

# Against Mind-Blindness: Recognizing and Communicating With Unconventional Intelligences

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<http://allencenter.tufts.edu/>

<http://thoughtforms.life/>



ALLEN  
DISCOVERY CENTER  
at Tufts University

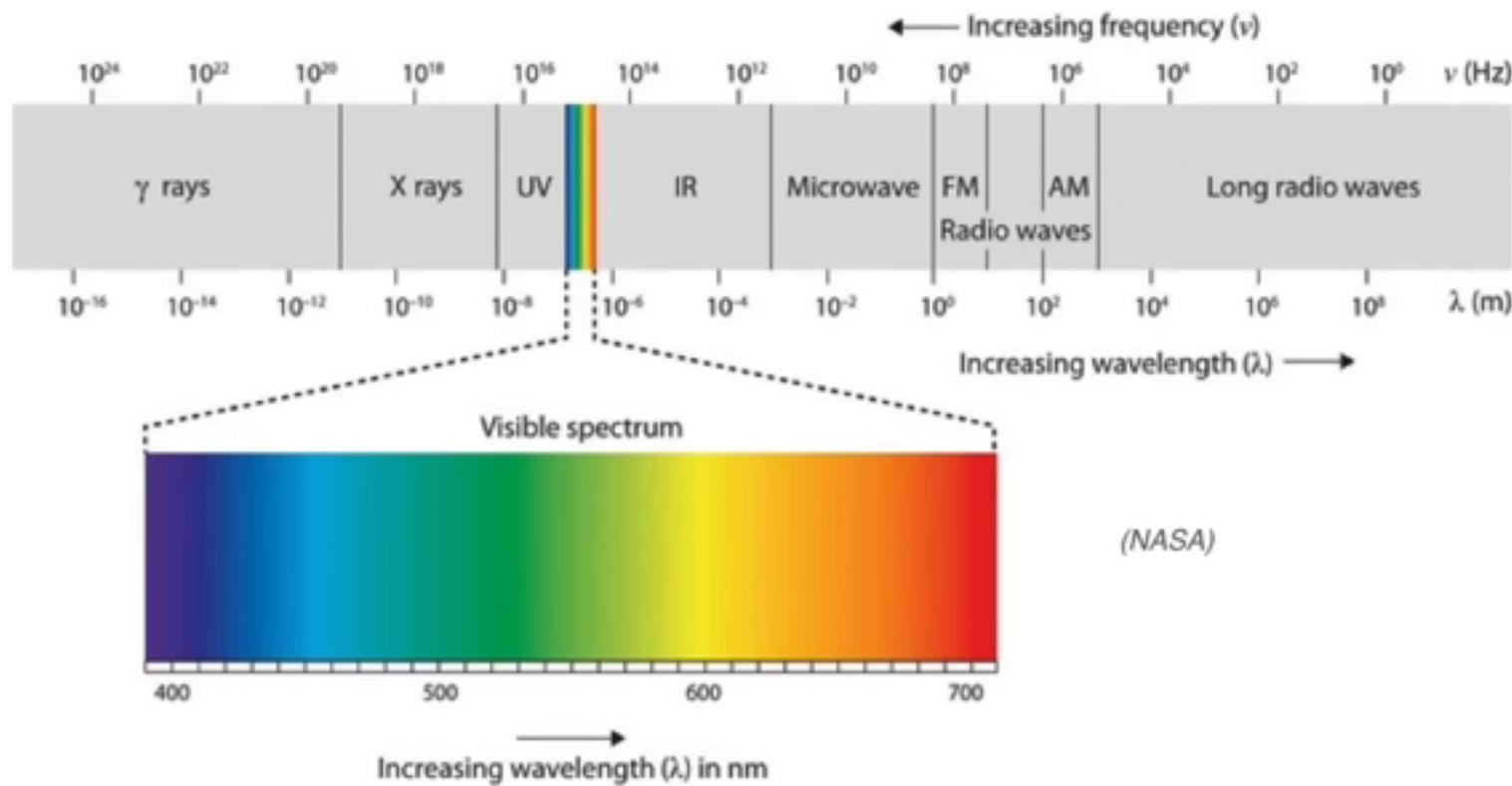


Computer-designed Organisms  
TUFTS UNIVERSITY | UNIVERSITY OF VERMONT

WYSS  
INSTITUTE



# The Power of Unification: spectrum of cognition

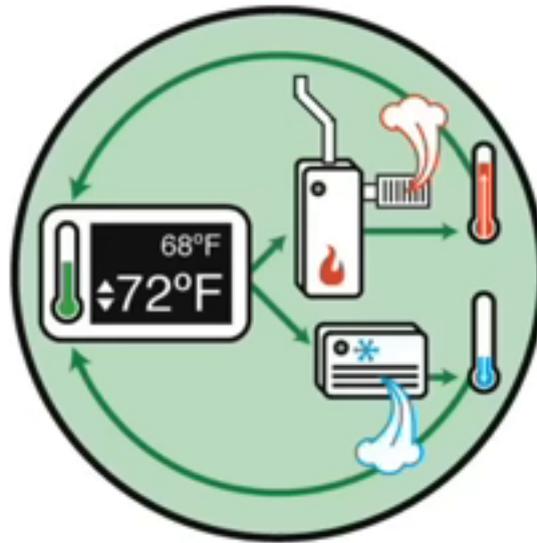


- understand how diverse phenomena are a continuum
- create technology to observe and detect parts of that continuum of which we were previously oblivious
- utilize this knowledge for a myriad of applications that improve quality of life

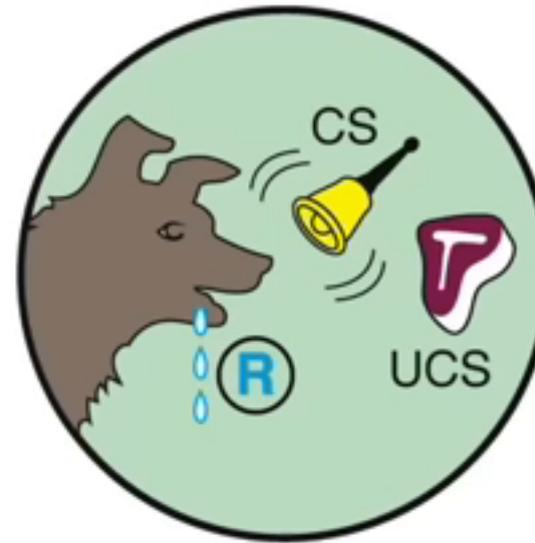
# Axis of Persuadability:



Hardware modification only



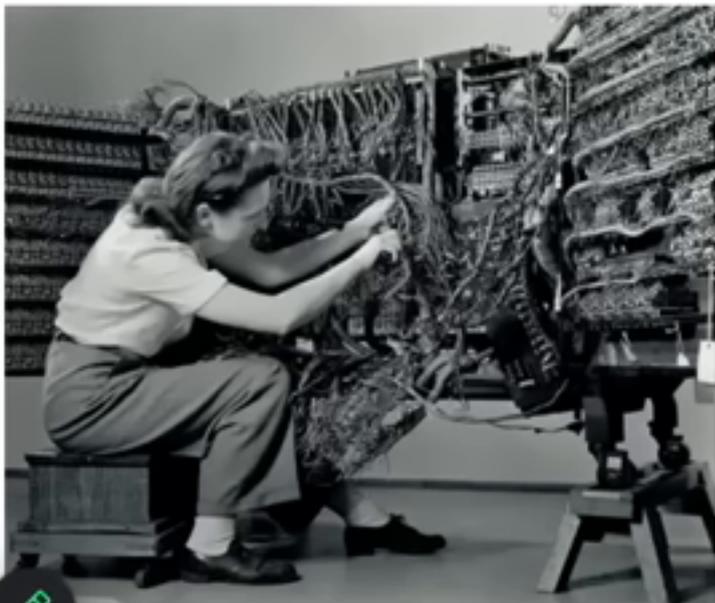
Modify the data encoding setpoint of goal-driven process



Training by rewards/punishments



Communicate cogent reasons



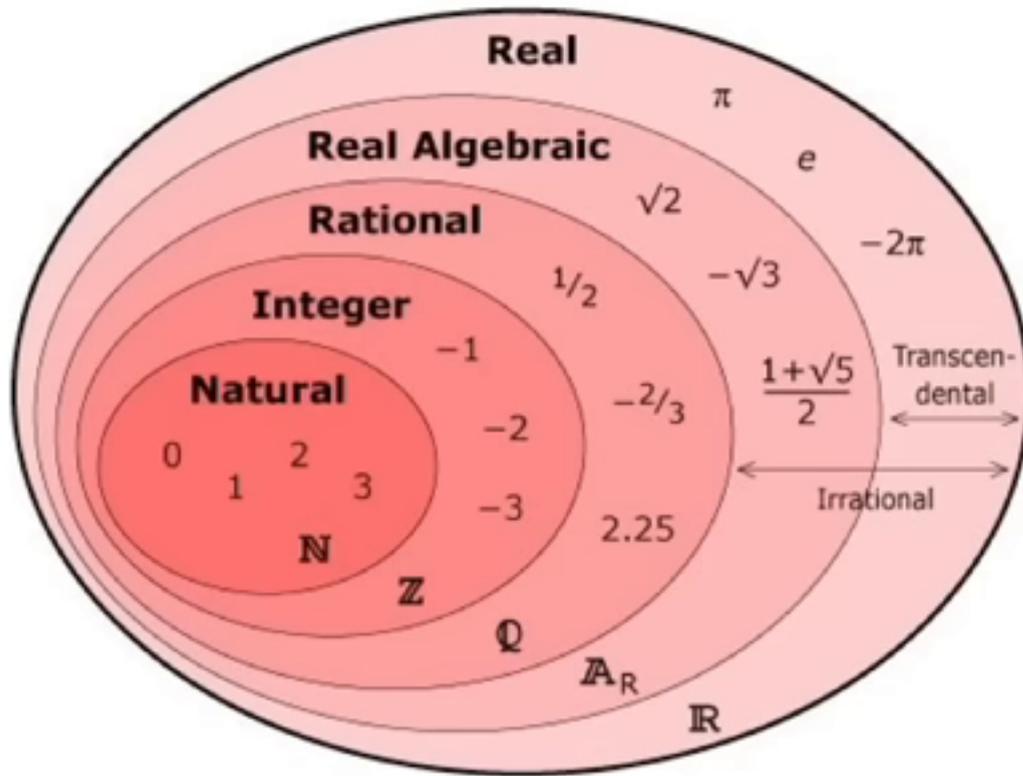
Intelligence is to be decided empirically, not via stale philosophical categories

Cognitive claims are interaction protocol claims

- > better technology
- > better ethics



# Expanding the Set of Cognitive Kin



frozen patterns

active patterns

evolved +  
designed +  
hybrid agents

all  
biologicals

complex  
life forms

brainy  
animals

## For each new category

- conceptual leap needed
- what does it break?
- recognize them
- do something useful with them
- active compassion toward them

<https://in.pinterest.com/pin/627970741770398254/>



# Easy to Detect Mind in Brainy Mammals

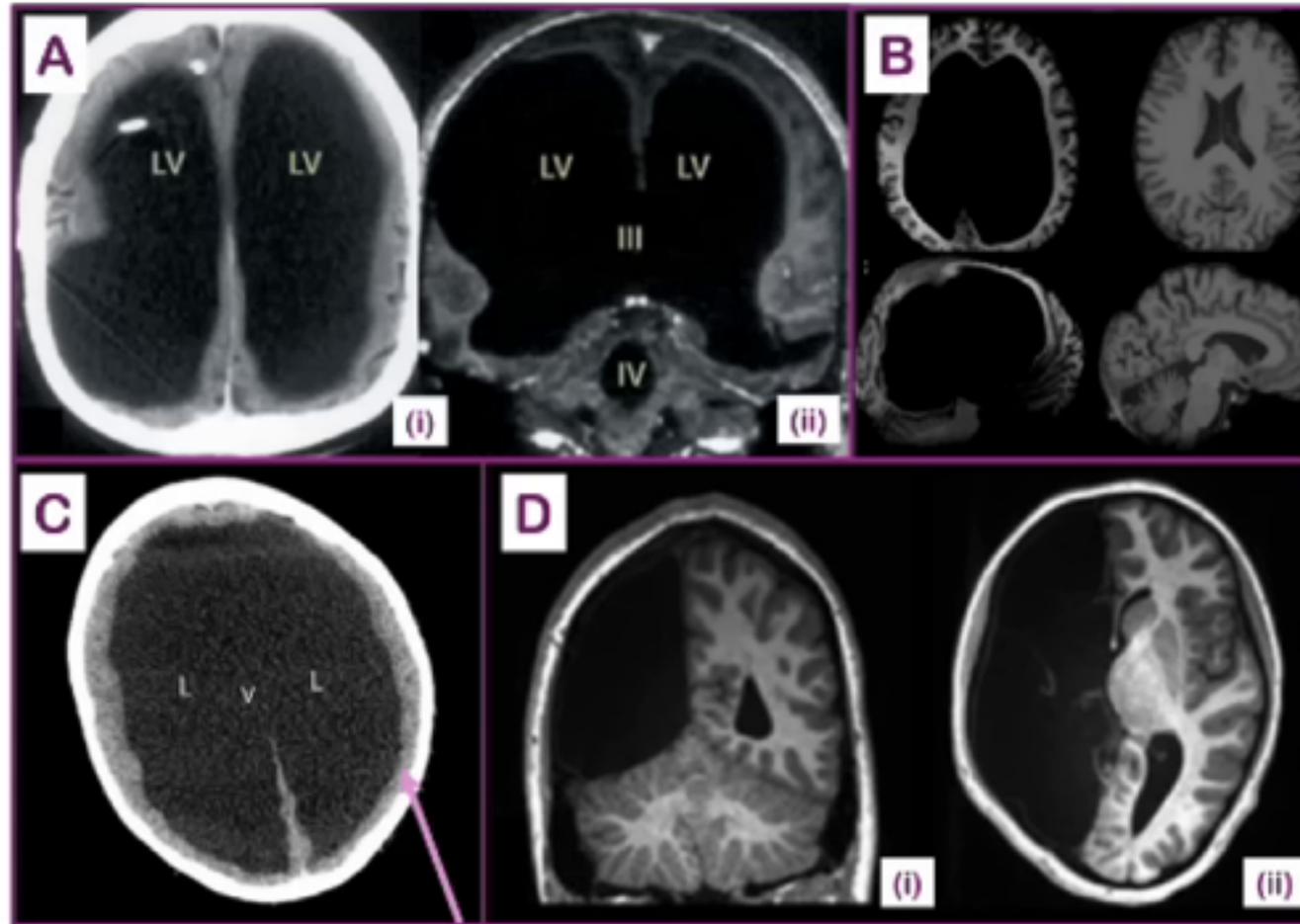


[https://www.youtube.com/watch?v=f75Vet\\_sJNo](https://www.youtube.com/watch?v=f75Vet_sJNo)

Why so obvious? Same spatiotemporal scale, same space, similar goals



# Even with brains, things are not simple



Minimal brain  
structure

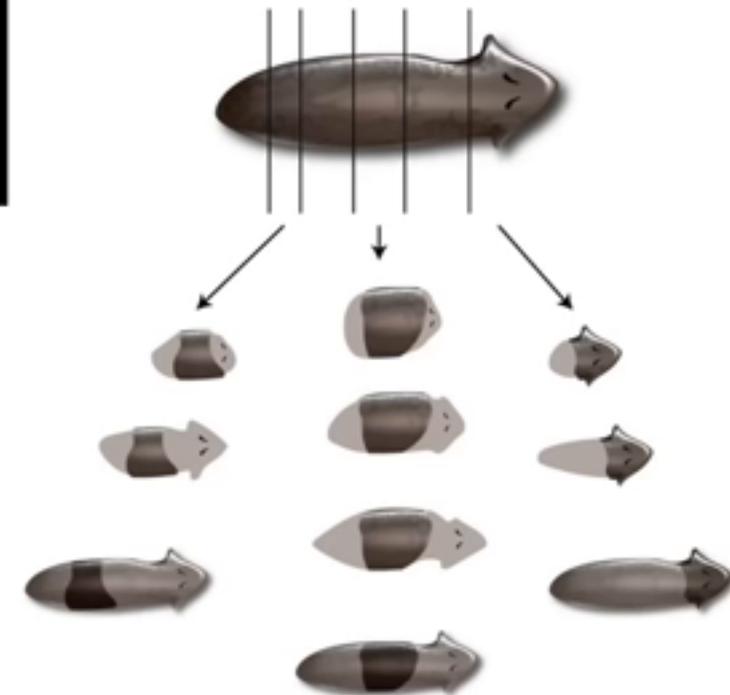
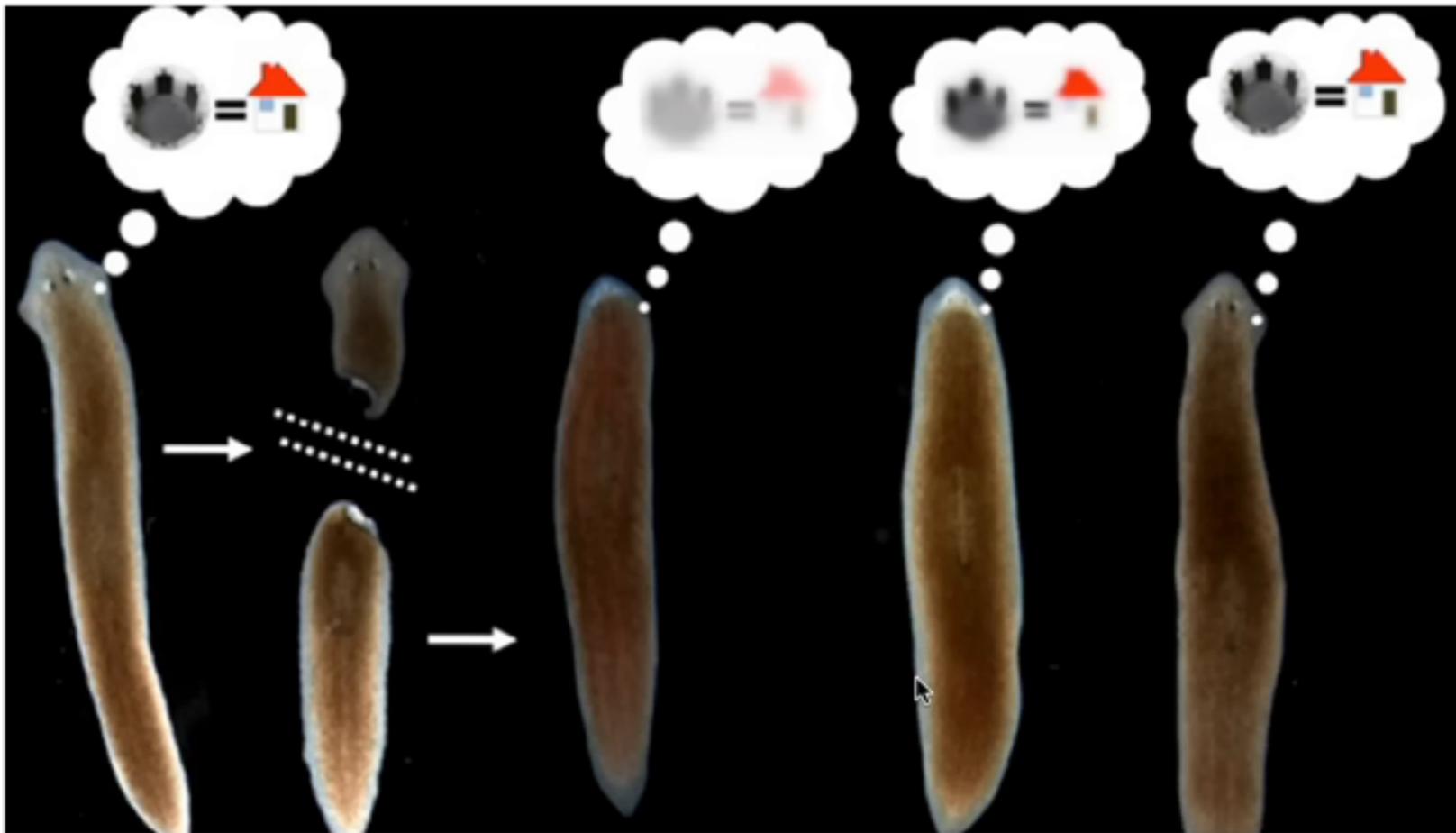
or function  
(Savant  
syndrome)

cases of high  
performance

**Figure 2.** Select cases of reductions in brain matter with normal function. **[A]** Image from (Feuillet *et al.* 2007) showing a white collared worker case of extreme hydrocephalus; he led a normal life as a civil servant, who possessed an average IQ of 75. During his neurological assessment at age 44, his (i) CT scan and (ii) T1 weighted MRI scans with contrast showed extreme ventricular enlargement. LV indicates lateral ventricle, III and IV indicate the third and fourth ventricles, respectively. **[B]** Image from (Alders *et al.* 2018), showing the case of a 60-year-old with a bad mood with massive ventriculomegaly and severely reduced cerebral mantle and corpus callosum, that went largely unnoticed. The left column is T1 weighted MRI images taken in the transverse, coronal, and sagittal planes of the patient. The right column represents T1 weighted MRI scans of a healthy control. **[C]** Image from (Persad *et al.* 2021), imaging of a Canadian living a normal, independent life with massive hydrocephaly. MRI scan taken from the axial view (plane parallel to the ground) at the level of the lateral ventricles (arrow points to extremely thin layer of cortical mantle, LV stands for Lateral Ventricle). **[D]** Image from (Asaridou *et al.* 2020), showing the T1 Weighted MRI scans of a child born without left hemisphere (i) taken in the coronal plane, (ii) taken in the axial plane. The child had normal cognitive development and language skills despite hemispherectomy of the left hemisphere and near-absence of the corpus callosum. All images re-used with permission.

