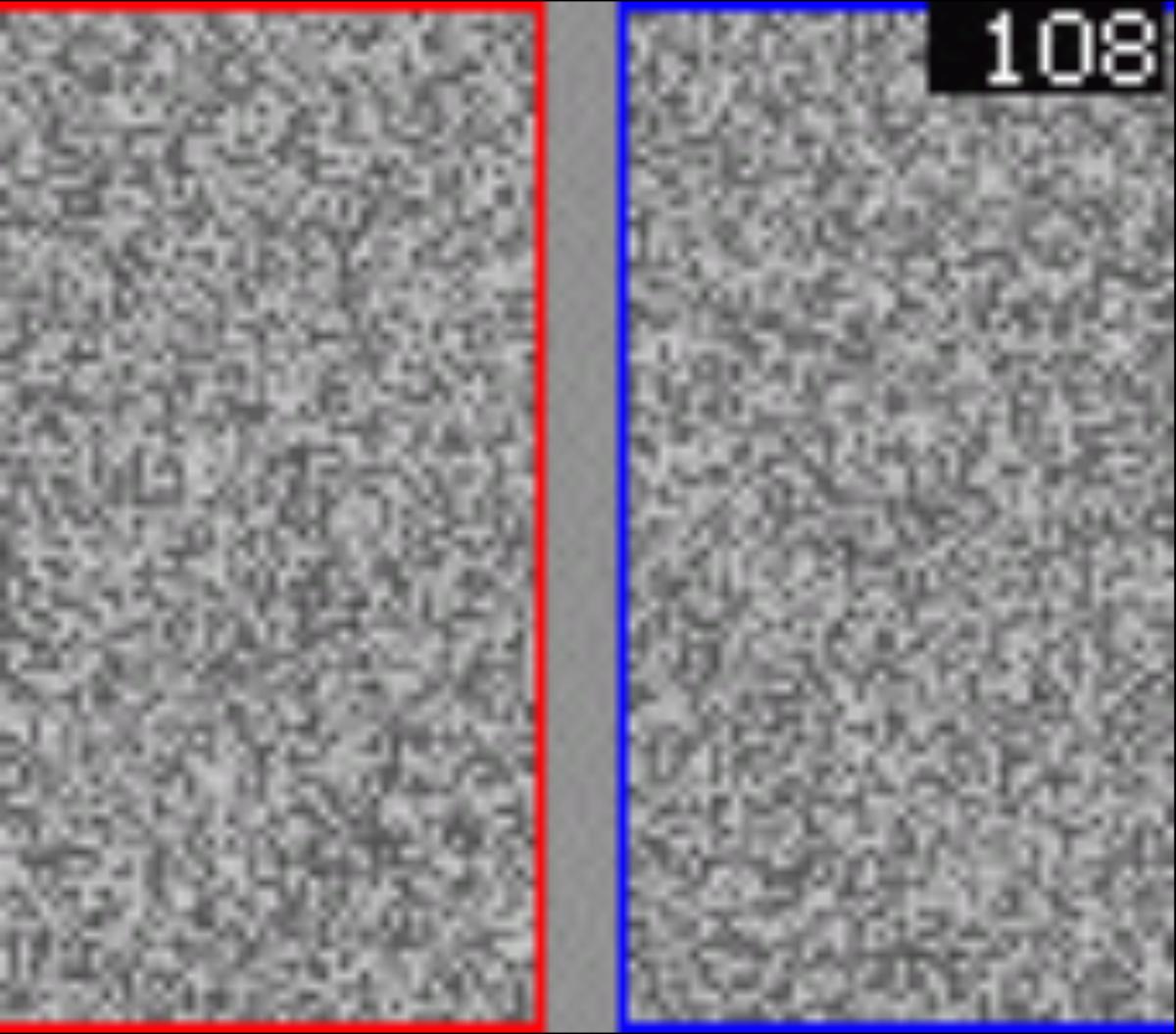
Statistical mechanics and visual signal processing.
M Potters & W Bialek, *J de Physique France I* 4, 1755-1775 (1994).