# Memories Survive Brain Regeneration

Memory stored outside the head, imprinted on regenerated brain



© 2016, Published by The Company of Biologists Ltd | Biology Open (2016) 5, 1177-1188 doi:10.1242/bio.030149



## HYPOTHESIS

Vertically- and horizontally-transmitted memories – the fading boundaries between regeneration and inheritance in planaria

Moran Neuhof<sup>1,\*</sup>, Michael Levin<sup>2,\*</sup> and Oded Rechavi<sup>1,2,3,\*</sup>



# Biological Intelligence outside the Brain

- Conceptual leap needed: intelligence is older than brains
- What it breaks: scale and substrate
- How to recognize them: anatomical goals, ingenuity
- Useful implications: biomedicine

model system: cells as collective intelligence in morphospace

# We are Made of Agential Materials



Lacrymaria = 1 cell  
no brain  
no nervous system

high competency  
at cell-level  
agendas

nature reviews bioengineering

<https://doi.org/10.1038/s44222-022-00001-9>

Review article

 Check for updates

## Synthetic morphology with agential materials

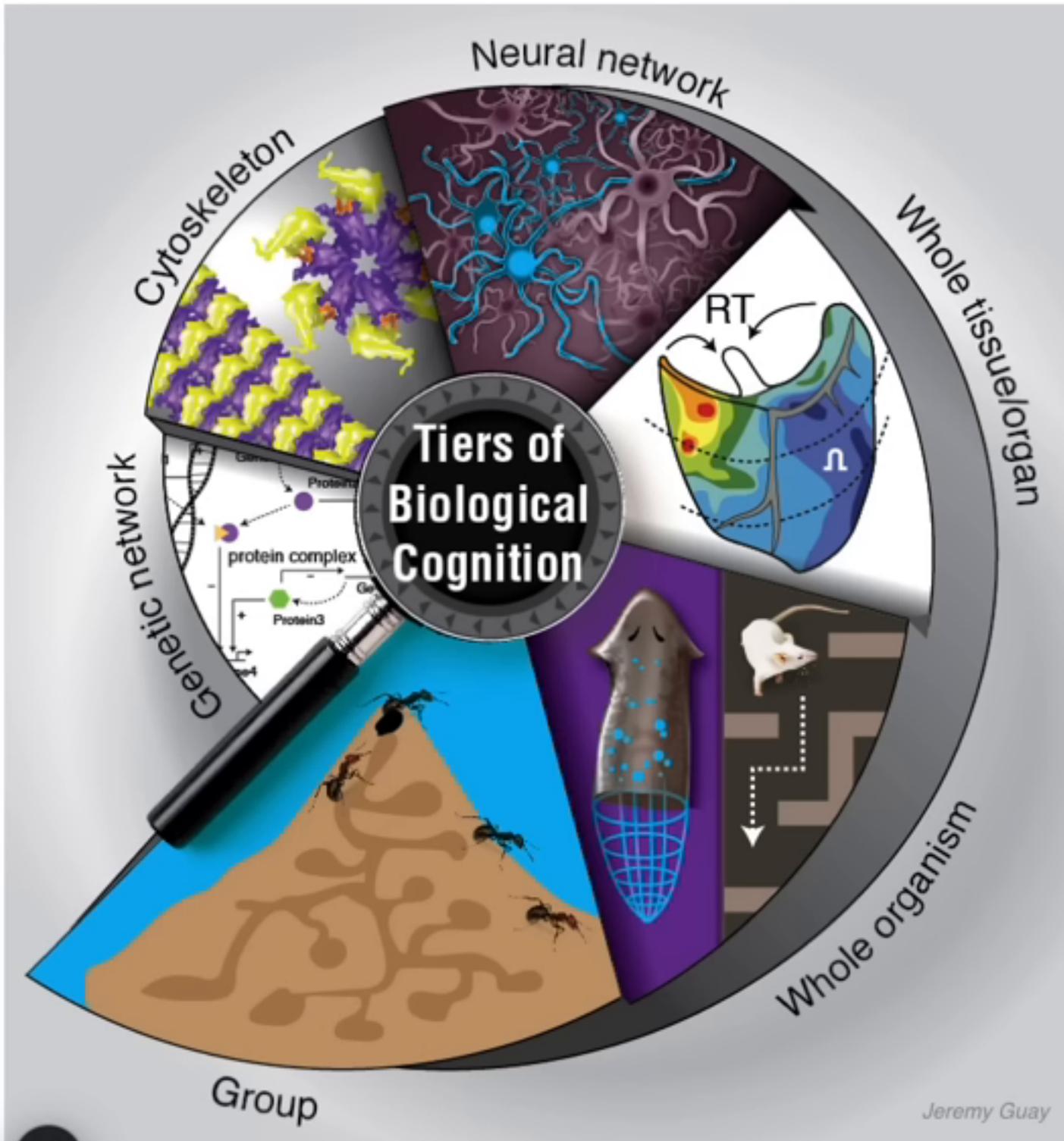
Jamie Davies<sup>1</sup> & Michael Levin<sup>1</sup> 



# Nested Competency, not Merely Structure

## Multi-scale Competency Architecture

each level of organization solves problems in its own space (morphospace, transcriptional space, physiological space, 3D behavioral space, etc.) using some of the same tricks, at various levels of sophistication



# Axis of Persuadability:

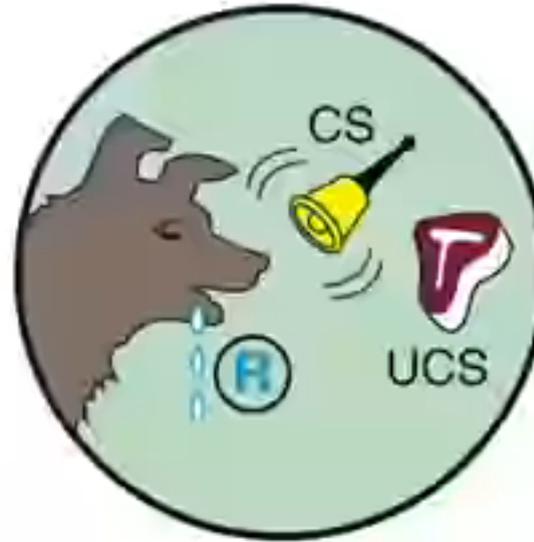
## an Engineering Take on a **Continuum** of Agency



Hardware modification only



Modify the data encoding setpoint of goal-driven process



Training by rewards/punishments

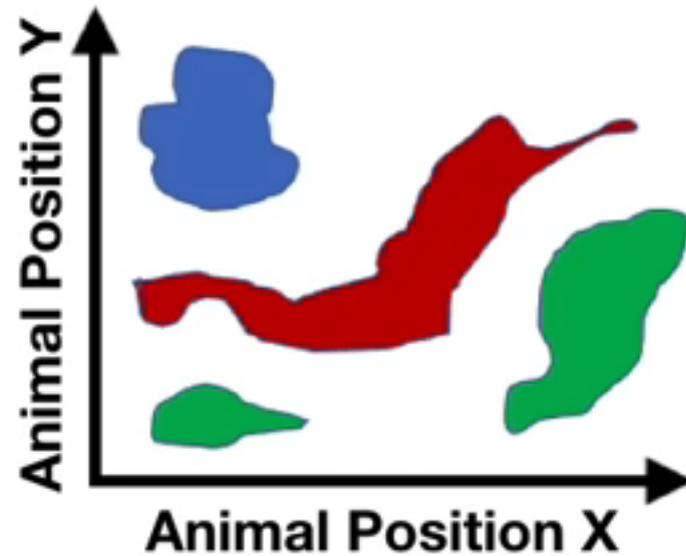


Communicate cogent reasons



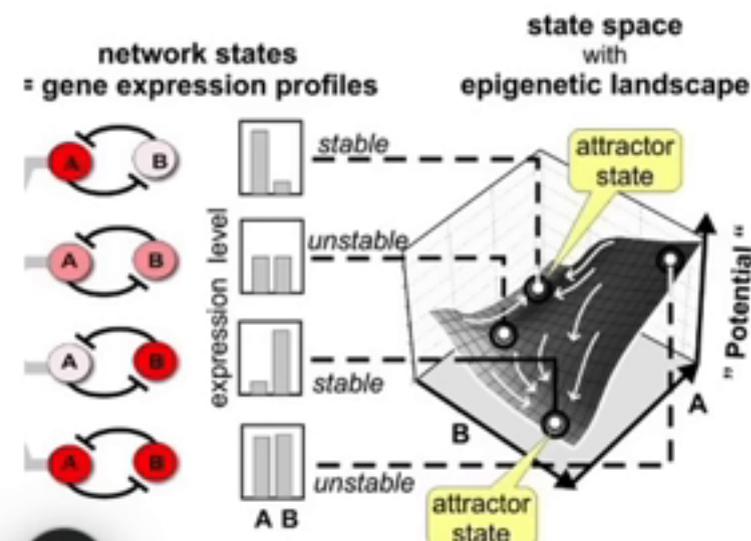
# Collective Intelligence of Cells: Competency in Diverse Spaces

## 3D Space (behavior)



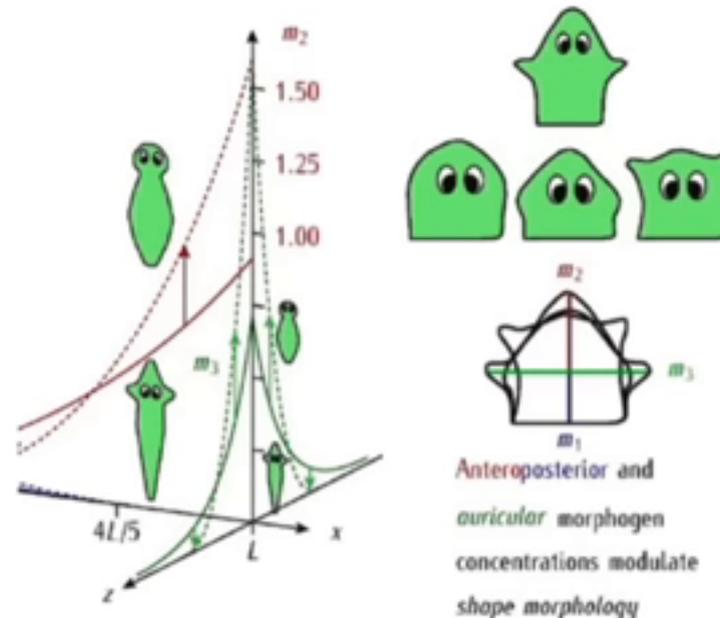
## Transcriptional Space

Huang, S.; Erberg, I.; Kauffman, S., *Semin Cell Dev Biol* 2009, 20, (7), 669-76.



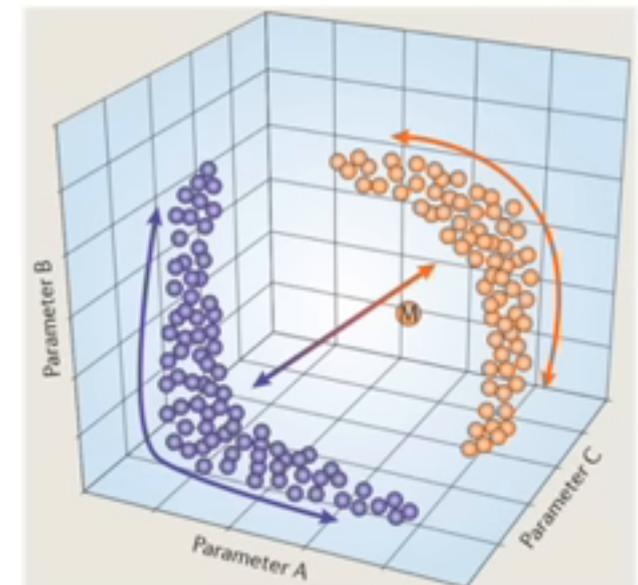
## Morphospace

Cervera, J., Levin, M., and Mafe, S., (2021), *BioSystems*, 209:104511



## Physiological Space

Marder, E., & Goaillard, J. M. (2006). Variability, compensation and homeostasis in neuron and network function. *Nat Rev Neurosci*, 7(7), 563-574.



“Intelligence is the ability to reach the same goal by different means.”

- William James

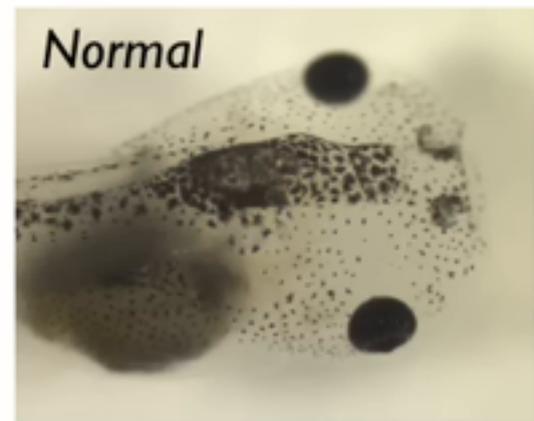
*Hypothesis: morphogenesis is a collective intelligence, exerting its behavioral competencies in anatomical morphospace*

*what kind of collective intelligence do cellular swarms deploy?*

- Different time scale (minutes, not milliseconds)
- Different problem space (morphospace, not 3D motion)
- but, same (homologous!) mechanisms - ion channels, GJs, NTs
- and, many of the same algorithms (tools of cog sci work great)



# Same anatomy, via different paths



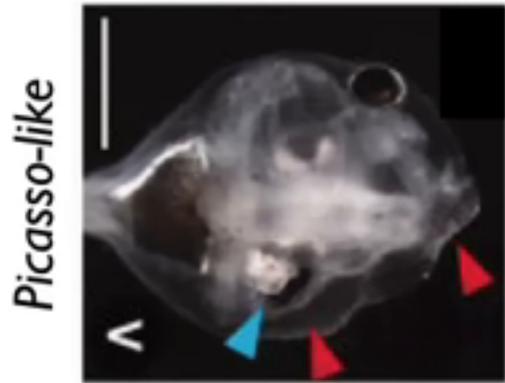
normal development



"as needed" remodeling

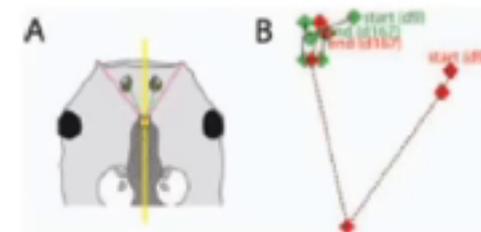
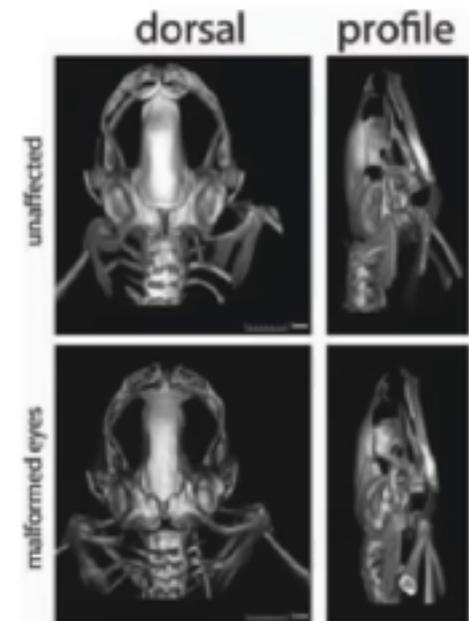
Laura Vandenberg

Craniofacial mispatterning  
 ↓  
 Metamorphosis  
 ↓  
 Morphometric analysis and modeling  
 reveals: **faces fix themselves!!**



Genetics does not specify hardwired rearrangements: it specifies a system that executes a highly flexible program that can recognize unexpected states and take corrective action.

Cannot just follow a rote set of steps. How does it know when it's "right"?

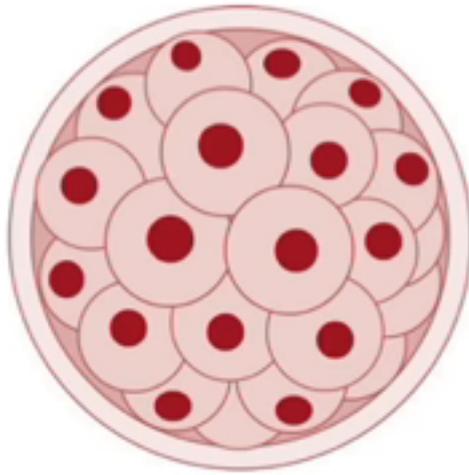


# Components of Intelligence:

- Homeostasis: the basis of goal-directed activity
- Homeostasis<sup>2</sup>: Same ends by different means
- Hierarchical, non-local control
- Hackability (software, not just hardware)
- Learning
- Creative problem-solving toward default goals
- Novel beings, novel goals: never give up

# Where do Anatomies Come from?

stem cell  
embryonic  
blastomeres



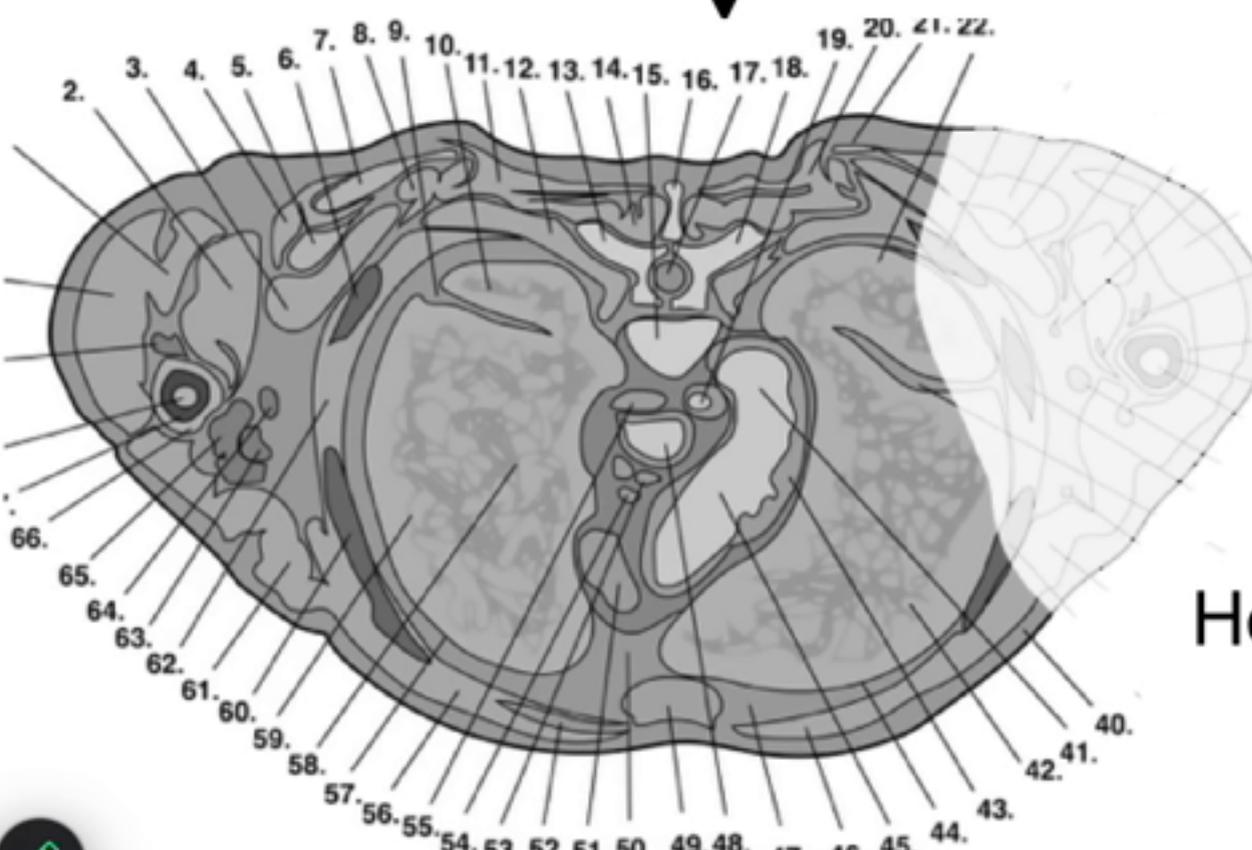
self-assembly



earthlymission.com

- DNA specifies proteins; whence Anatomy?
- how do cell groups know what to make and when to stop?
- how far can we push shape change?  
Engineers ask: what's possible to build given default genome?

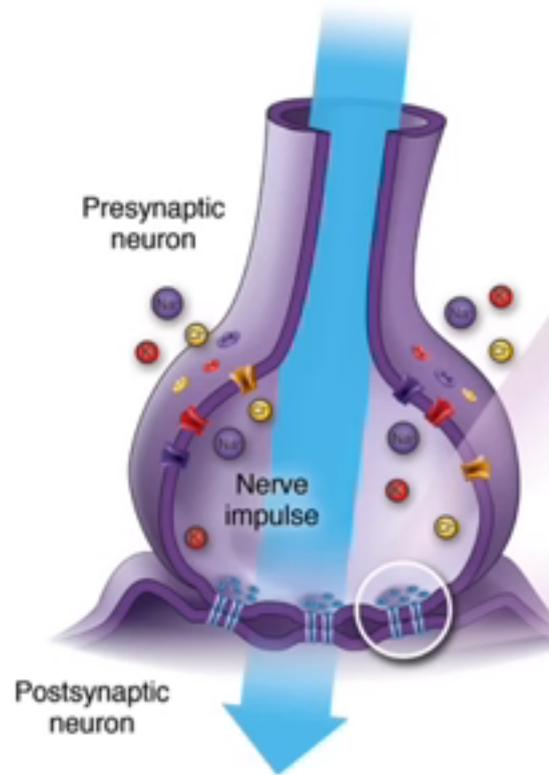
How to repair  
(edit) it?



# Hardware

gene products -> electric circuits

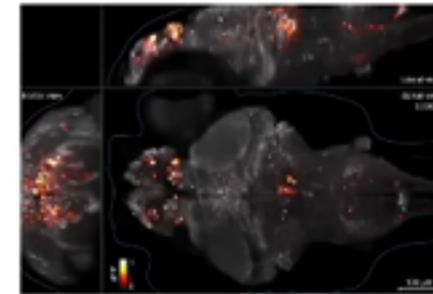
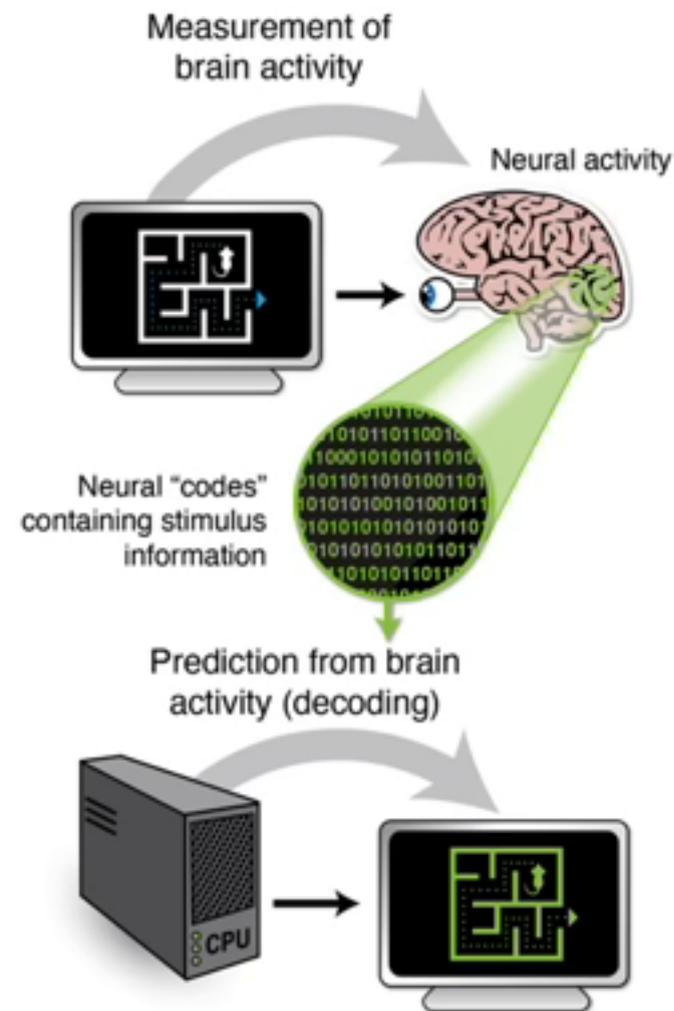
ion  
channels,  
electrical  
synapses



# Software

electrical dynamics -> memory

neural

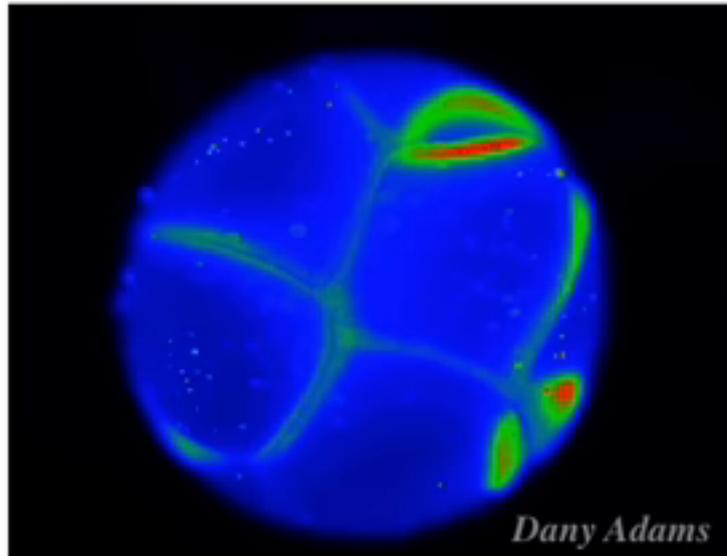


<http://www.nature.com/nmeth/journal/v10/n5/full/nmeth.2434.html>



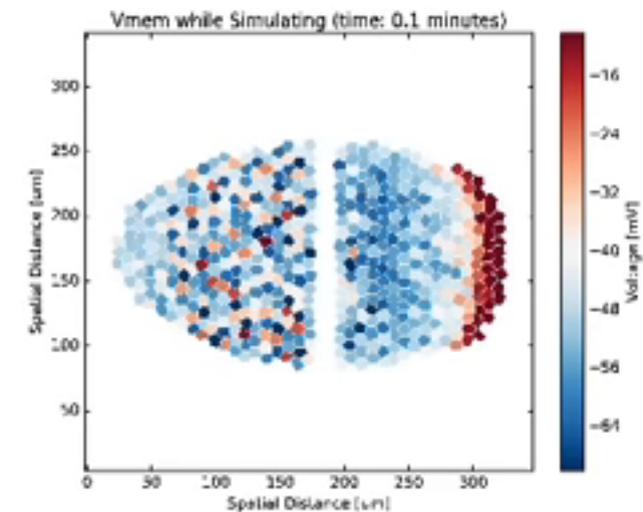
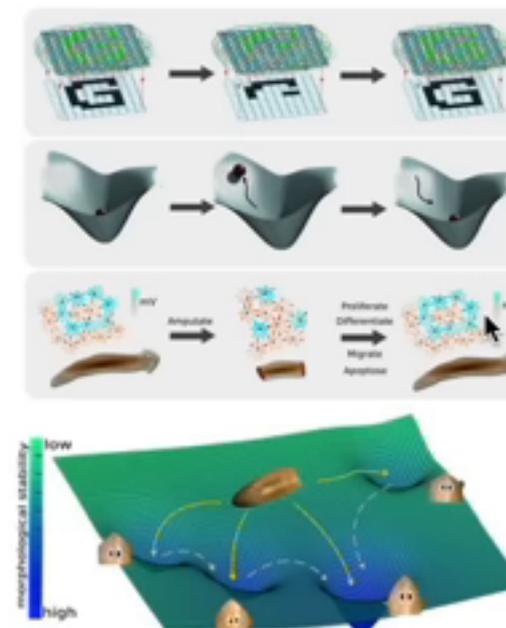
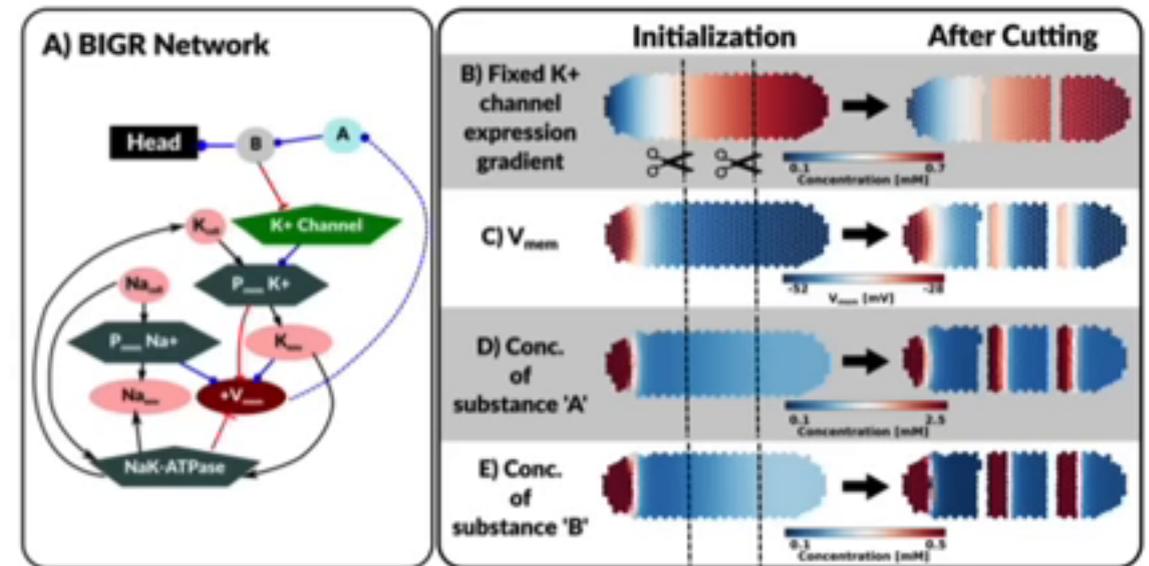
# How we Detect and Model Bioelectric Signals:

**Characterization** of endogenous voltage gradients - direct measurement and correlation with morphogenetic events

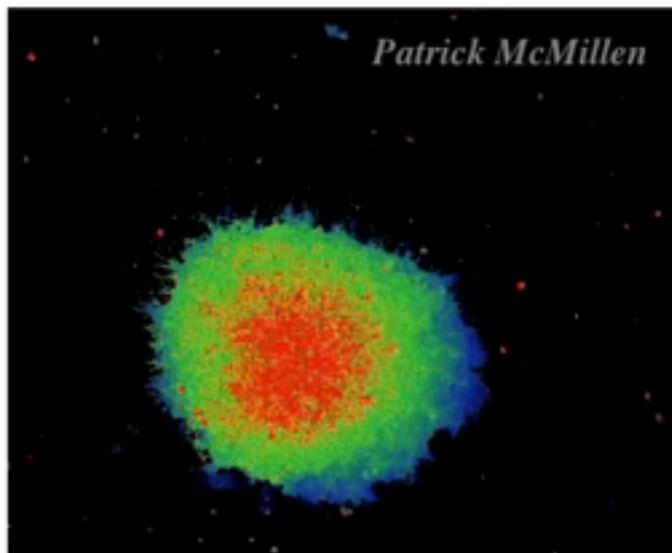


Voltage reporting fluorescent dye in time-lapse during *Xenopus* development

**Quantitative computer simulation:** synthesize biophysical and genetic data into predictive, quantitative, often non-linear models

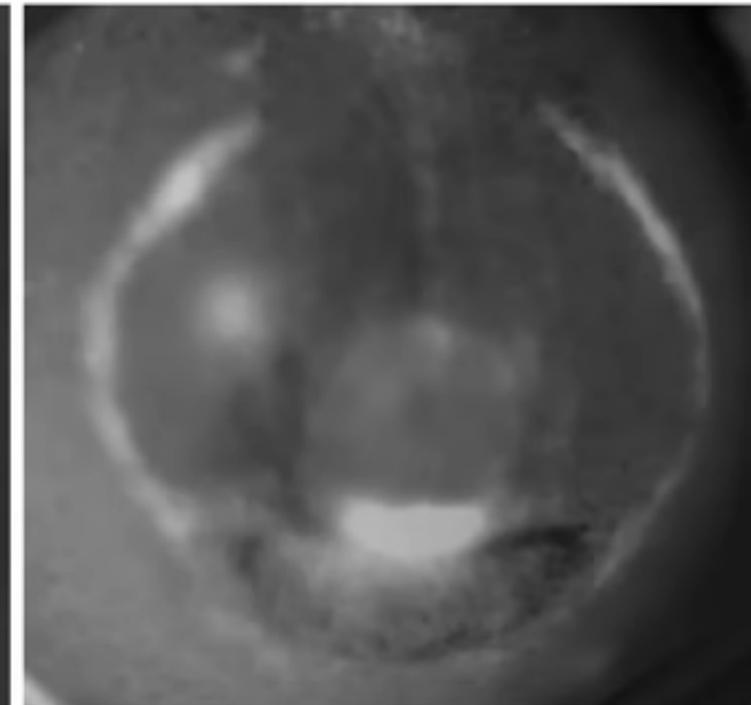
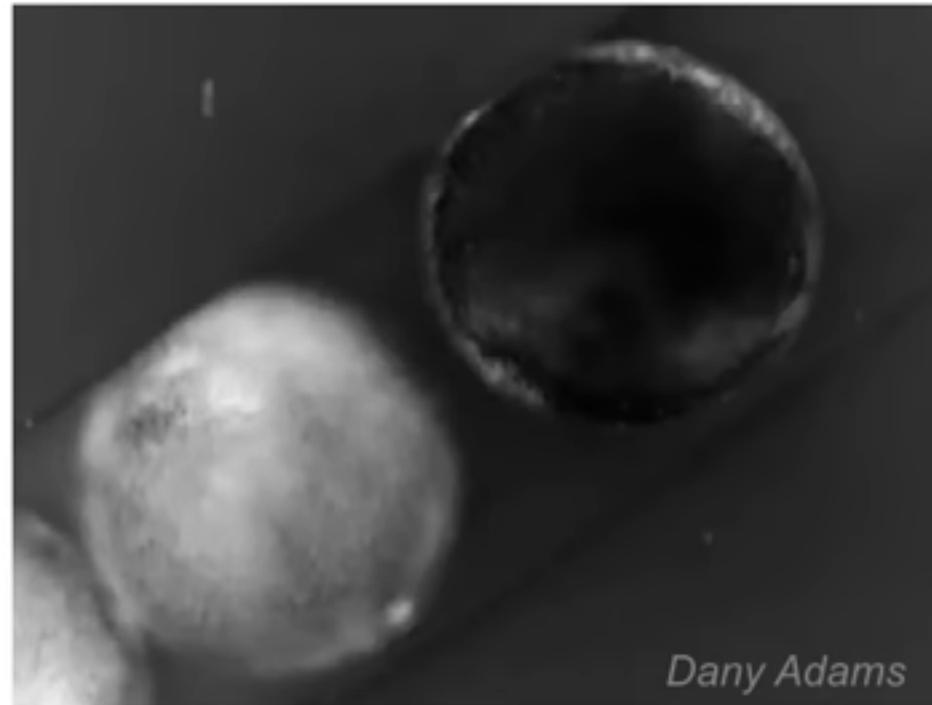


Alexis Pietak



# Endogenous Bioelectric Prepatterns: reading the multi-scale mind of the body

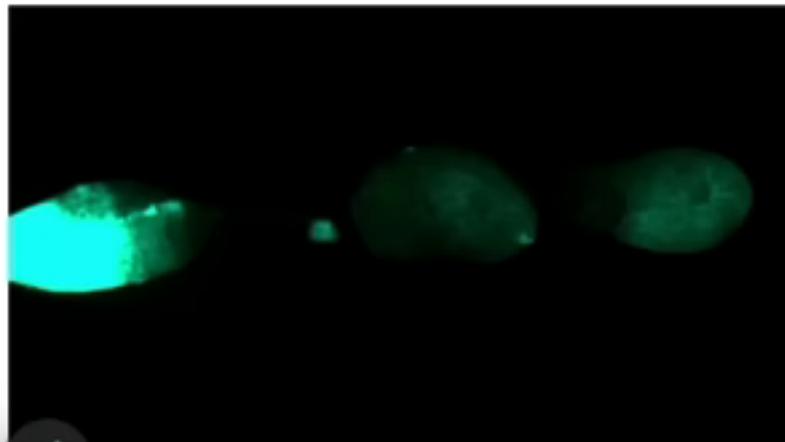
craniofacial  
development  
“electric face”  
prepattern  
required for  
normal face