Real world data
SR Sinha & RR de Ruyter van Steveninck

difference from
one moment
to the next



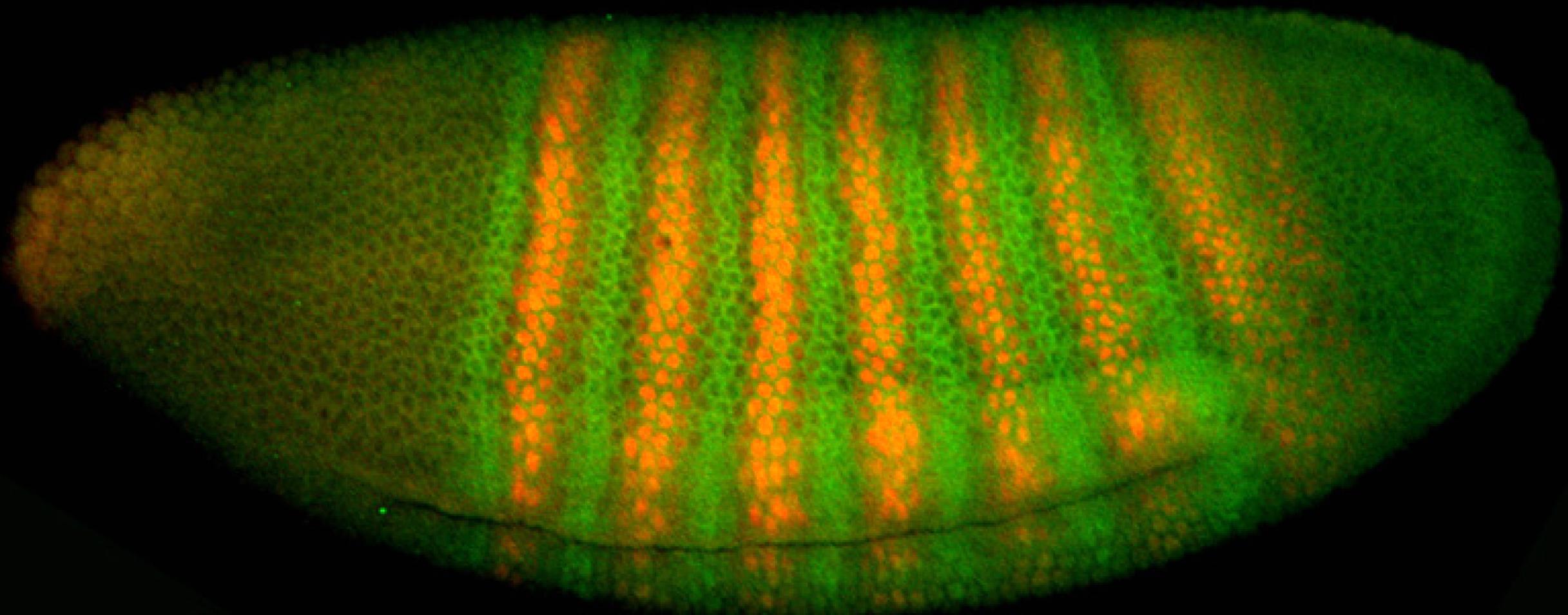
difference between
neighboring pixels



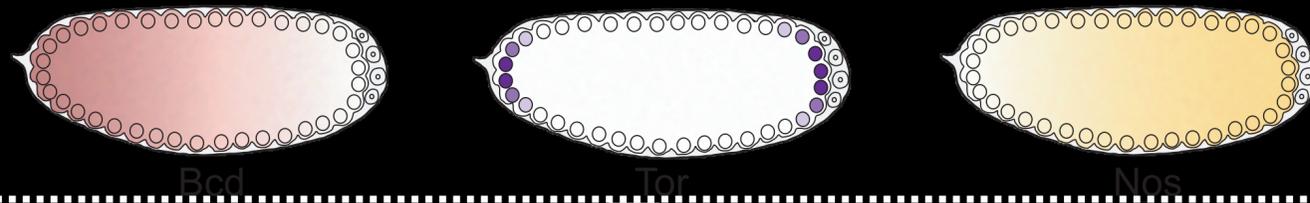
Even if you do the optimal
computation, you can be fooled.



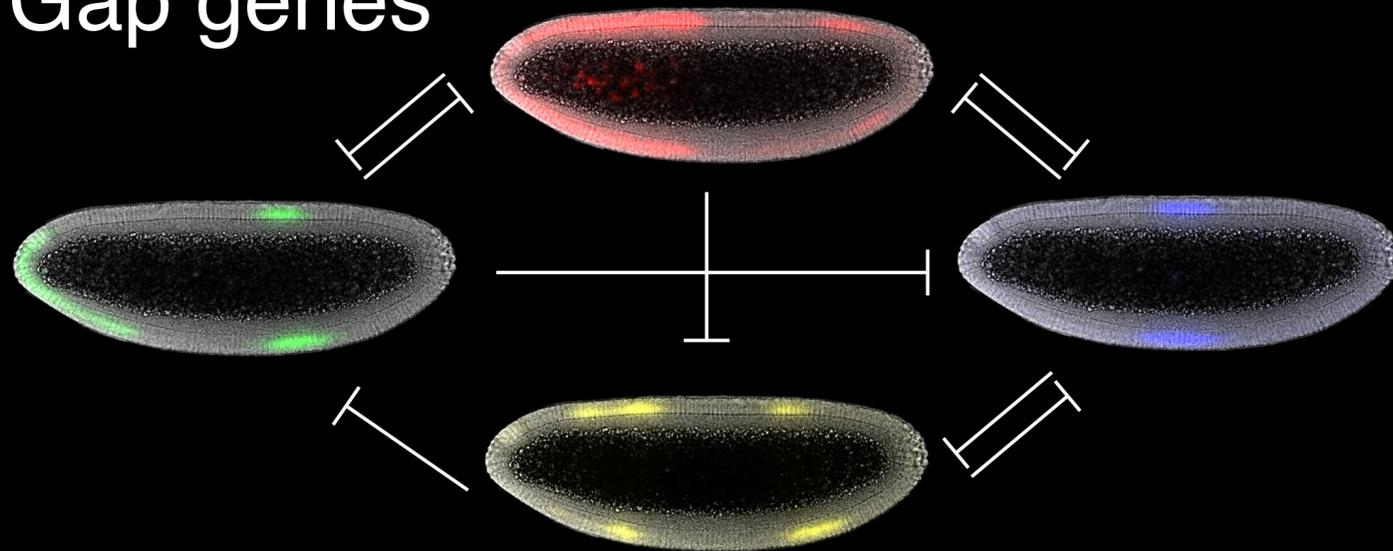
**How do animals
establish their
body plans?**



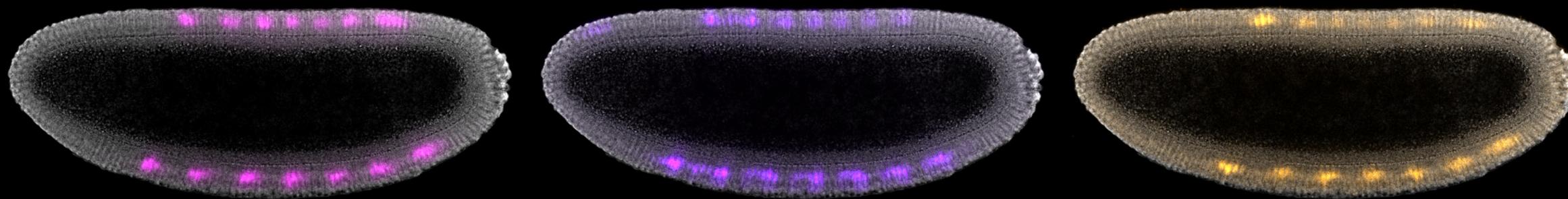
Primary maternal morphogens



Gap genes

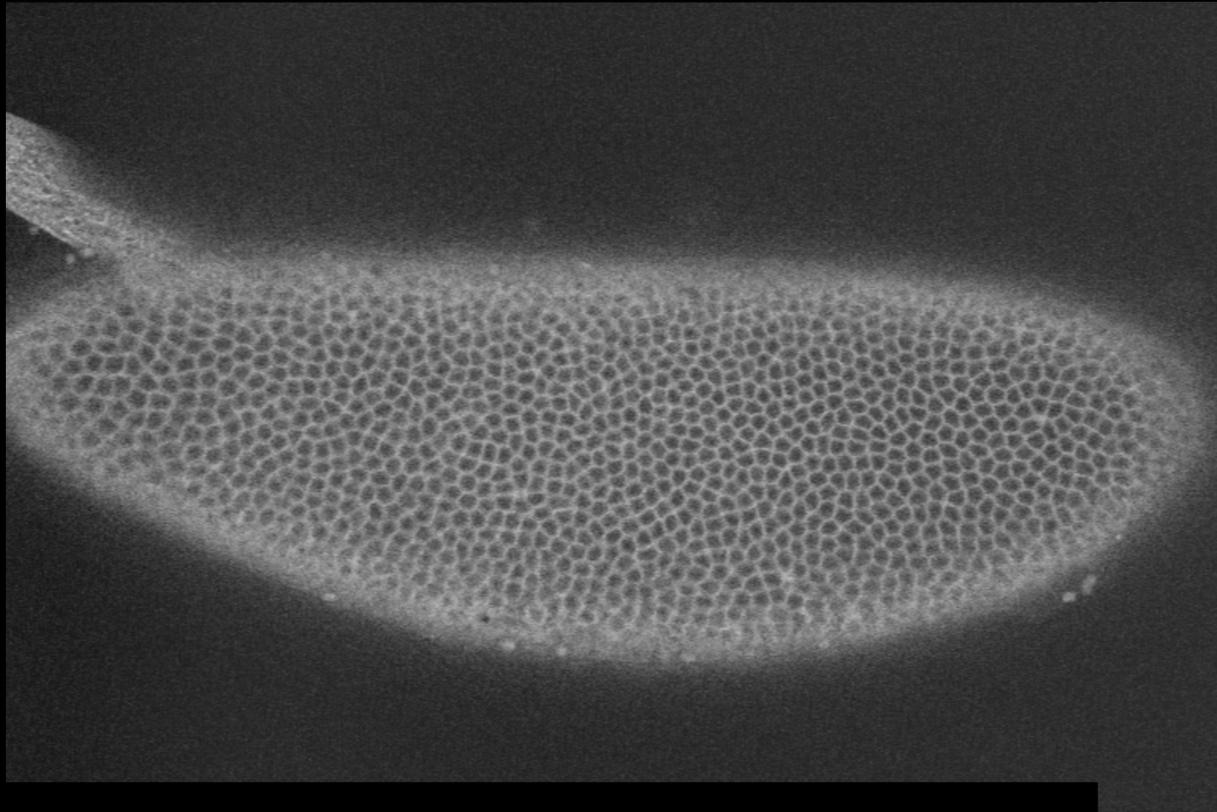
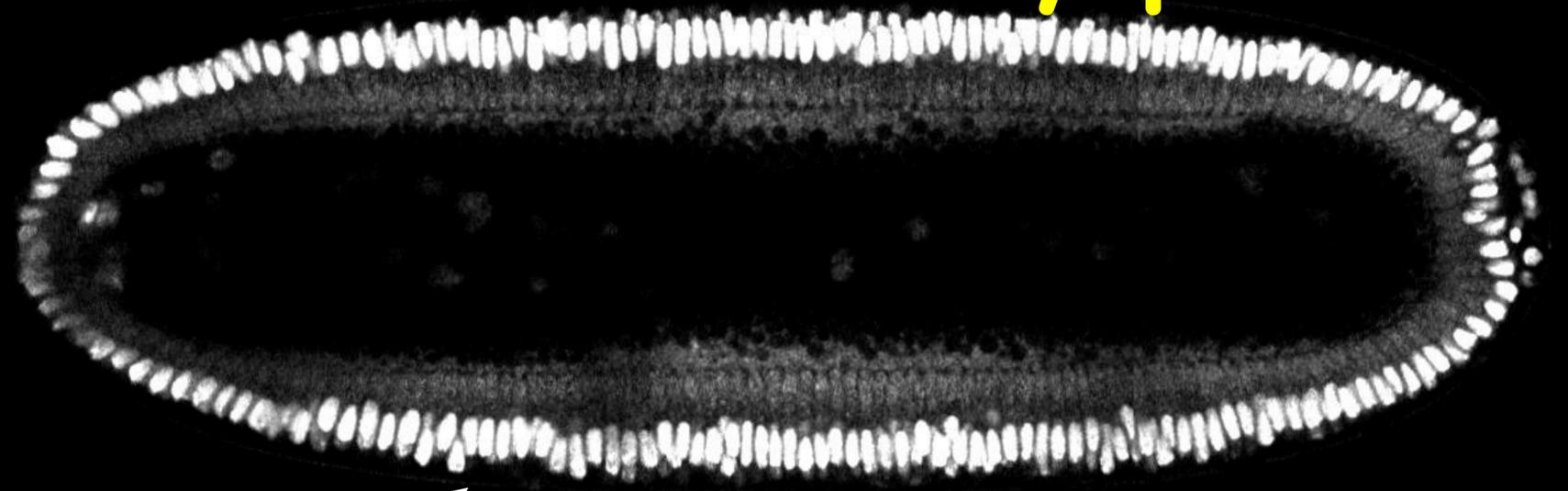
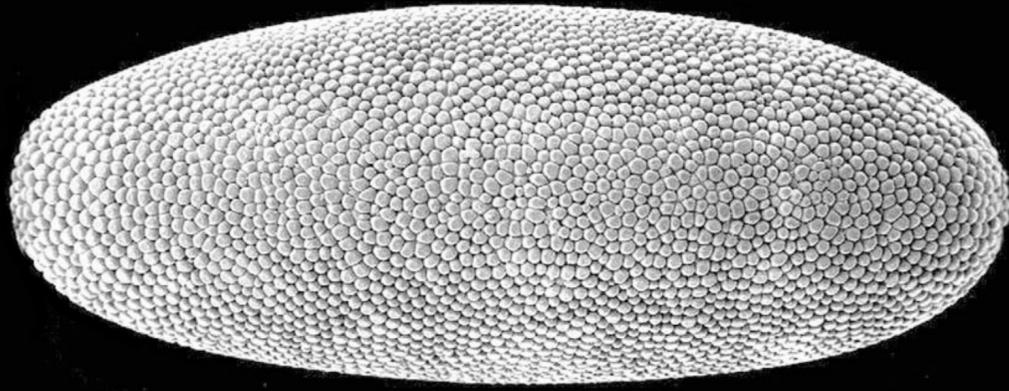