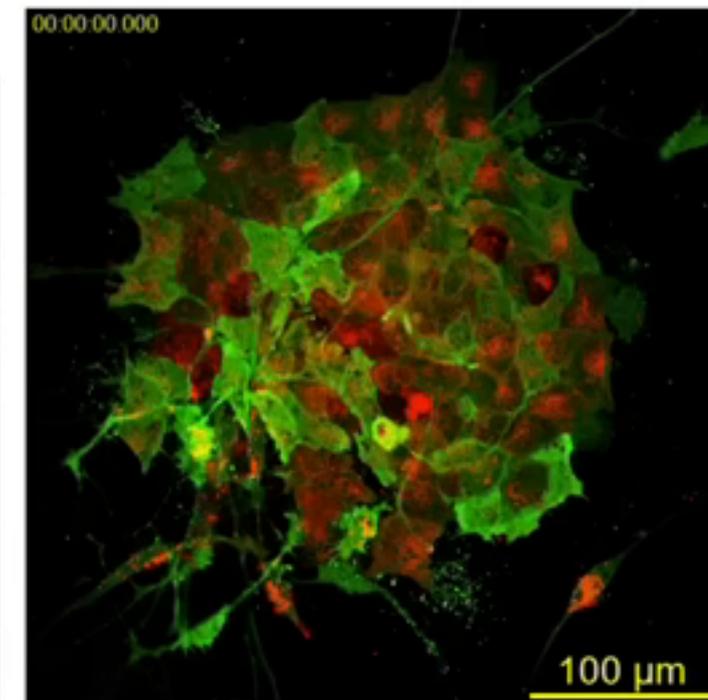
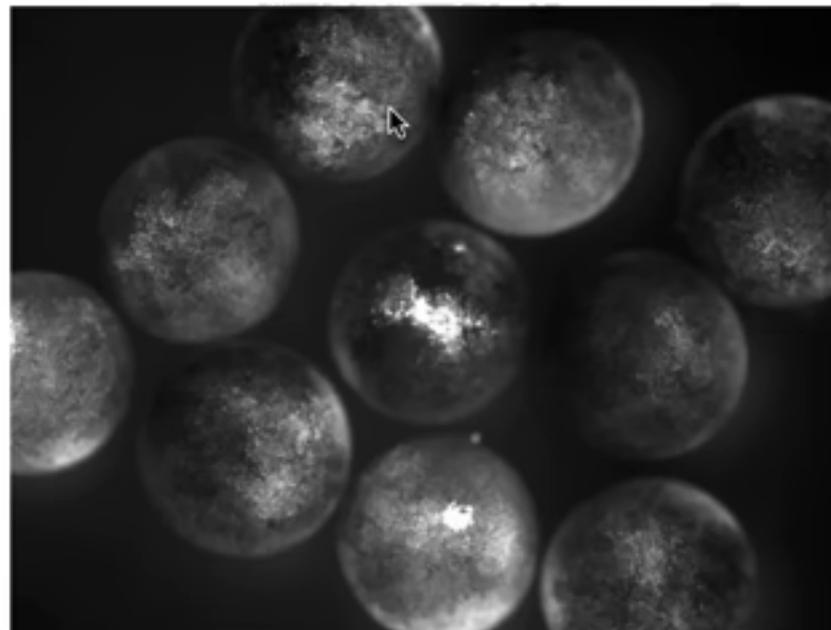
hyperpolarized  depolarized

cognitive glue on 2 scales:  
cells -> embryo  
embryos -> hyperembryo

*Patrick McMillen*



*Angela Tung, Megan Sperry*

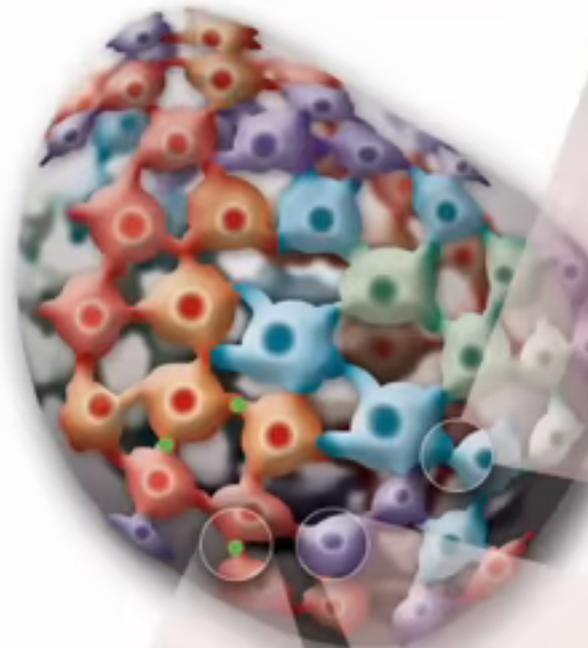


# Rewriting Somatic Pattern Memories

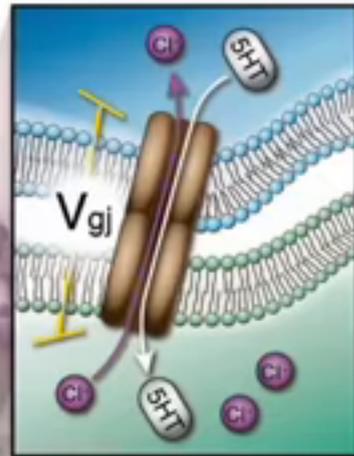
Non-neural cell group



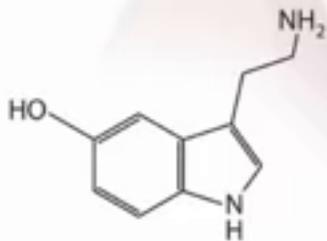
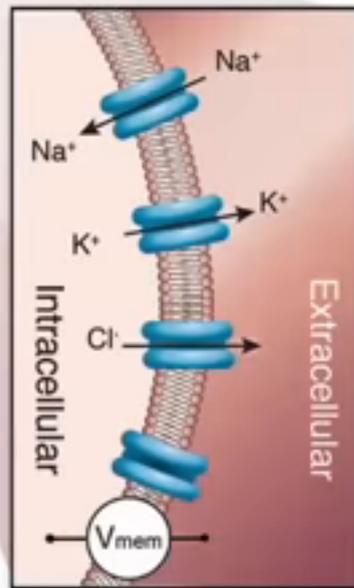
hyperpolarized ← → depolarized



Gap Junctions  
(electrical synapse)



Ion channels  
(setting  $V_{mem}$ )



● Neurotransmitter  
(moving via  $V_{mem}$ )

- Transporter or receptor mutant overexpression
- Drug agonists or antagonists of receptors or transporters
- Photo-uncaging of neurotransmitter

## Tools we developed

(no applied fields!)

- Dominant negative Connexin protein
- GJC drug blocker
- Cx mutant with altered gating or permeability

Synaptic  
plasticity

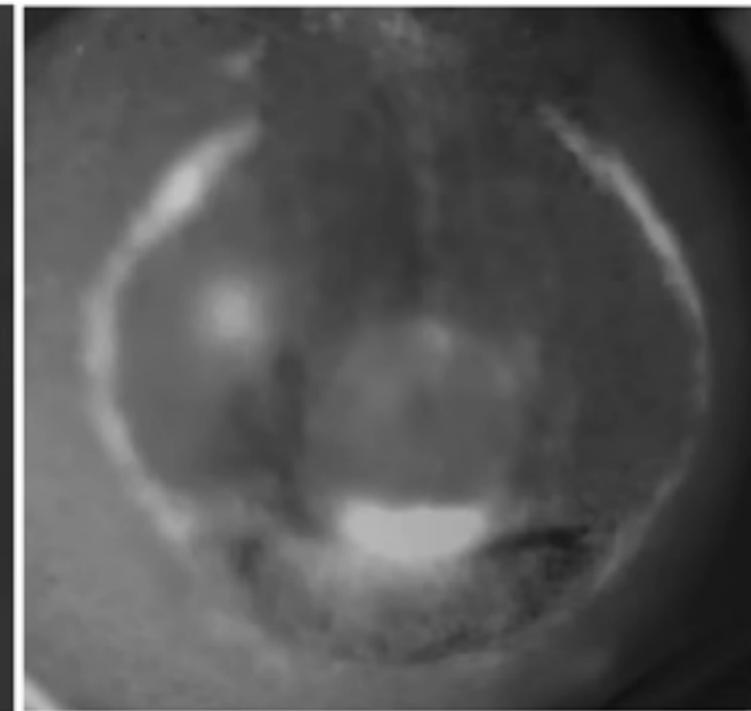
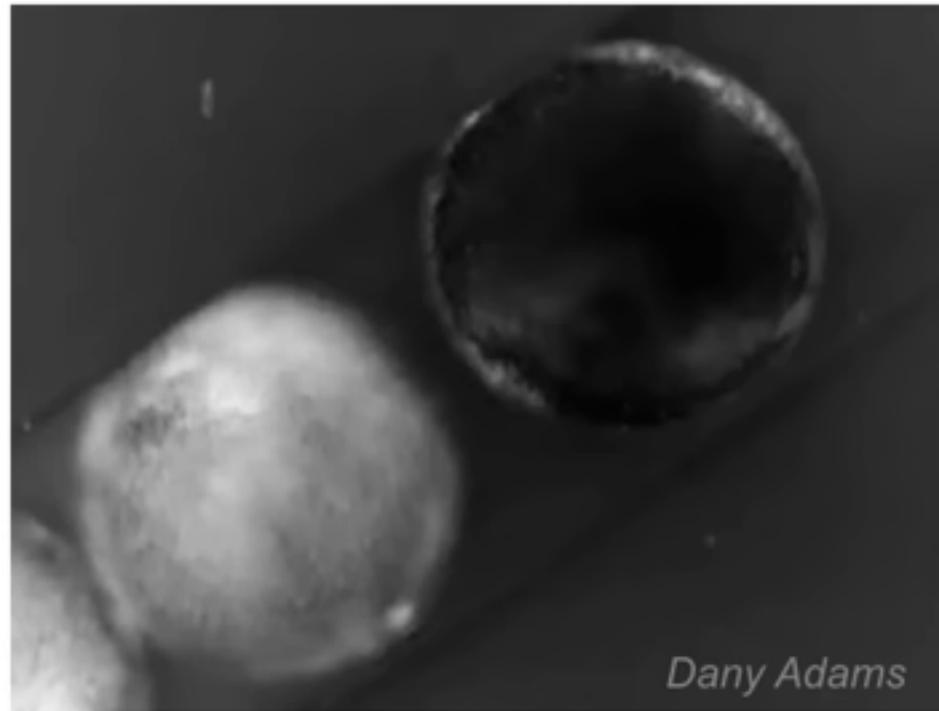
- Dominant ion channel over-expression (depolarizing or hyperpolarizing, light-gated, drug-gated)
- Drug blocker of native channel
- Drug opener of native channel

Intrinsic  
plasticity



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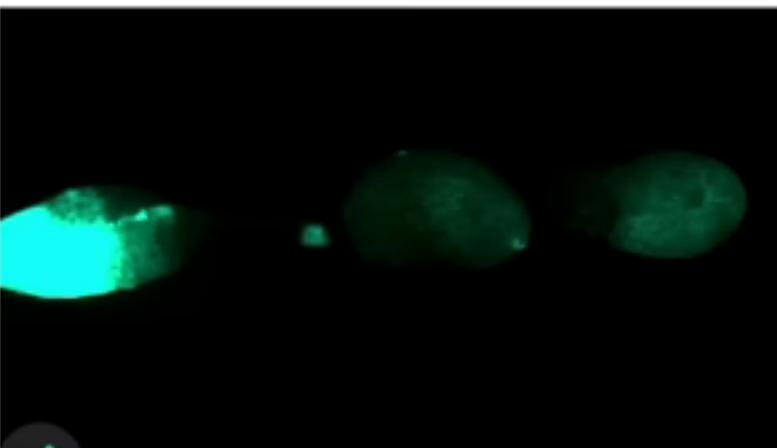
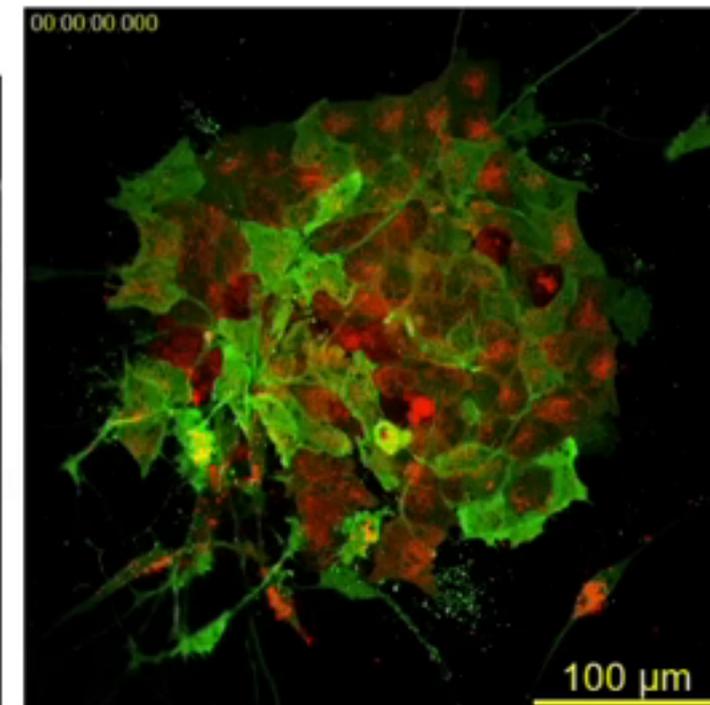
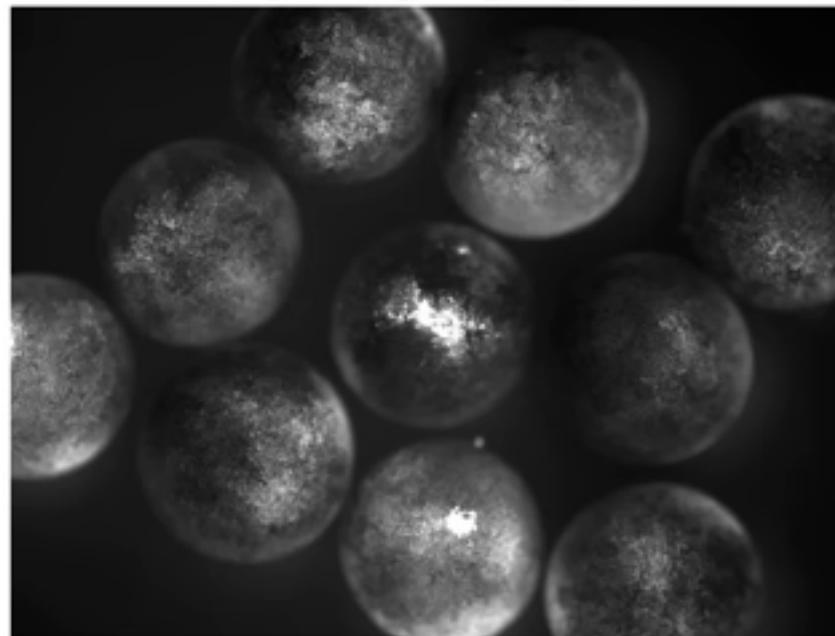


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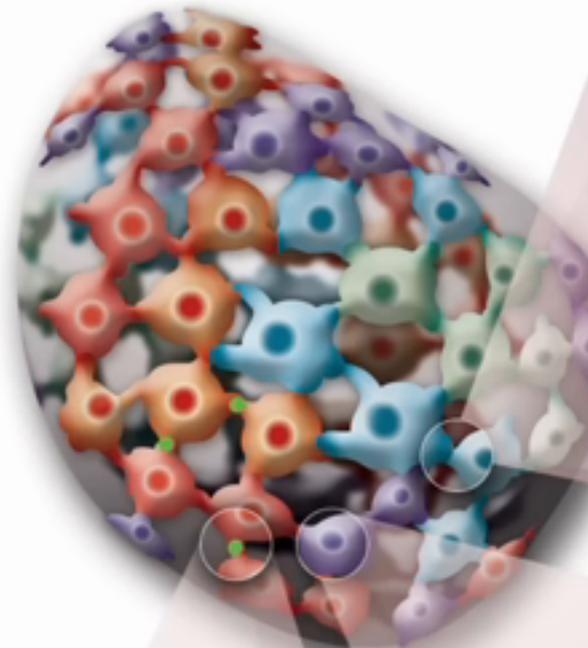


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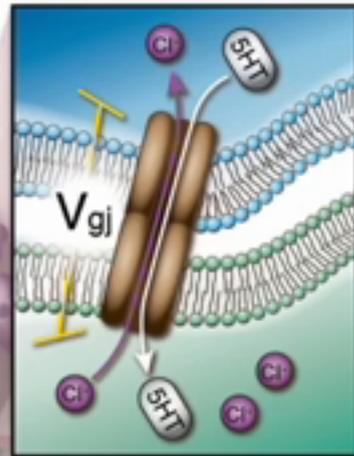
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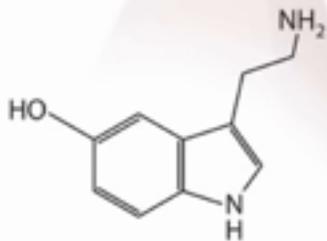
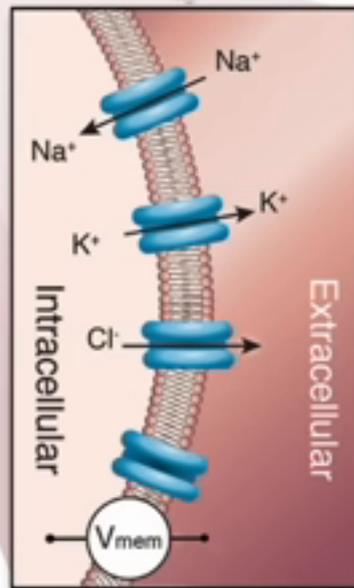
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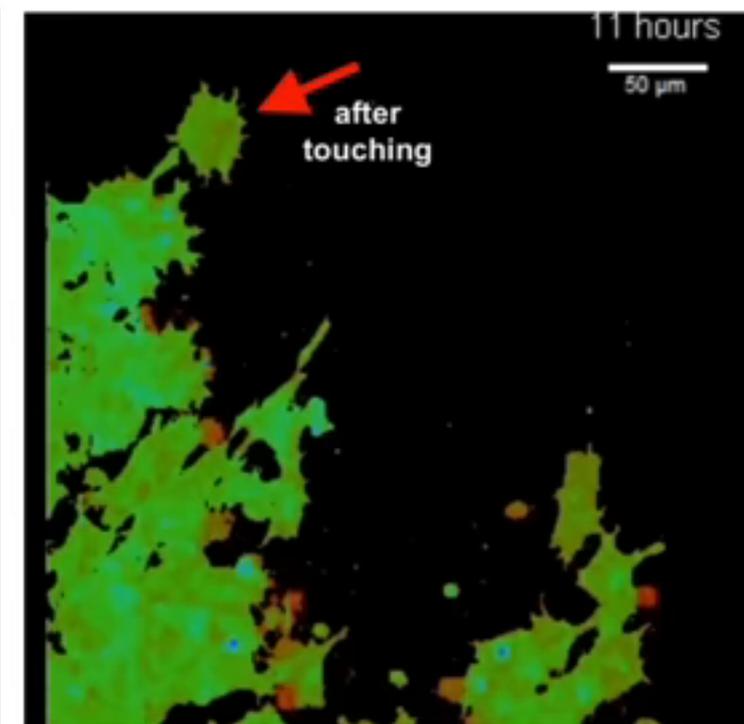
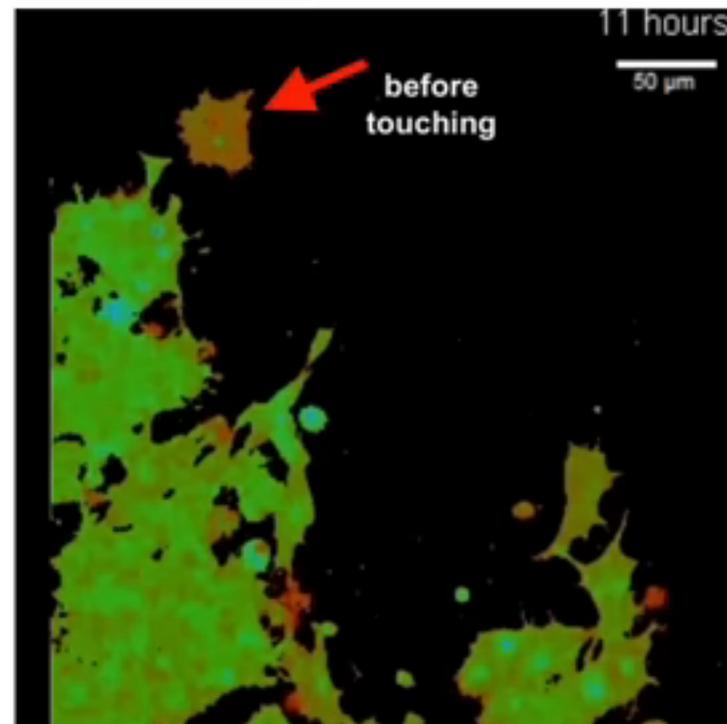
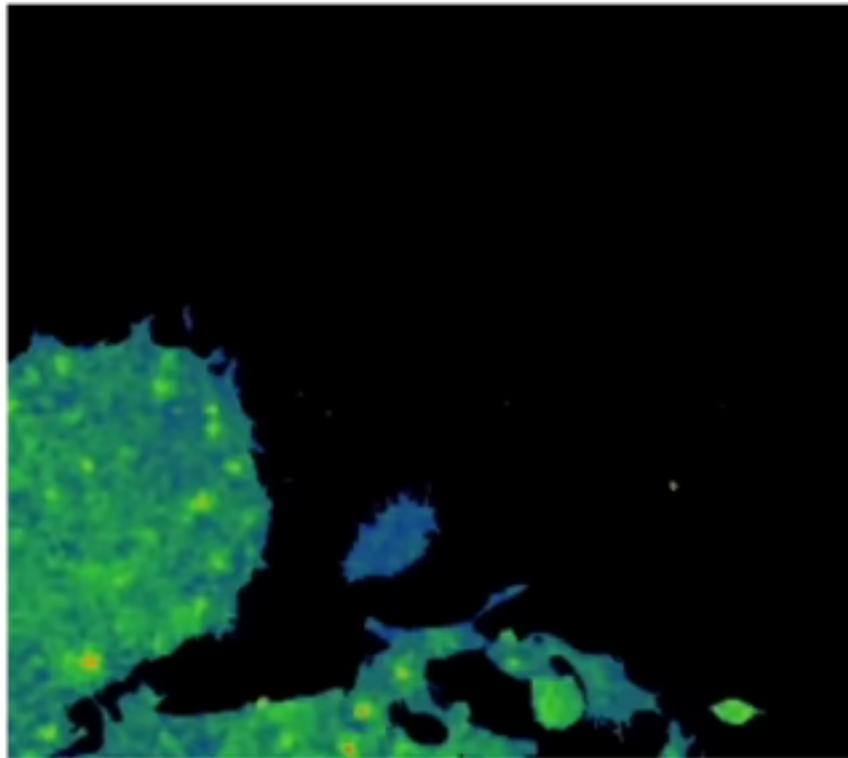
Synaptic  
plasticity