Pair rule genes

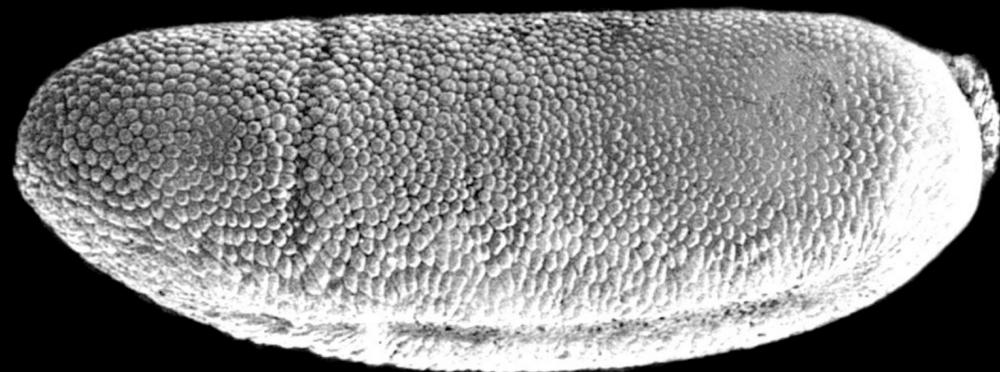
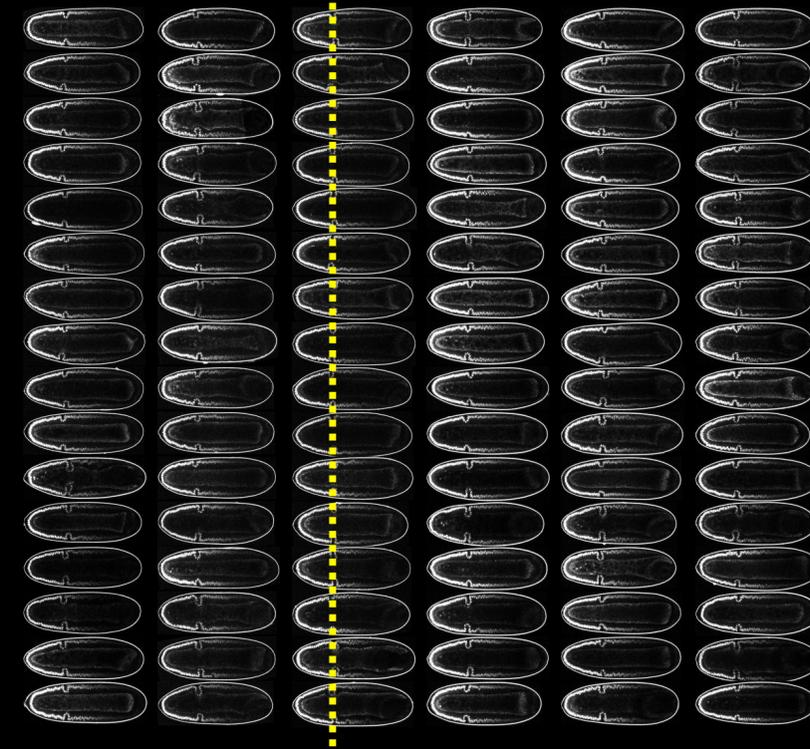