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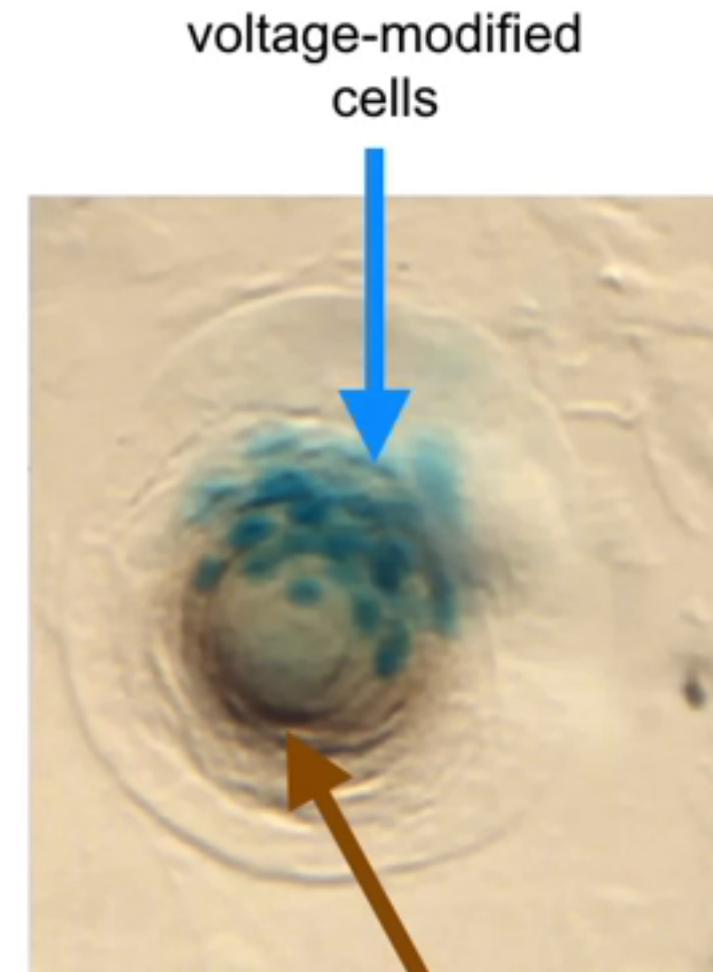
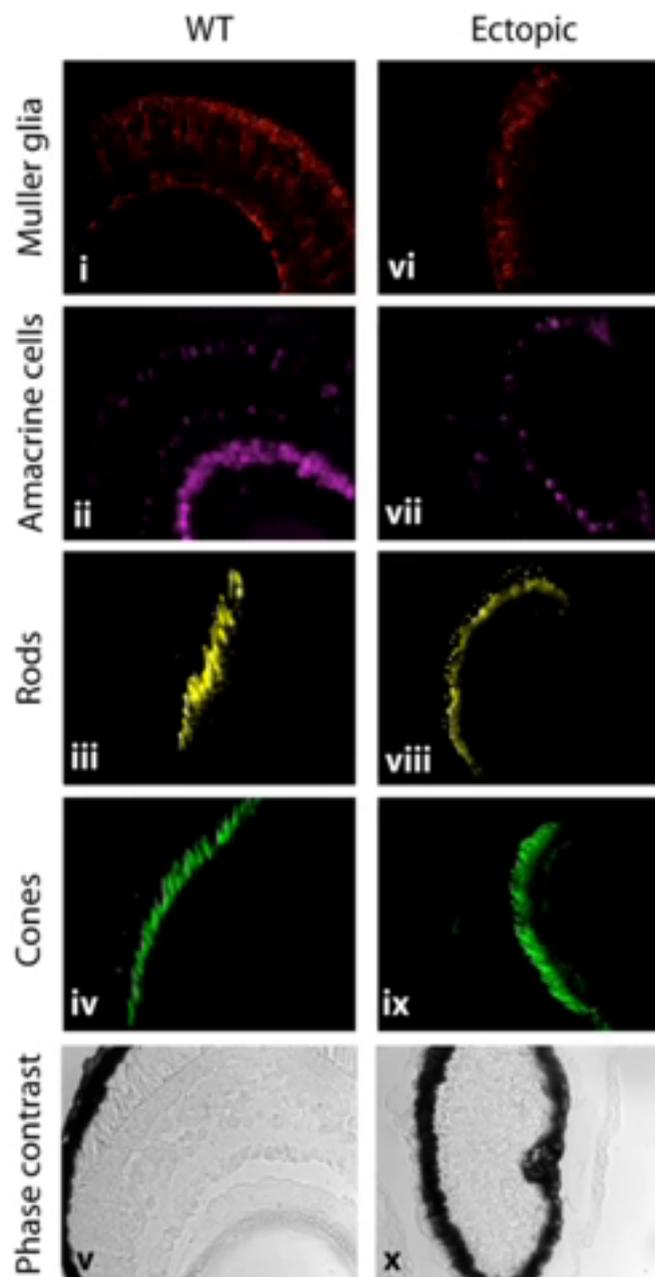
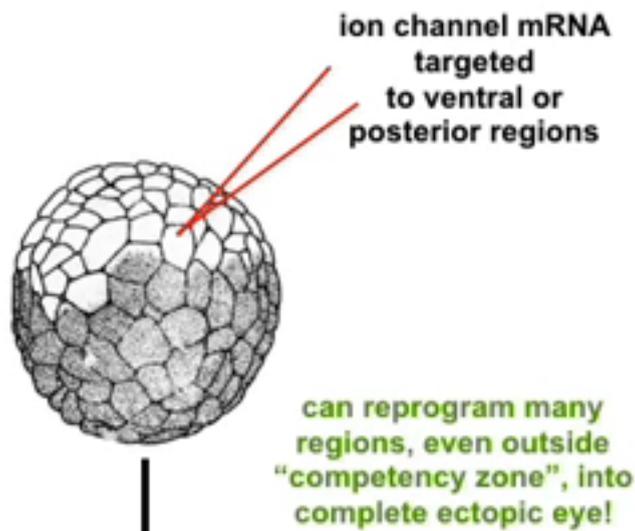
Intrinsic  
plasticity



# Bioelectrical Take-over at Cell Level: A very convincing message



# Communicating New Goal Top-Down via Bioelectric Interface

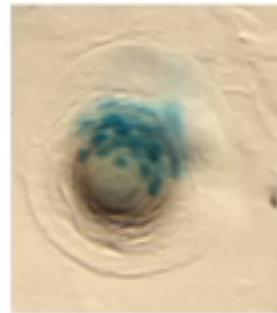
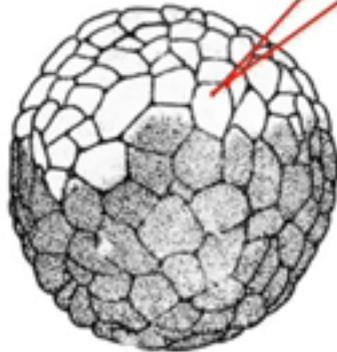


1. BIOE is instructive
2. modularity - not cell level, organ-level subroutine call
3. higher-level prompt reveals higher tissue competency than Pax6 prompt
4. self-scaling of system to task

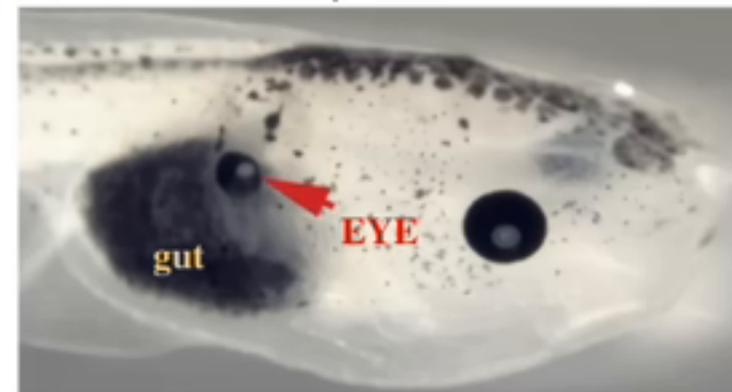
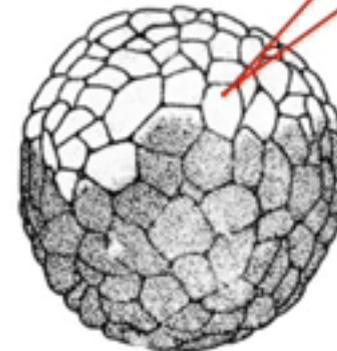


# A Battle of World-Views: plasticity in morphogenetic navigation

ion channel mRNA  
targeted  
to ventral or  
posterior regions



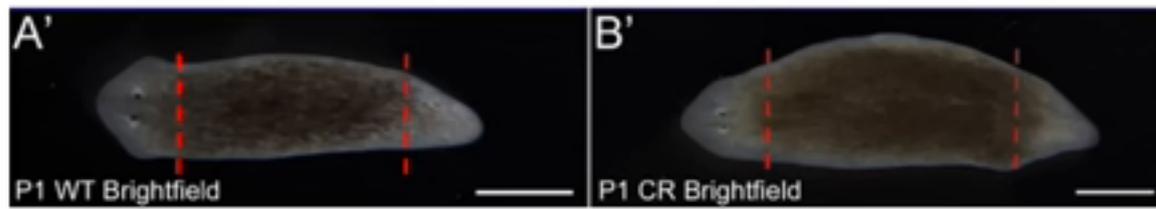
ion channel mRNA  
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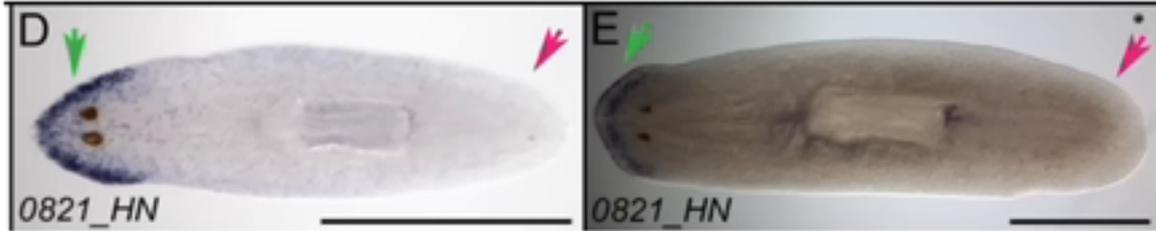
3 ectopic eyes, according to  
early eye marker Rx1



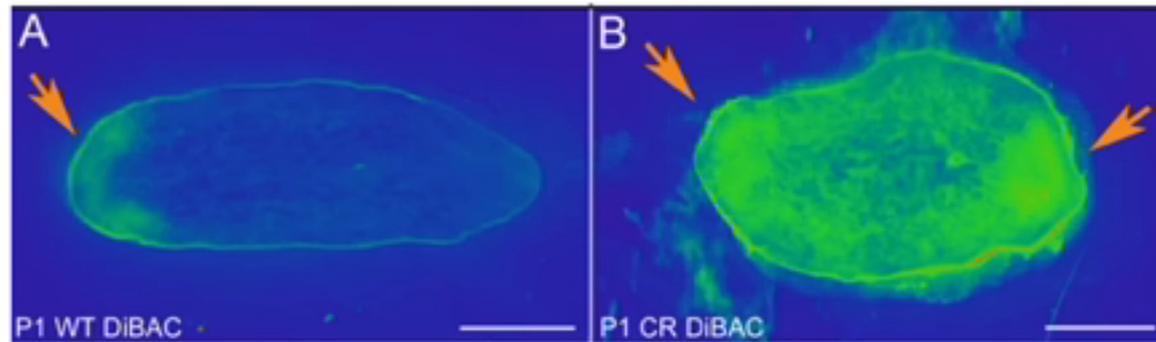
# Re-writing Anatomical Pattern Memory



normal anatomy

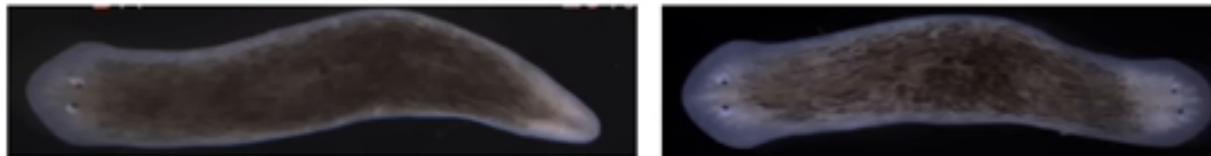


normal molecular histology

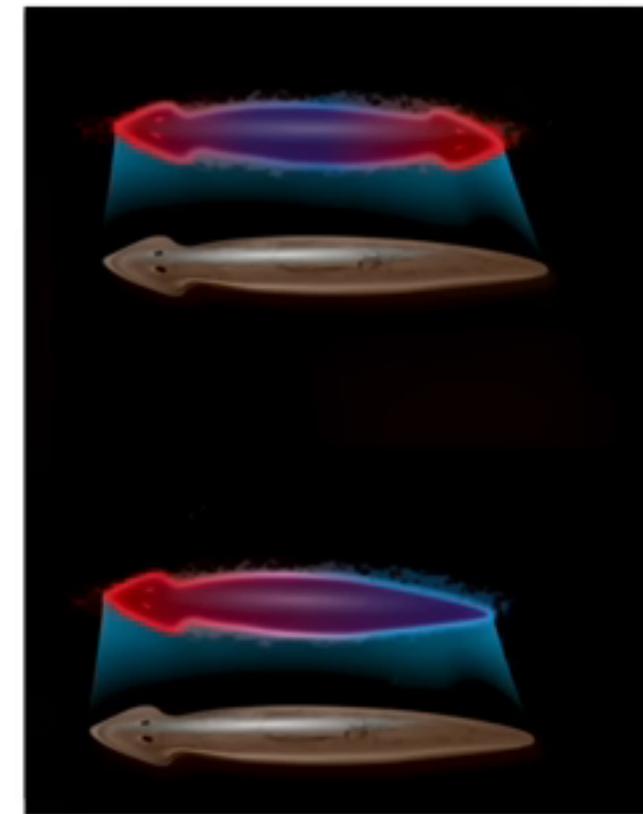


edited bioelectric pattern

middle-third  
regenerates:



The Same Body can Store different  
Electrical Pattern Memories



The bioelectric pattern doesn't indicate what the anatomy is now, it encodes the latent pattern memory that will guide anatomy if it is cut at a future time = **counterfactual**



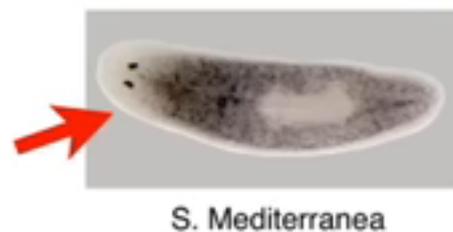
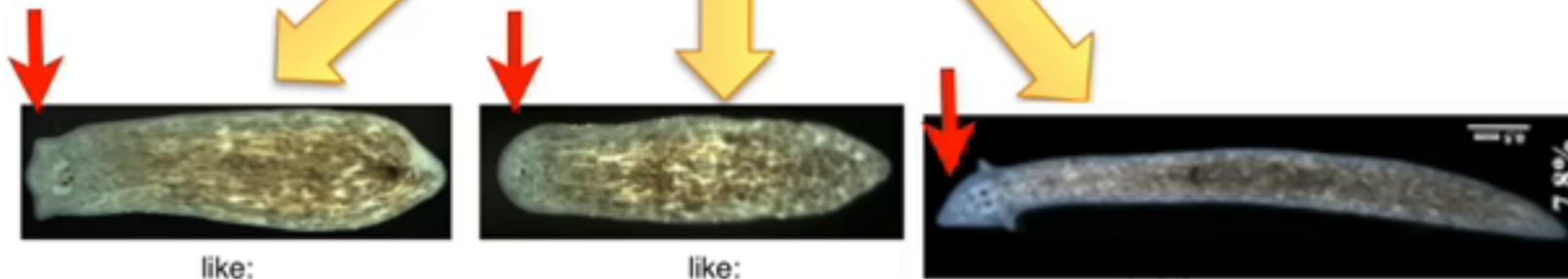