Imagine how many parameters are hidden in this diagram ...

A hint: this process is extraordinarily precise

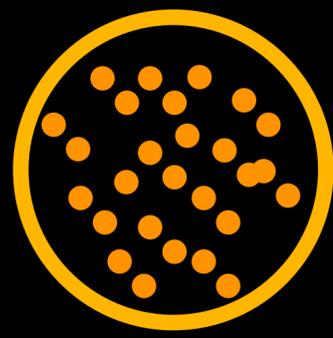
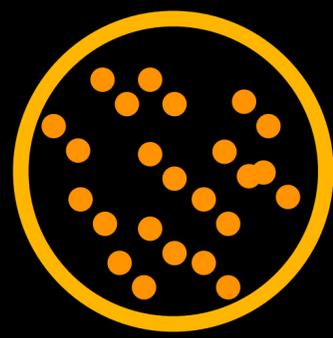


**cephalic
furrow**



**Precision: 1% of embryo
length, or ± 1 cell (!).**

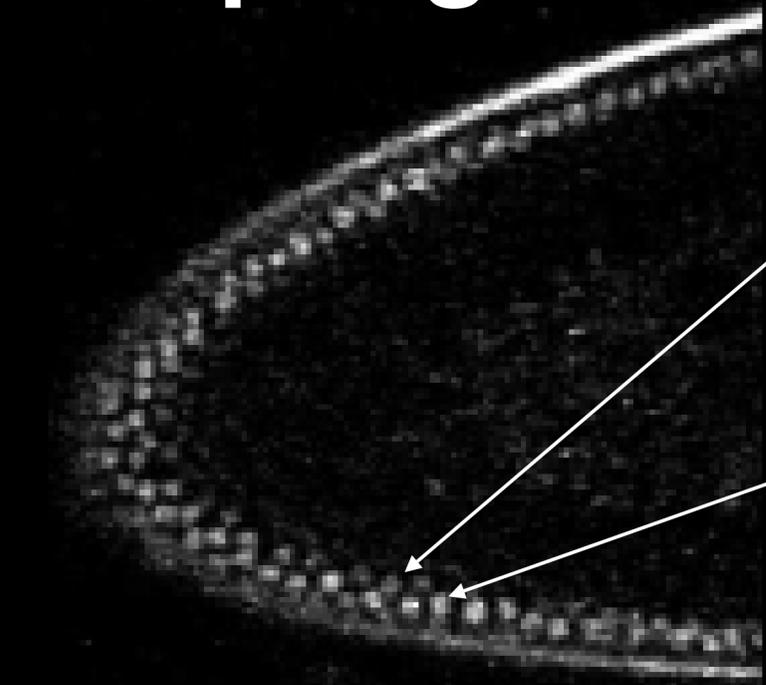
zoom in on the primary morphogens



~1000 molecules
~10% differences

But the cells cannot "stand outside" to look at all the molecules.

In order to have an effect, molecules must bind to a small target along the cell's DNA.