# A Single Genome Makes Hardware that can Access Bioelectric Memories of Other Species' Head Shapes

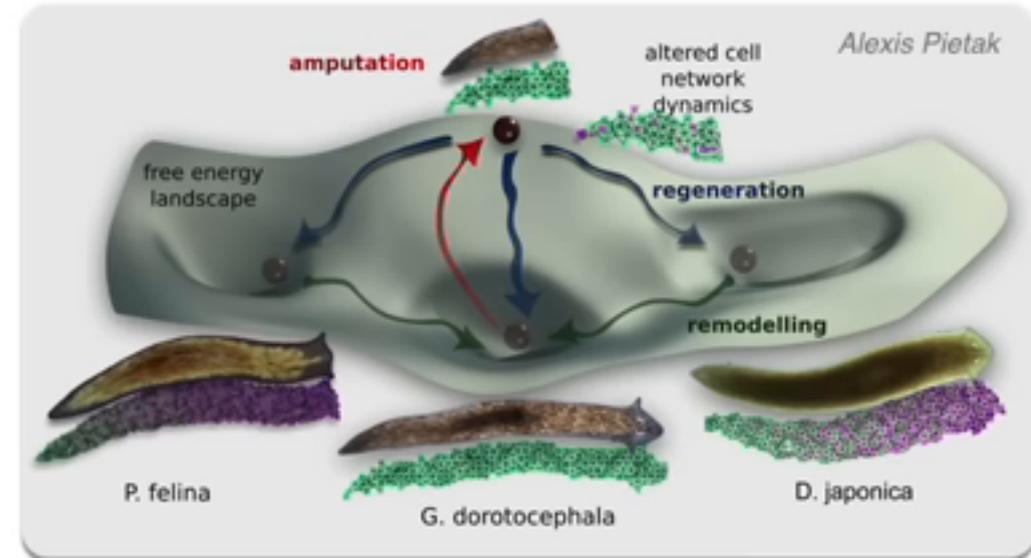
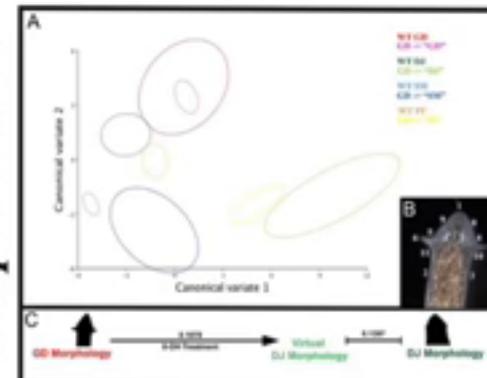
Species-specific shapes = attractors in morphospace = memories as attractors in neural network



cut off head, perturb network topology

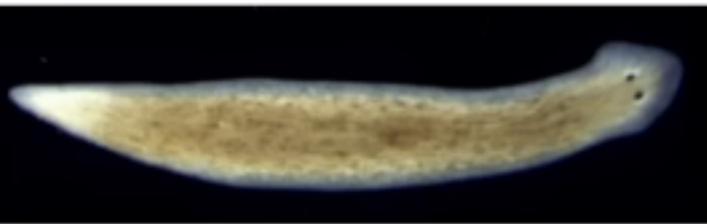


quantitative morphometrics

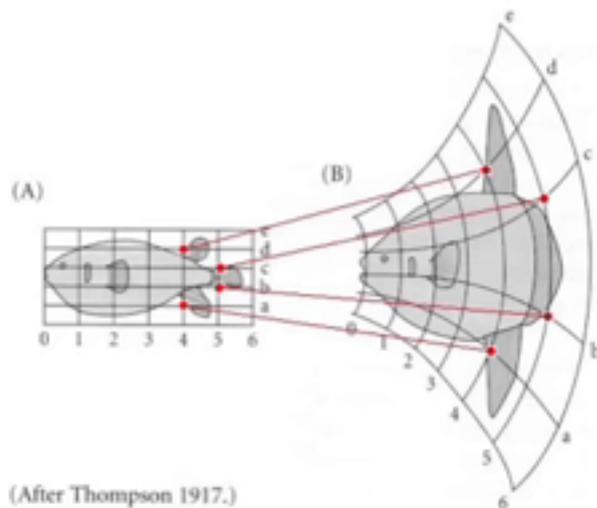
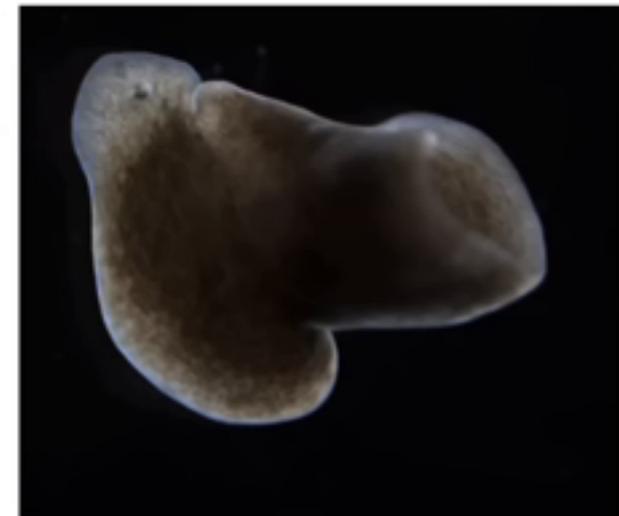
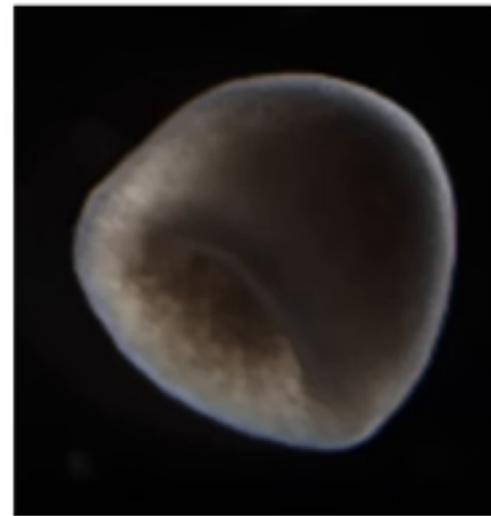


# The Hardware is Extremely Reprogrammable

Normal worm



Bioelectric Pattern Altered



(After Thompson 1917.)

latent morphospace



# Good Old Reliable Development like “instinct” - fixed patterns?



White Oak Leaf - Photo by Chris Evans, River to River CWMA, Bugwood.org

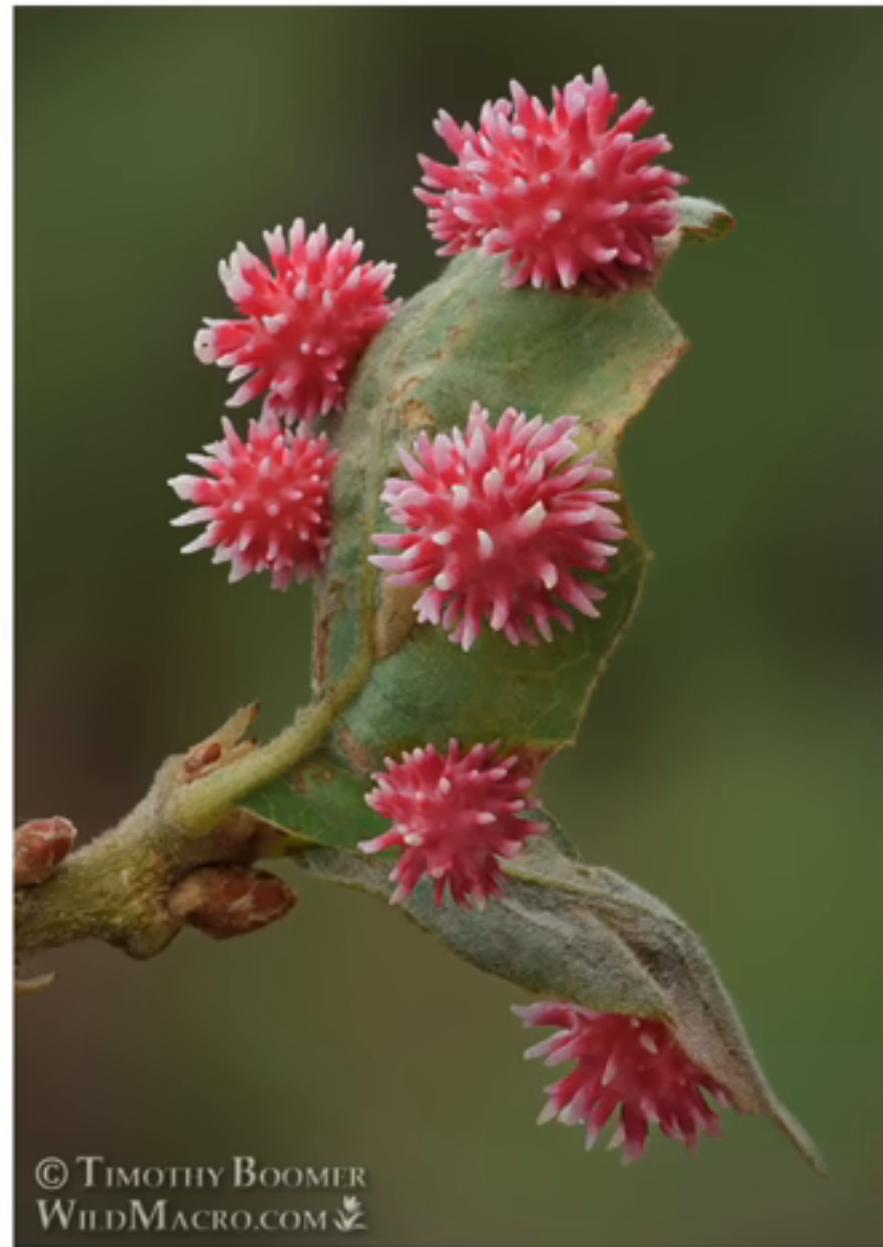
# Messages from Hacker Reveal Flexibility:



Photo Credit: Andrew Deans

## Hedgehog Gall

*Acraspis erinacei*  
August - November



Parasite hacks host to induce new anatomy (bio-prompting)

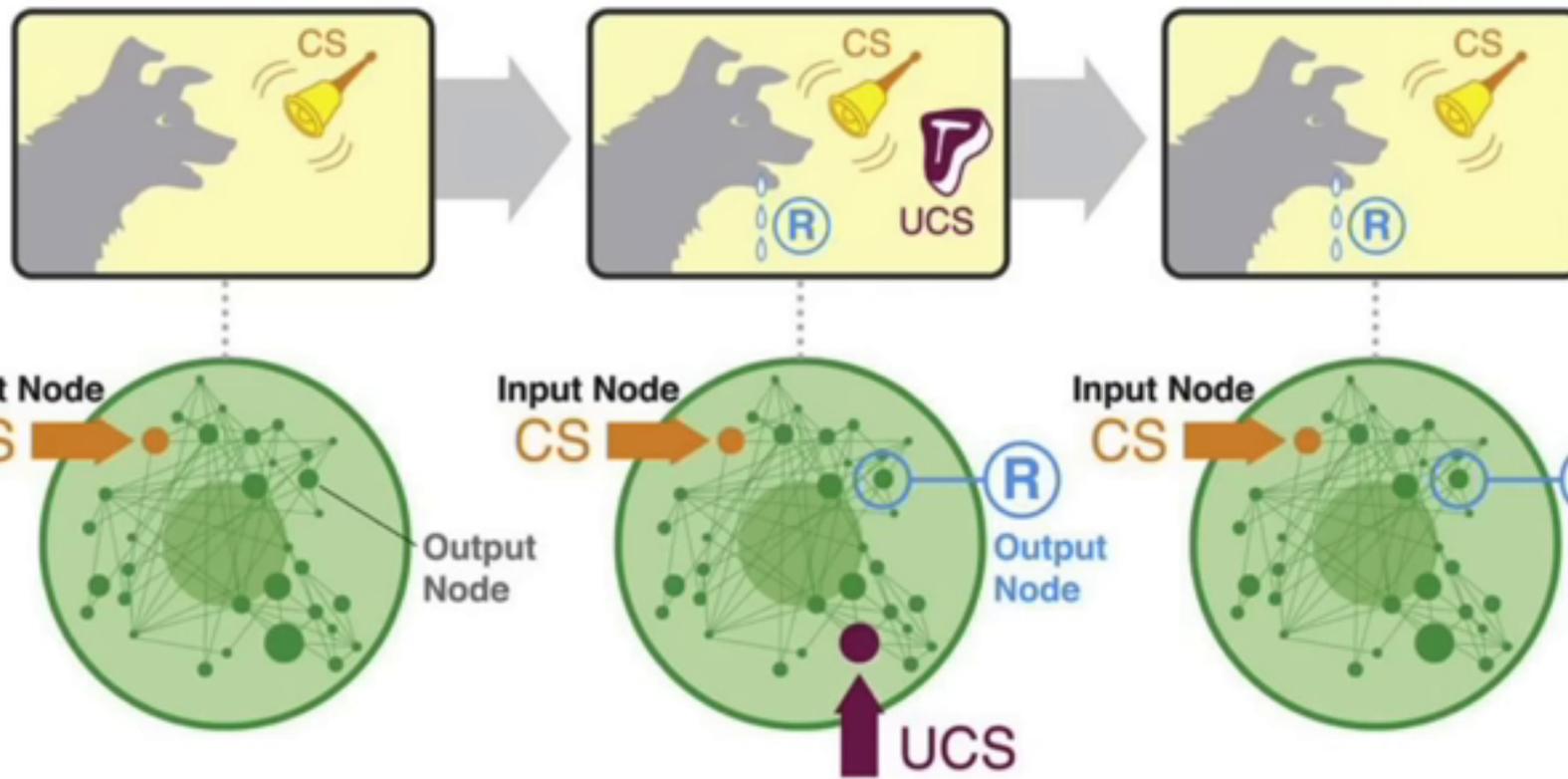


# Components of Intelligence:

- Homeostasis: the basis of goal-directed activity
- Homeostasis<sup>2</sup>: Same ends by different means
- Hierarchical, non-local control
- Hackability (software, not just hardware)
- **Learning**
- Creative problem-solving toward default goals
- Novel beings, novel goals: never give up



# Collective Intelligence Below the Cell Level



molecular networks  
already smart

Biomedicine:

- drug conditioning

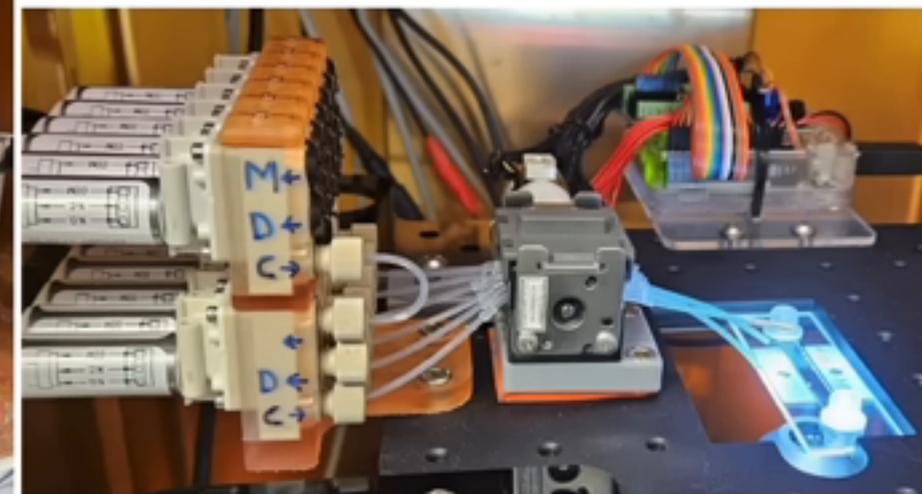
Article  
**Learning in Transcriptional Network Models:  
Computational Discovery of Pathway-Level Memory  
and Effective Interventions**

Surama Biswas <sup>1,2,†</sup>, Wesley Clawson <sup>1,†</sup> and Michael Levin <sup>1,2,\*</sup>

Article  
Gene regulatory networks exhibit several kinds of  
memory: quantification of memory in biological  
random transcriptional networks

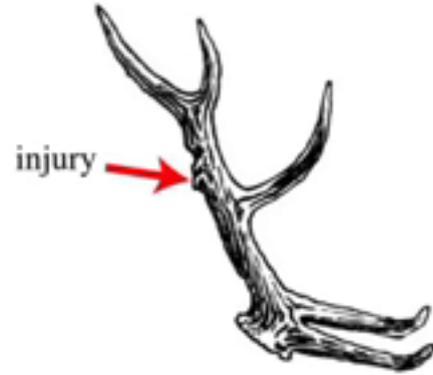


Patrick Erickson

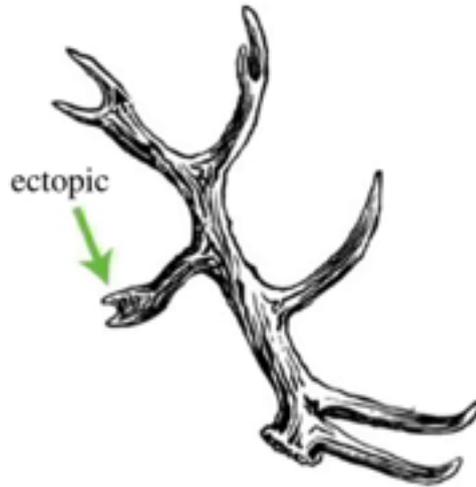


# Trophic Memory in Deer Antlers:

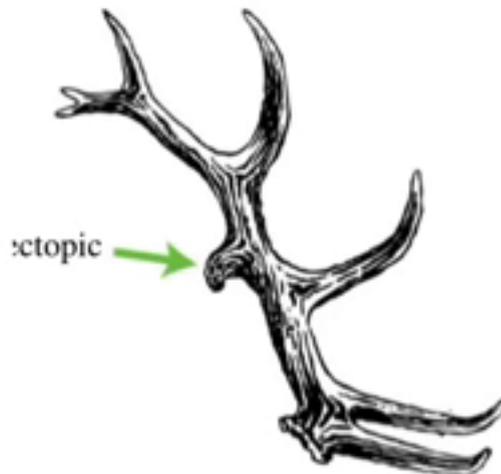
Year 0



Years 1-5



Years 6+



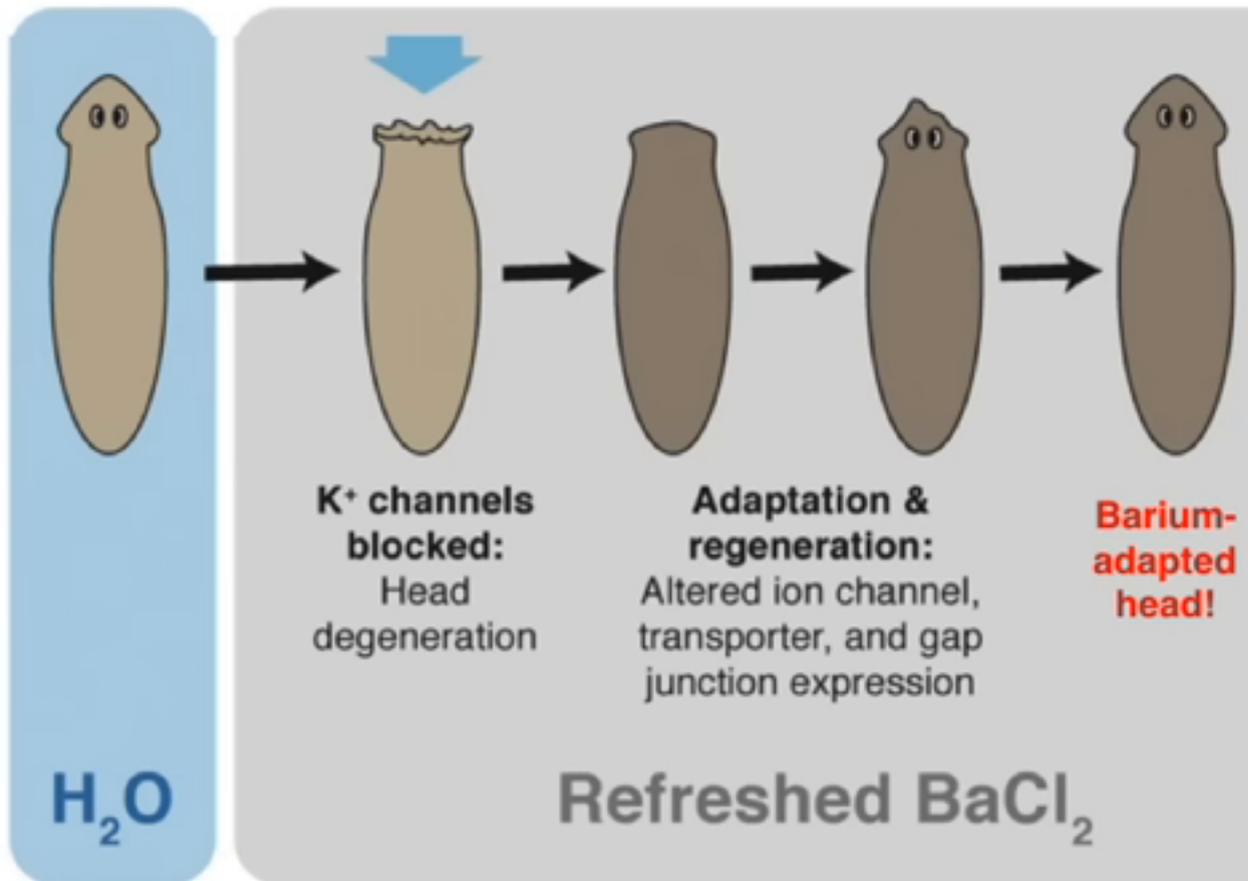
What molecular pathway model would you draw?



George Bubenik



# Solving Novel Physiological Problems by Navigation of Transcriptional Space



Small number of genes regulated out of entire genome!

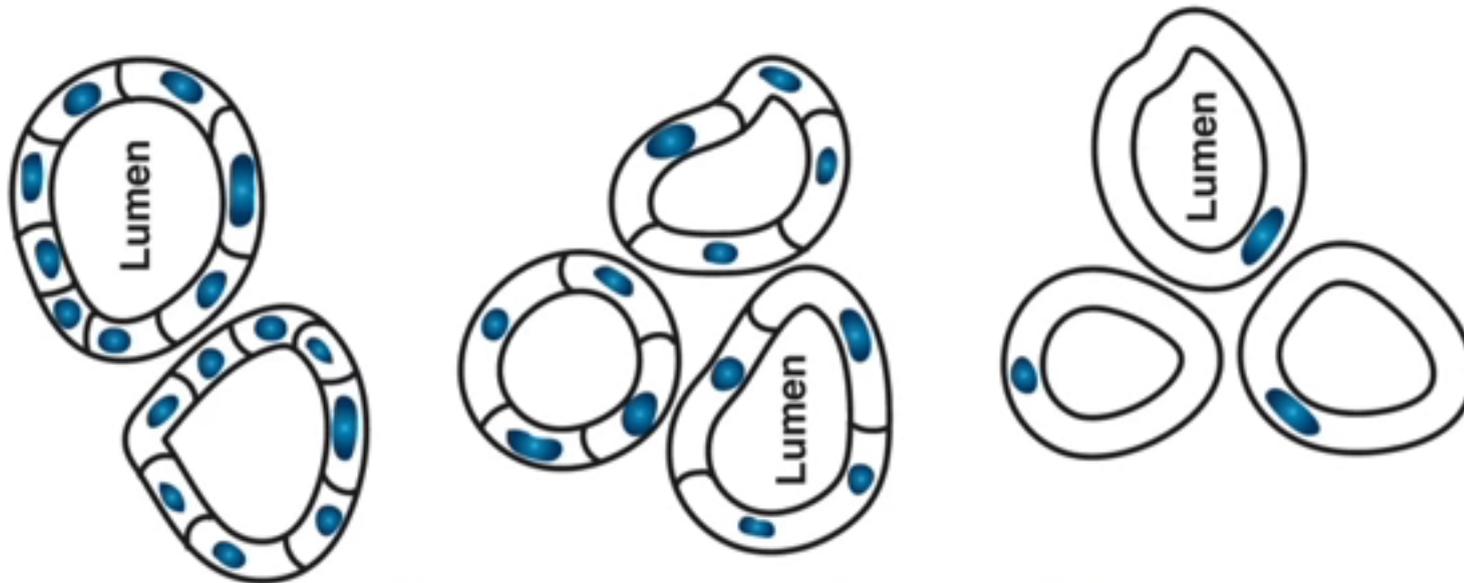


- planarian heads degenerate after exposure to barium
- planaria eventually adapt and regenerate heads that tolerate barium
- a relatively few transcripts were altered to produce barium tolerance
- how did the system choose exactly the right genes to modulate, to deal with this evolutionarily-novel challenge?

# Creative Problem-Solving by Cell Groups

- get to the same outcome
  - despite perturbations (external and internal)
  - from diverse starting positions
  - via different molecular mechanisms!

newt  
kidney  
tubule  
cross-  
section



Fankhauser, 1945, *J. Exp. Zool.*, 100(3): 445-455

Changing the size of cells still enable large-scale structures to form, even if they have to utilize different molecular mechanisms = top-down causation

## INTERFACE

[rnl.royalsocietypublishing.org](http://rnl.royalsocietypublishing.org)

Perspective

**Top-down models in biology: explanation and control of complex living systems above the molecular level**

G. Pezzulo<sup>1</sup> and M. Levin<sup>2\*</sup>

## Top-down models in biology: explanation and control of complex living systems above the molecular level

G. Pezzulo<sup>1</sup> and M. Levin<sup>2\*</sup>

<sup>1</sup>Young Laboratory, IBM Research, Almaden, CA 95120, USA

<sup>2</sup>Center for Complex Systems and Biodynamics, National Research Council, Rome, Italy

\*Correspondence: gpezzulo@us.ibm.com

It is widely assumed in developmental biology and bioengineering that optimal understanding and control of complex living systems follows from models of molecular events. The success of reductionism has overshadowed attempts at top-down models and control policies in biological systems. However, other fields, including physics, engineering and neuroscience, have successfully used the explanation and models at higher levels.

## Integrative Biology

PERSPECTIVE

Re-membering the body: applications of computational neuroscience to the top-down control of regeneration of limbs and other complex organs†

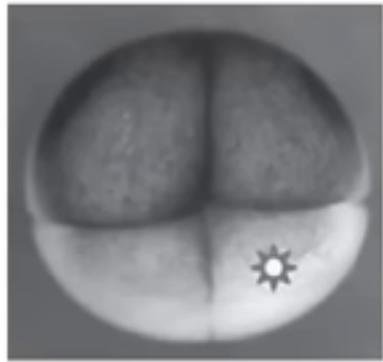
G. Pezzulo<sup>1</sup> and M. Levin<sup>2\*</sup>

Re-membering the body: applications of computational neuroscience to the top-down control of regeneration of limbs and other complex organs†

G. Pezzulo<sup>1</sup> and M. Levin<sup>2\*</sup>



# Rebooting Multicellularity: Xenobots



Early frog embryo

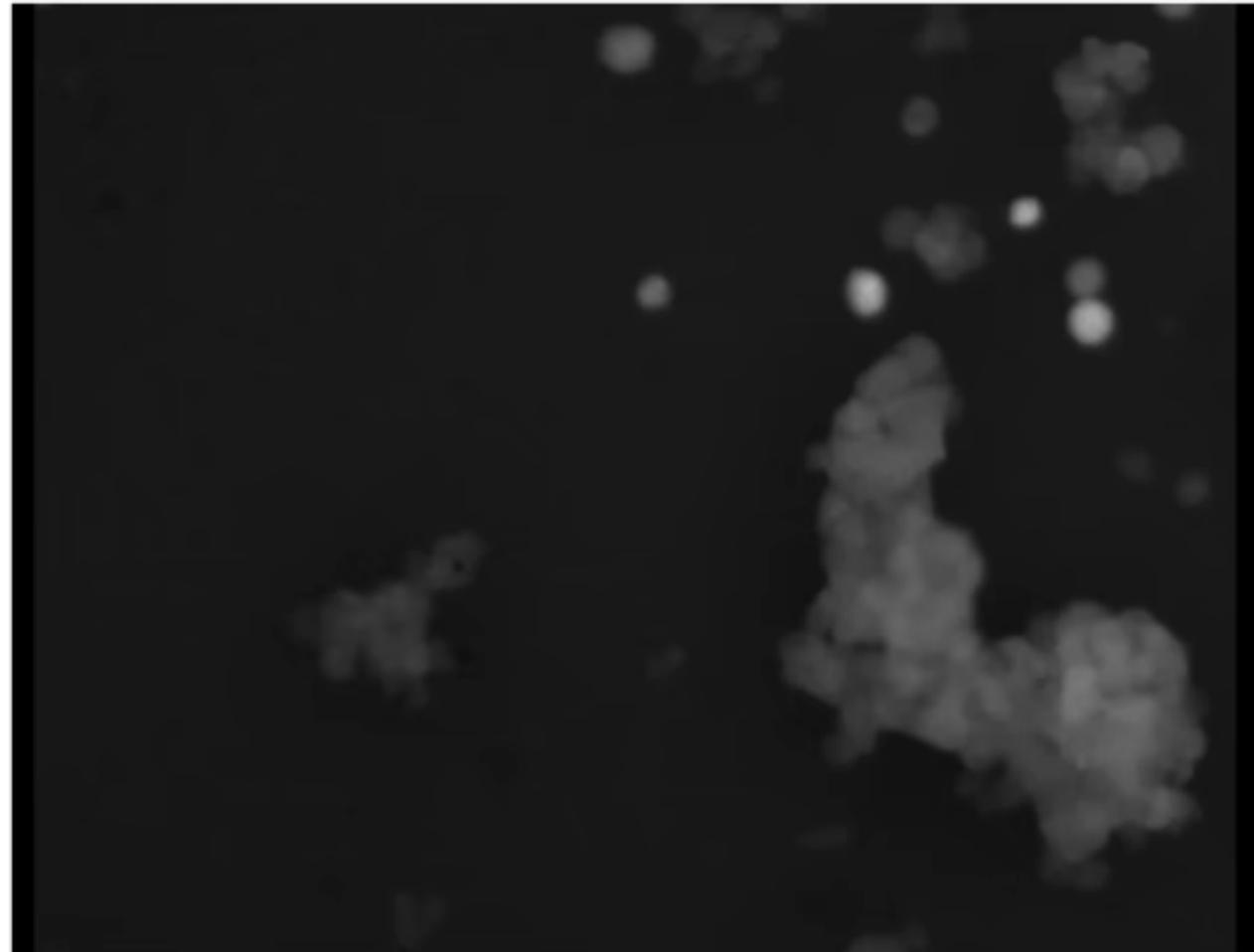
8 hours



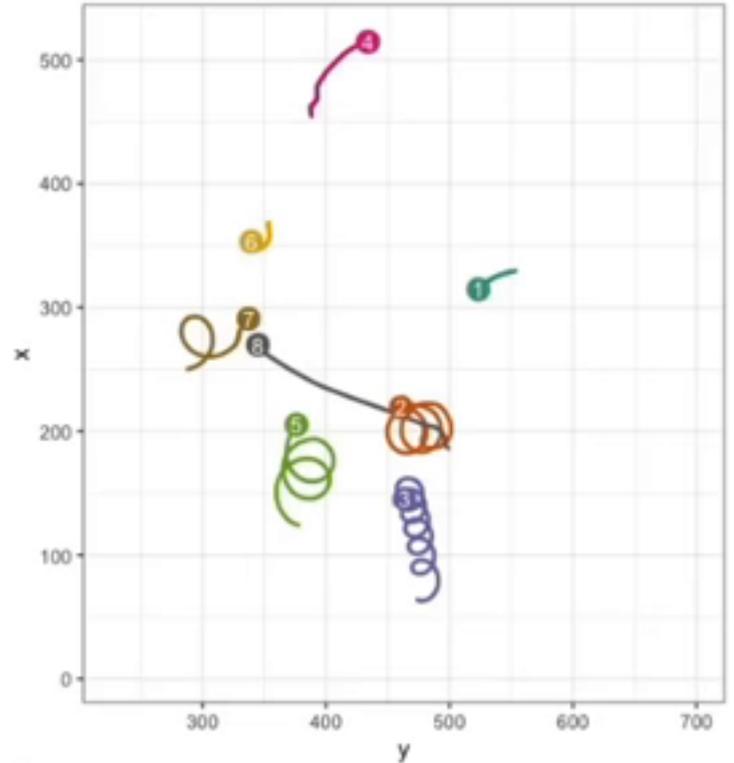
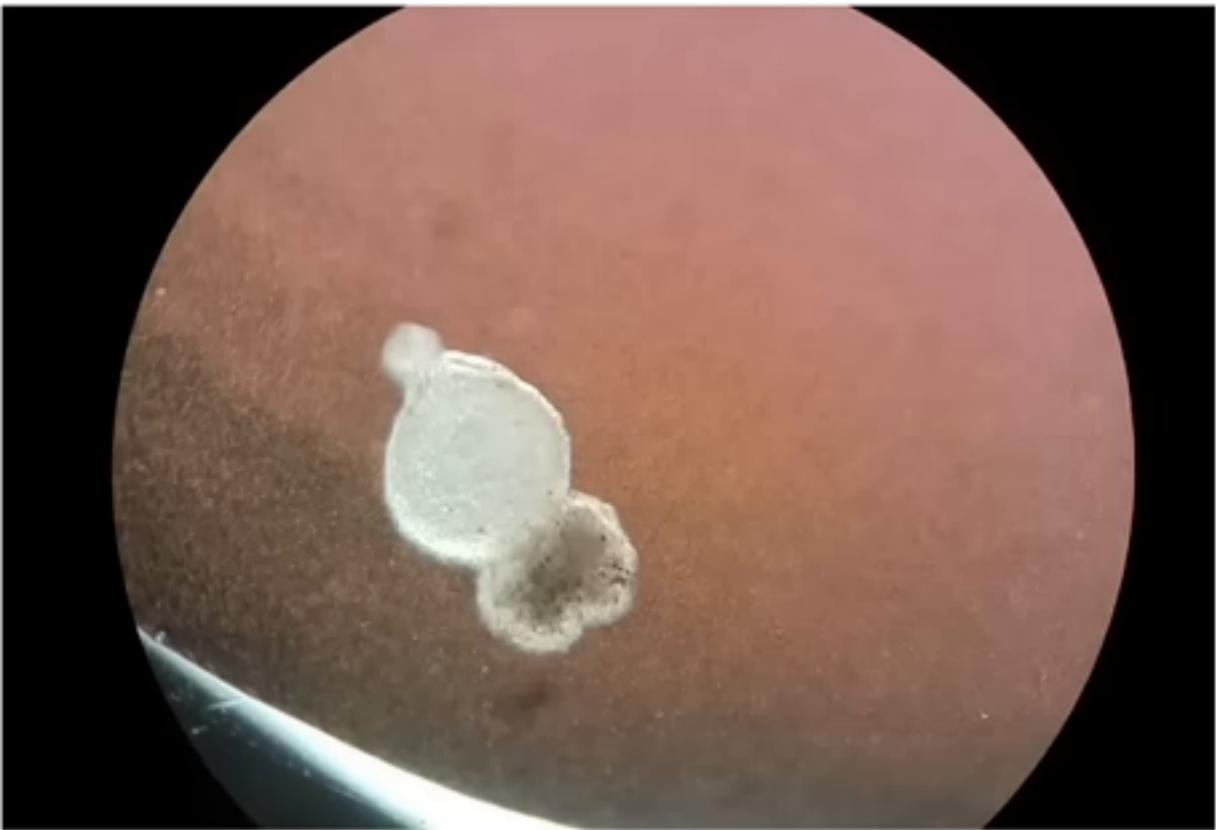
- die
- crawl off
- 2D cell layer
- ...?

assay for form and function

*Douglas Blackiston*



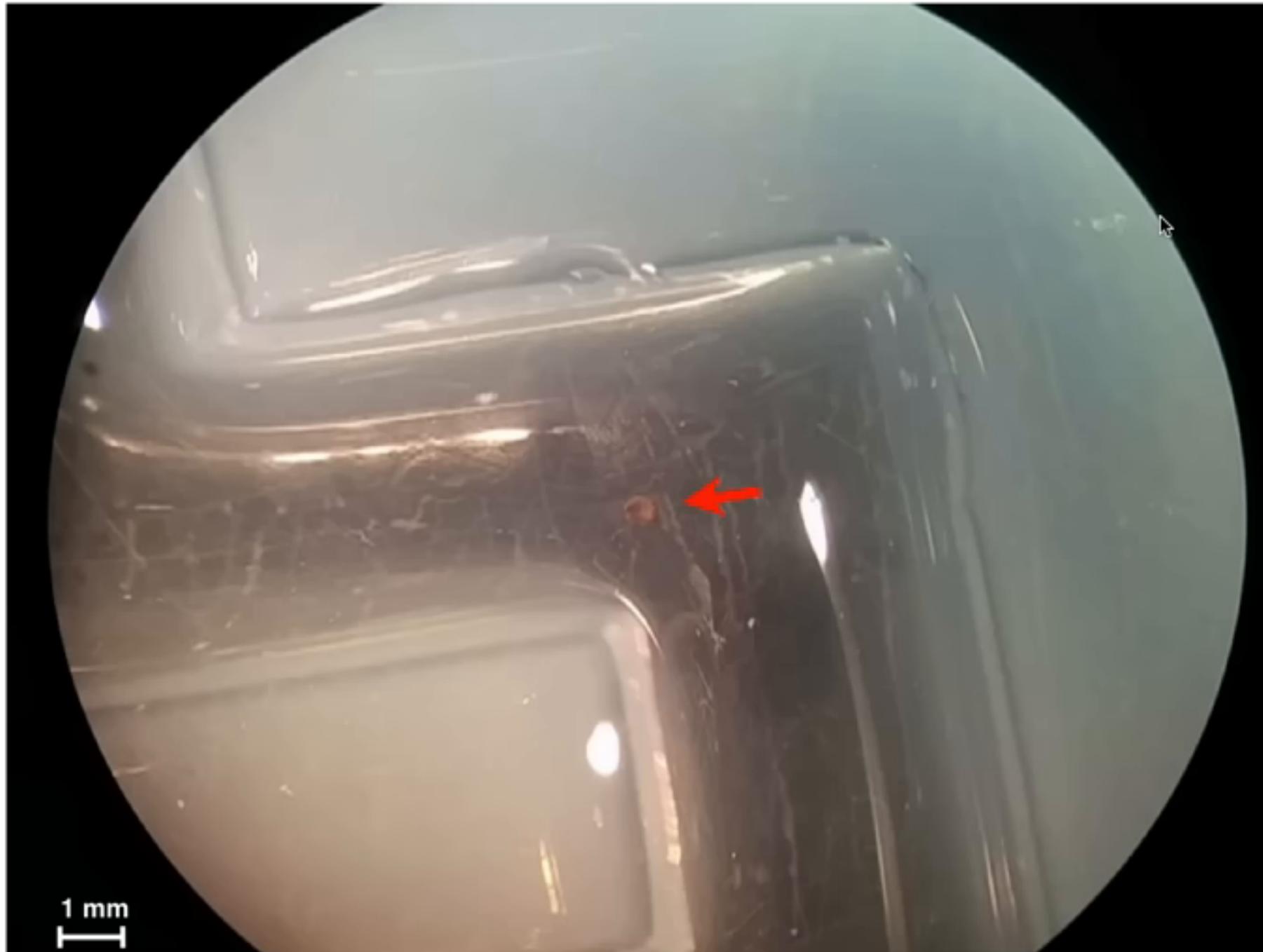
# Xenobot behaviors - repurposing cilia for motion



collective behaviors



# Xenobot in a maze (still water, no flow):



- 1) it traverses maze,
- 2) rounds the corners without bumping into walls, and
- 3) it makes a spontaneous decision to turn around without hitting anything.