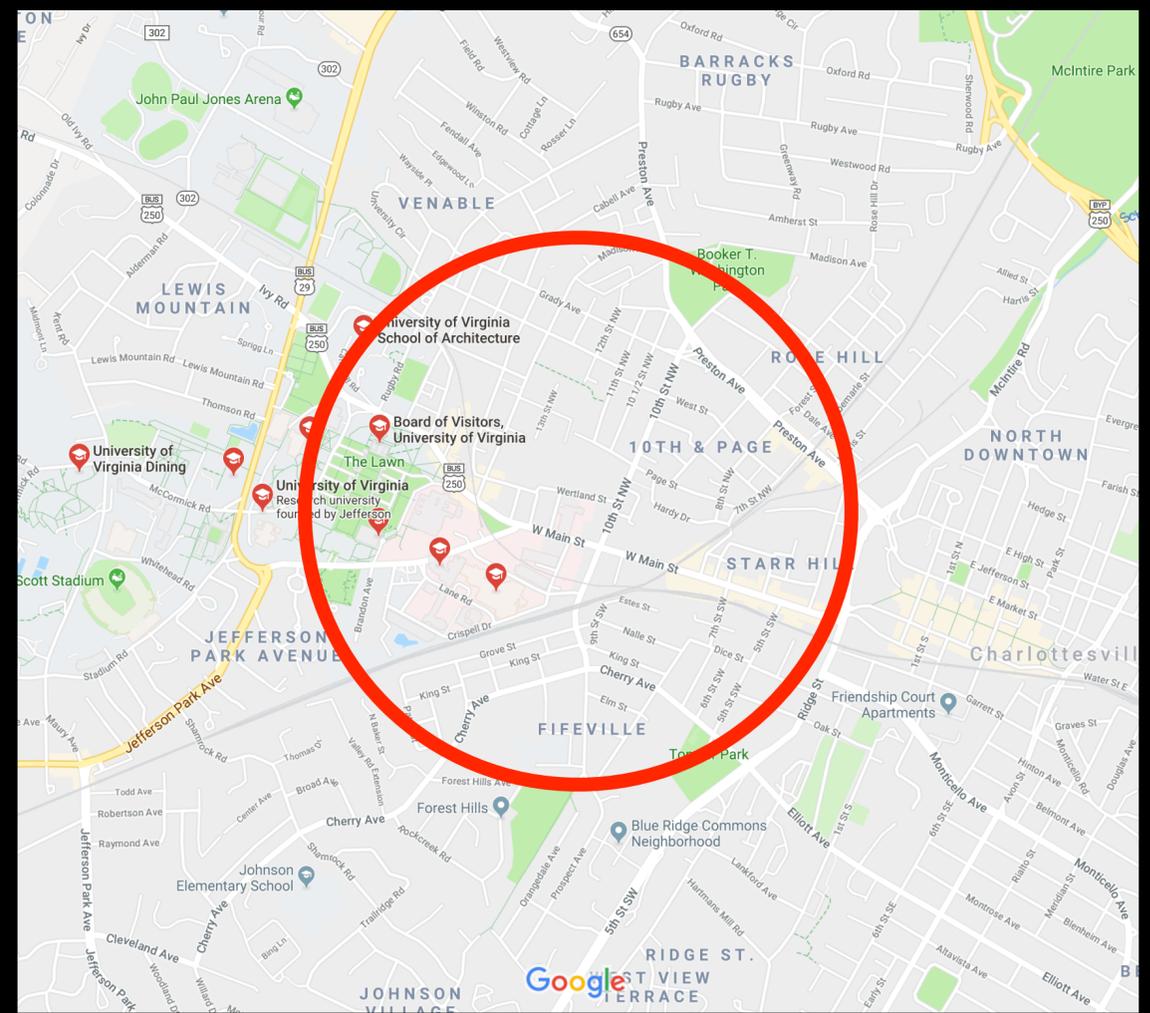


size of nucleus ~ 6 microns

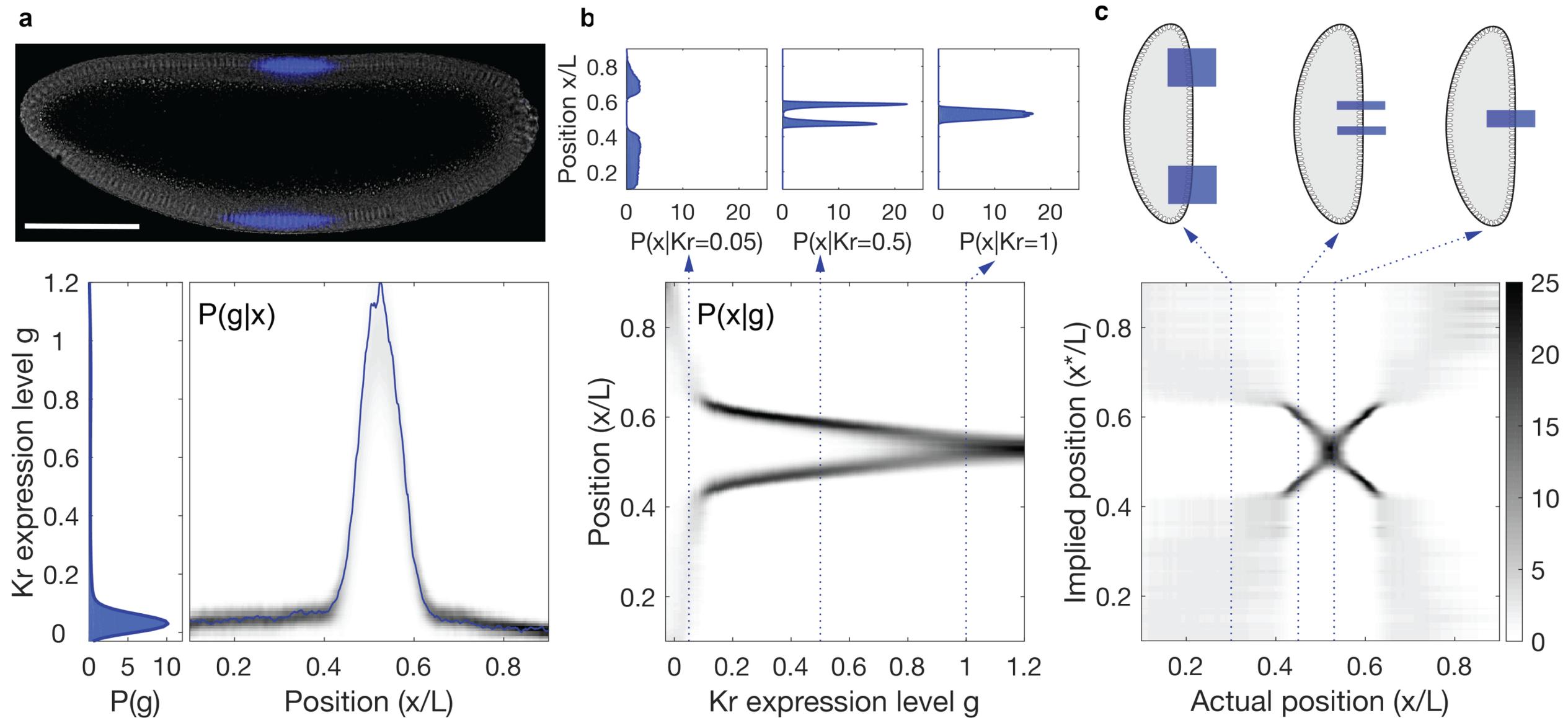
target site on DNA ~ 3 nanometers

suppose the nucleus were the size of our local neighborhood, ~ 1 km

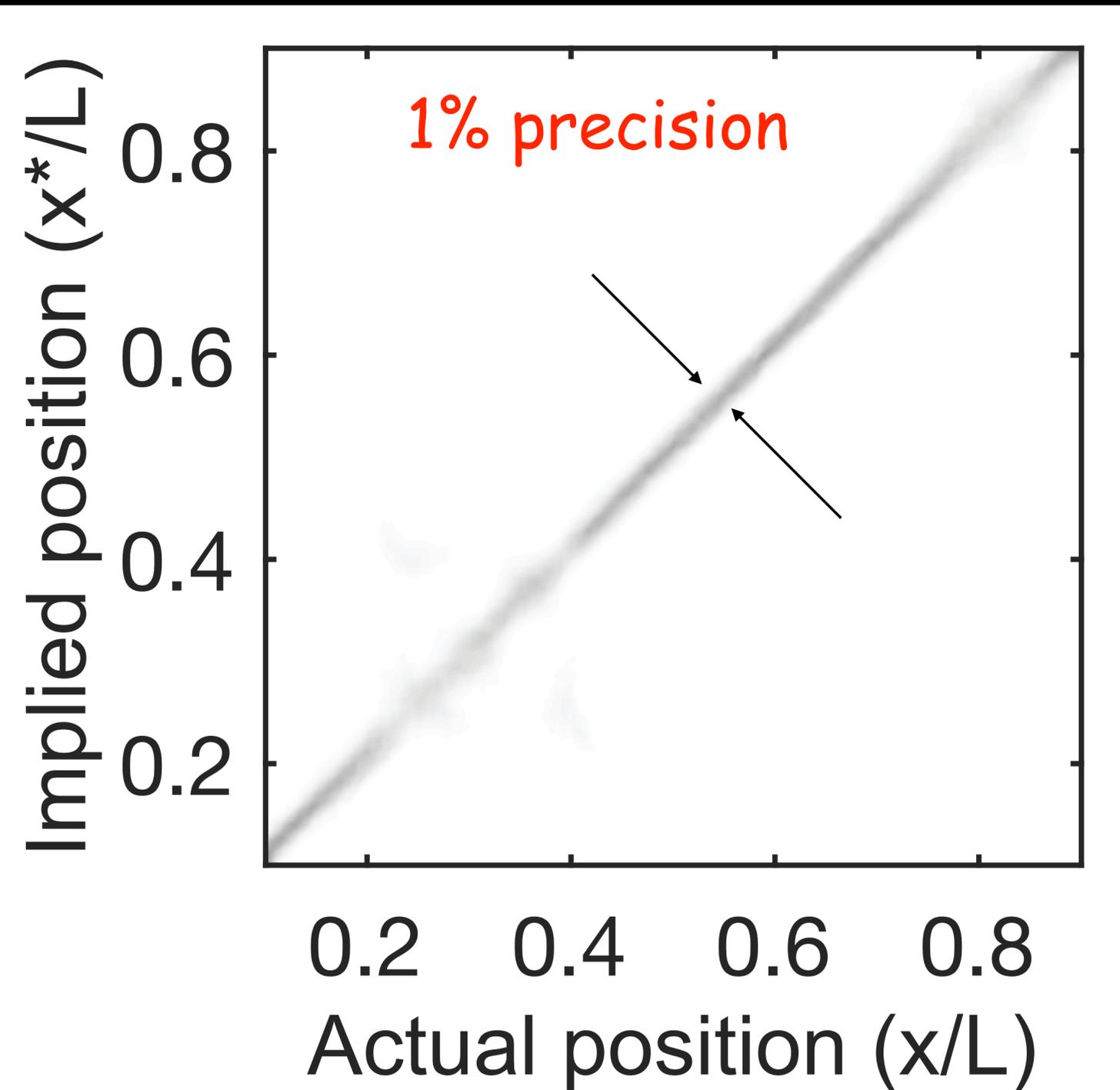
the target would be 1/2 meter in size!



Could the parameters be chosen to squeeze as much information as possible out of the limited number of molecules?



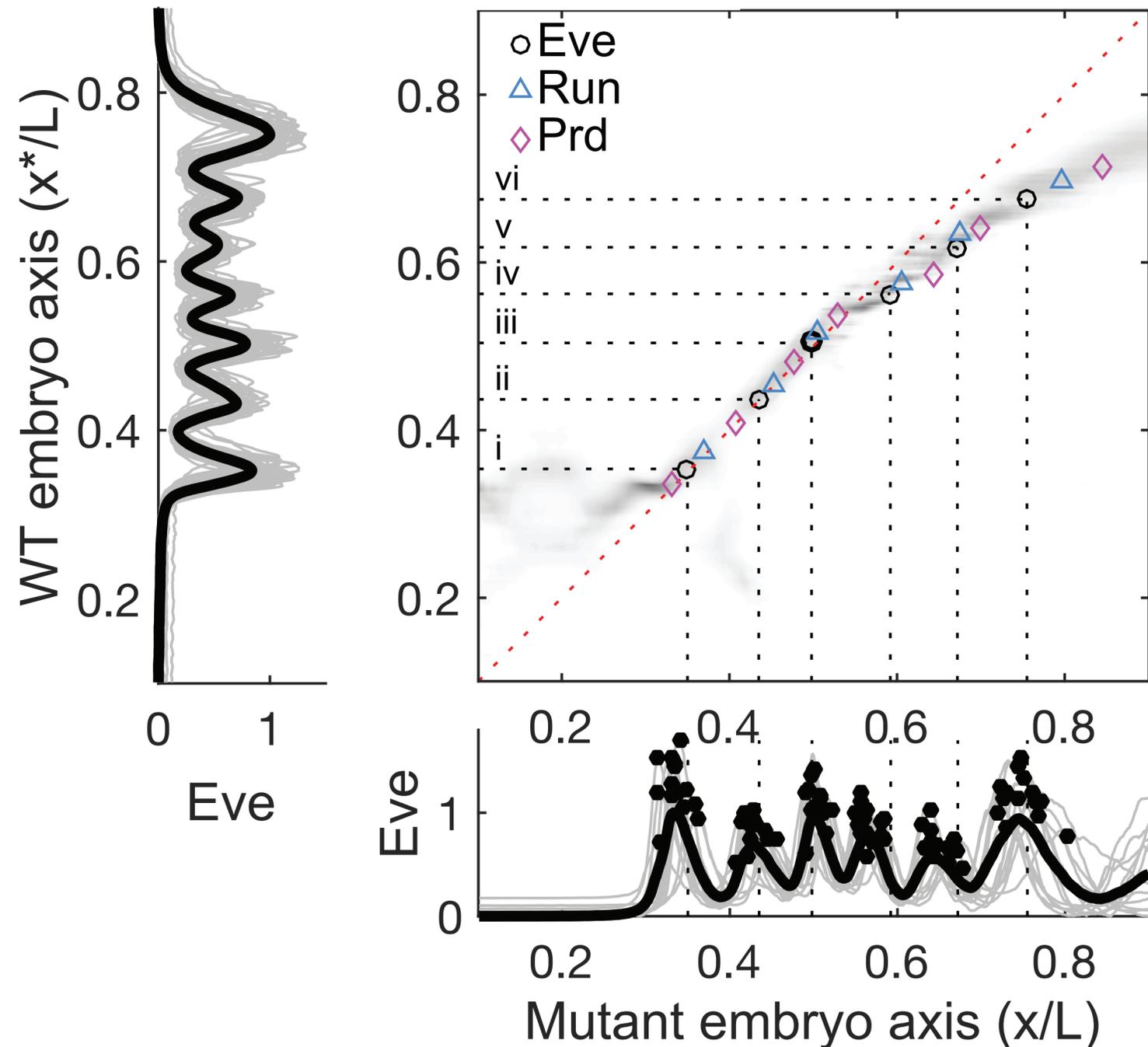
If you put together information from all four gap genes, the ambiguities are resolved.



No parameters!
But is this the rule that
the fly uses for “decoding”?

Let's look in mutants,
where we knock out one of
the primary maternal
morphogen inputs ...

Decoding from mutant flies generates distorted "maps."



When the map points to a position where the normal fly makes a stripe, the mutant should make a stripe. And it does.

Optimal decoding of information from a genetic network.
MD Petkova, G Tkacik, W Bialek, EF Wieschaus, and T Gregor,
arXiv 1612.08084 (2016).