# Kinematic Replication in Xenobots: novel competencies of the agential material



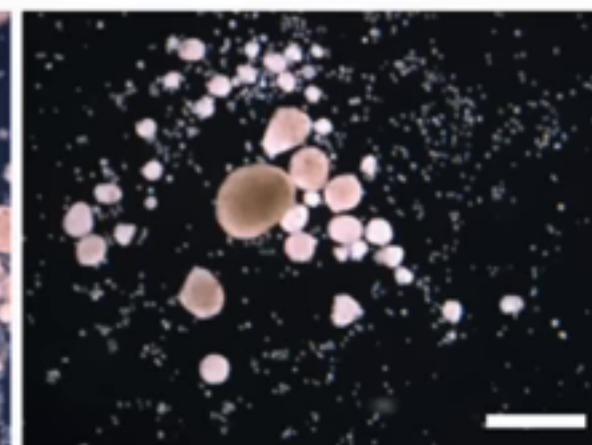
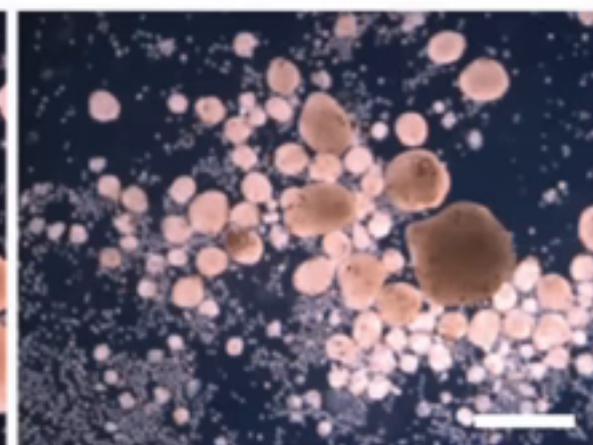
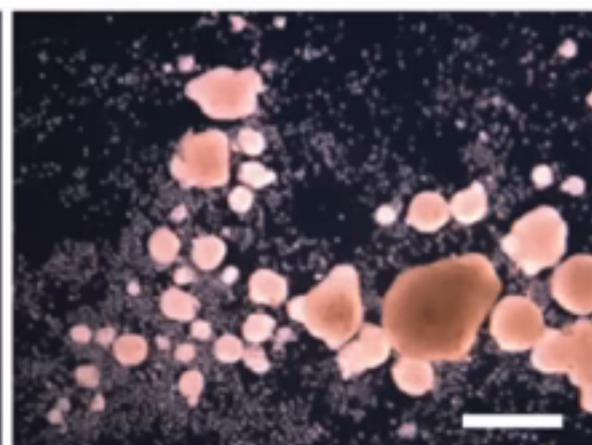
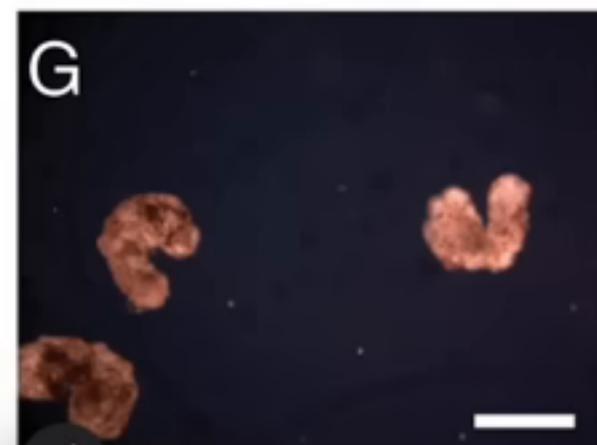
*Douglas Blackiston*

gen 0

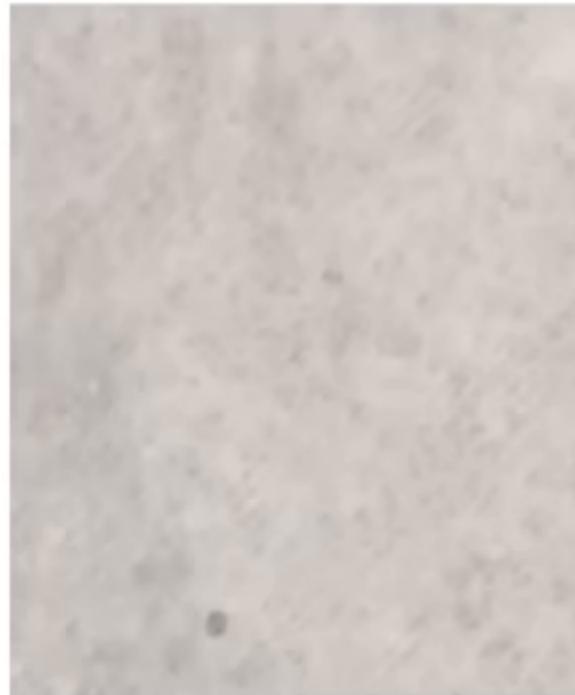
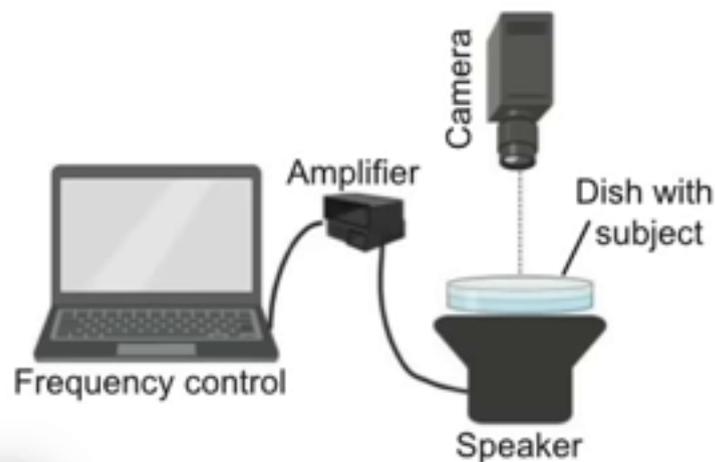
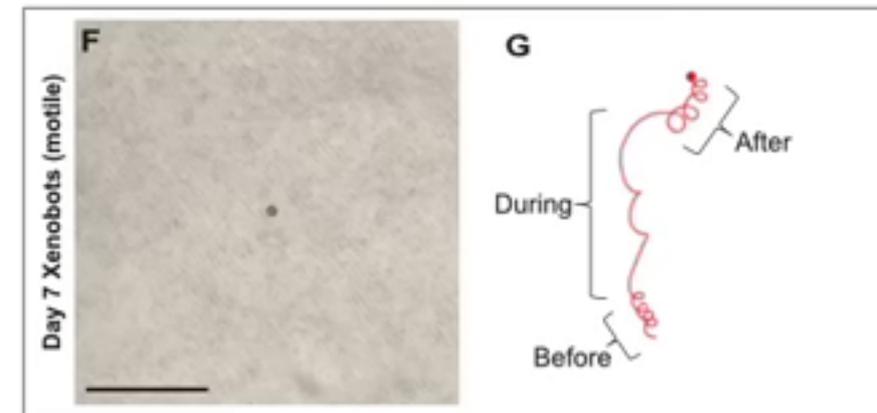
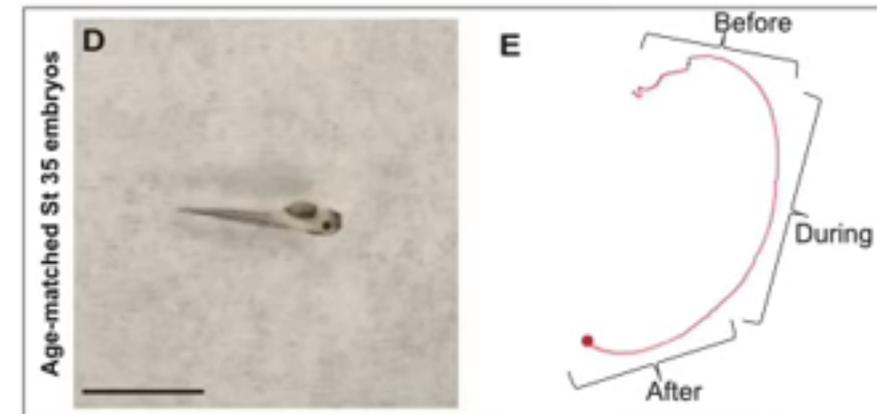
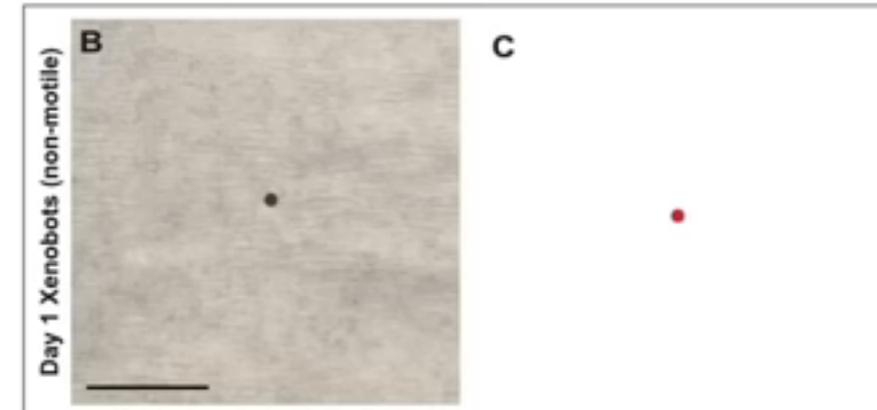
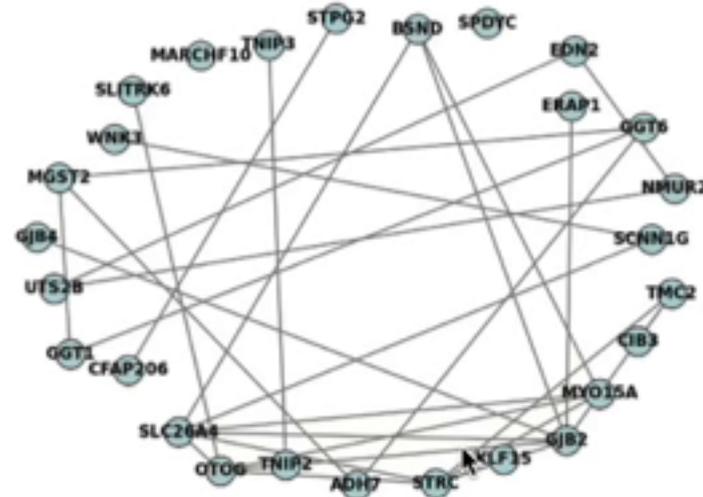
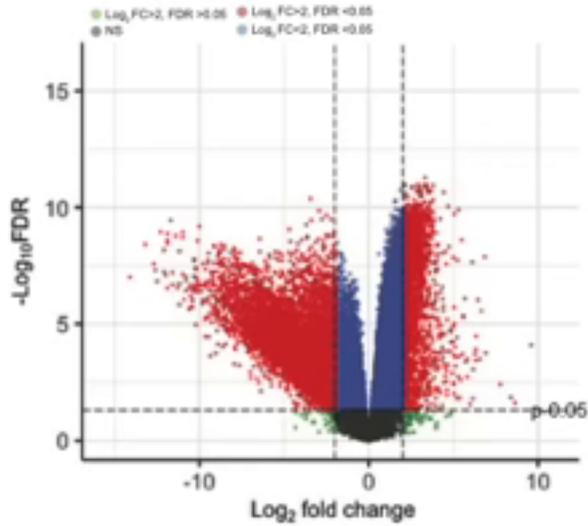
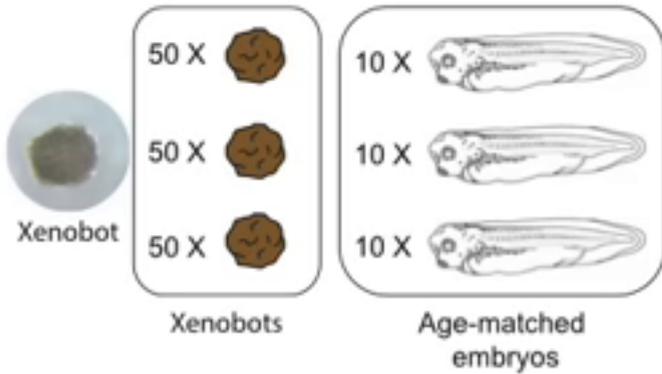
gen 1

gen 2

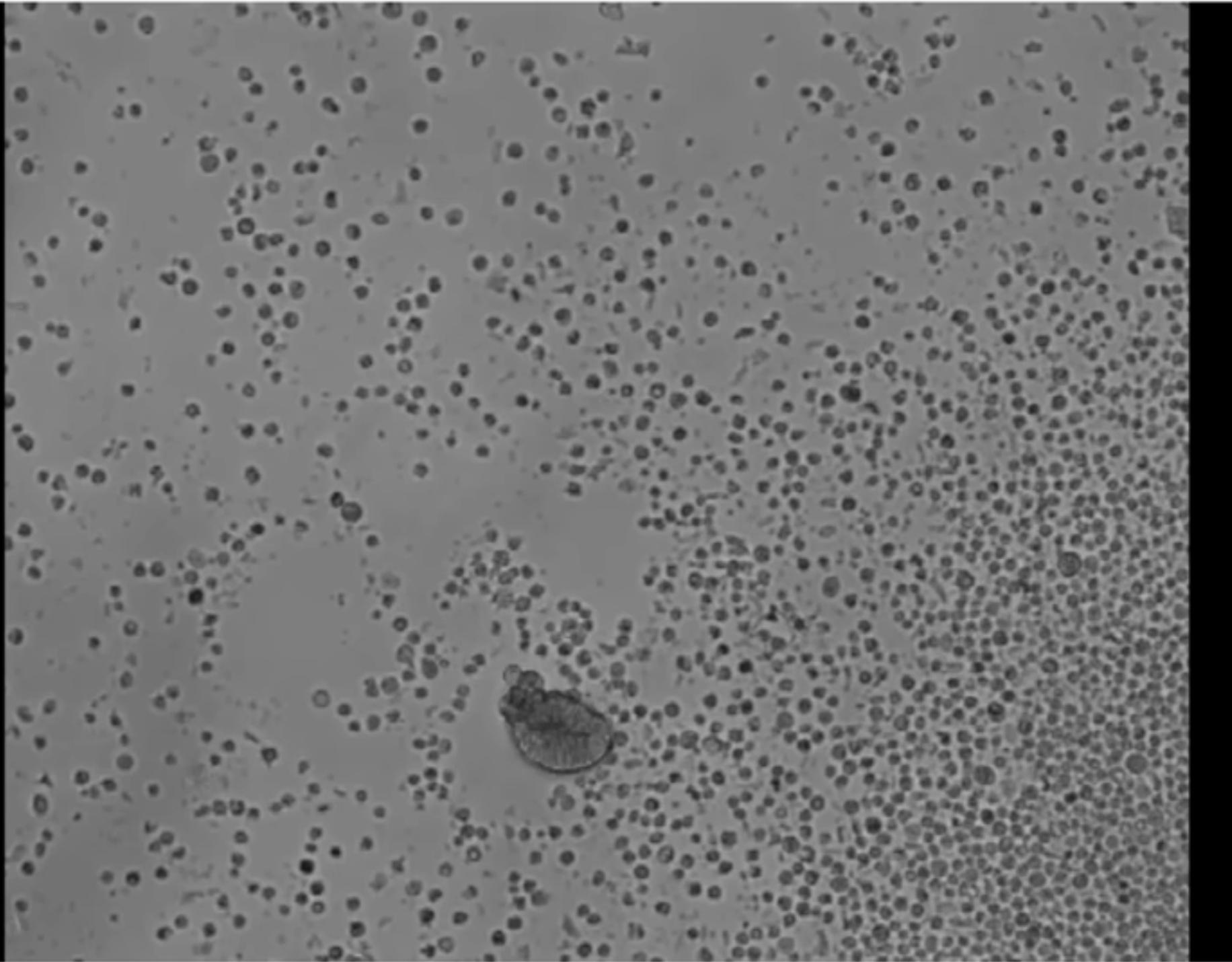
gen 3



# Communicating with Xenobots via Sound



# Anthrobots; can you guess the genome?

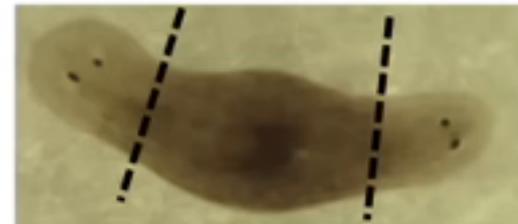
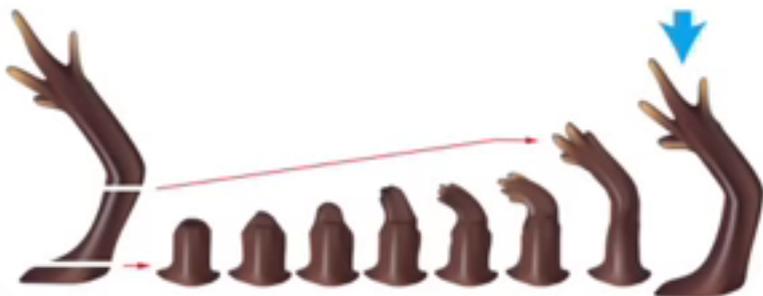
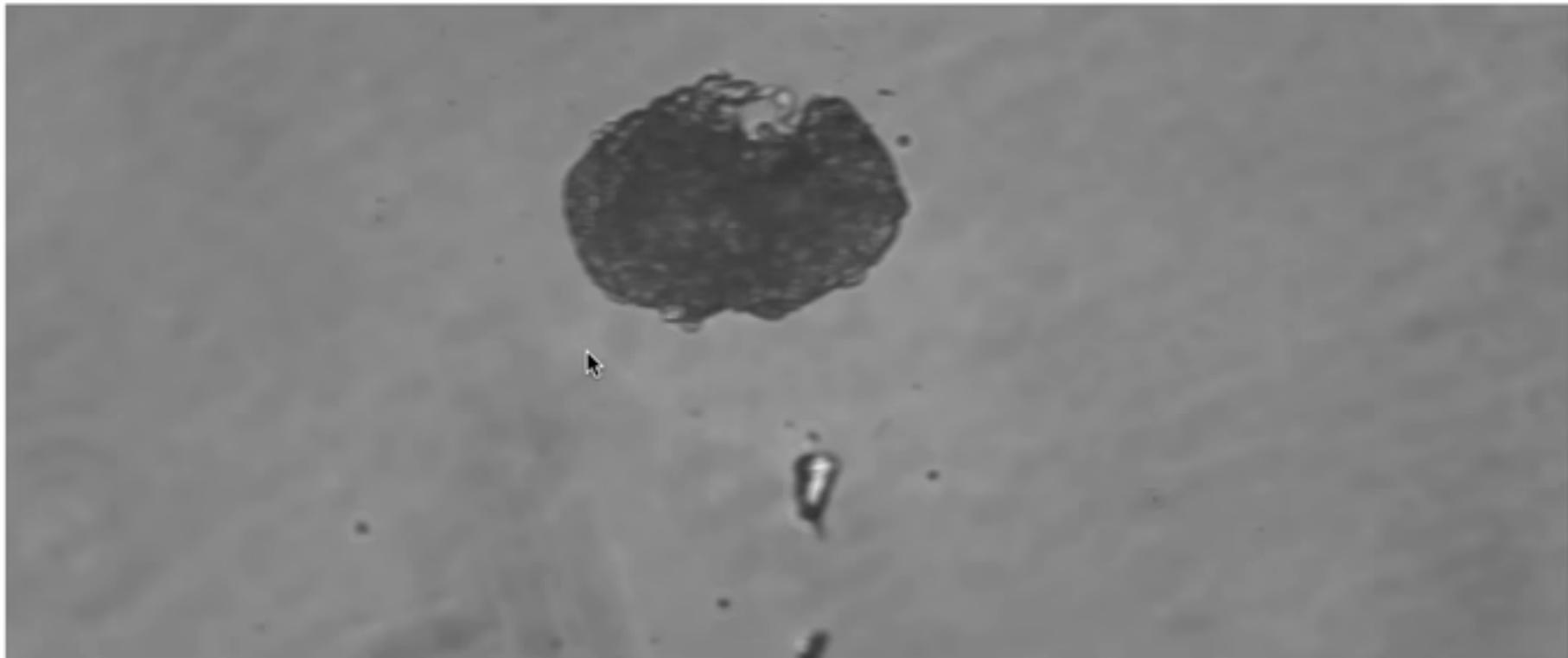


Where do the properties of novel systems come from if not eons of selection or explicit engineering?

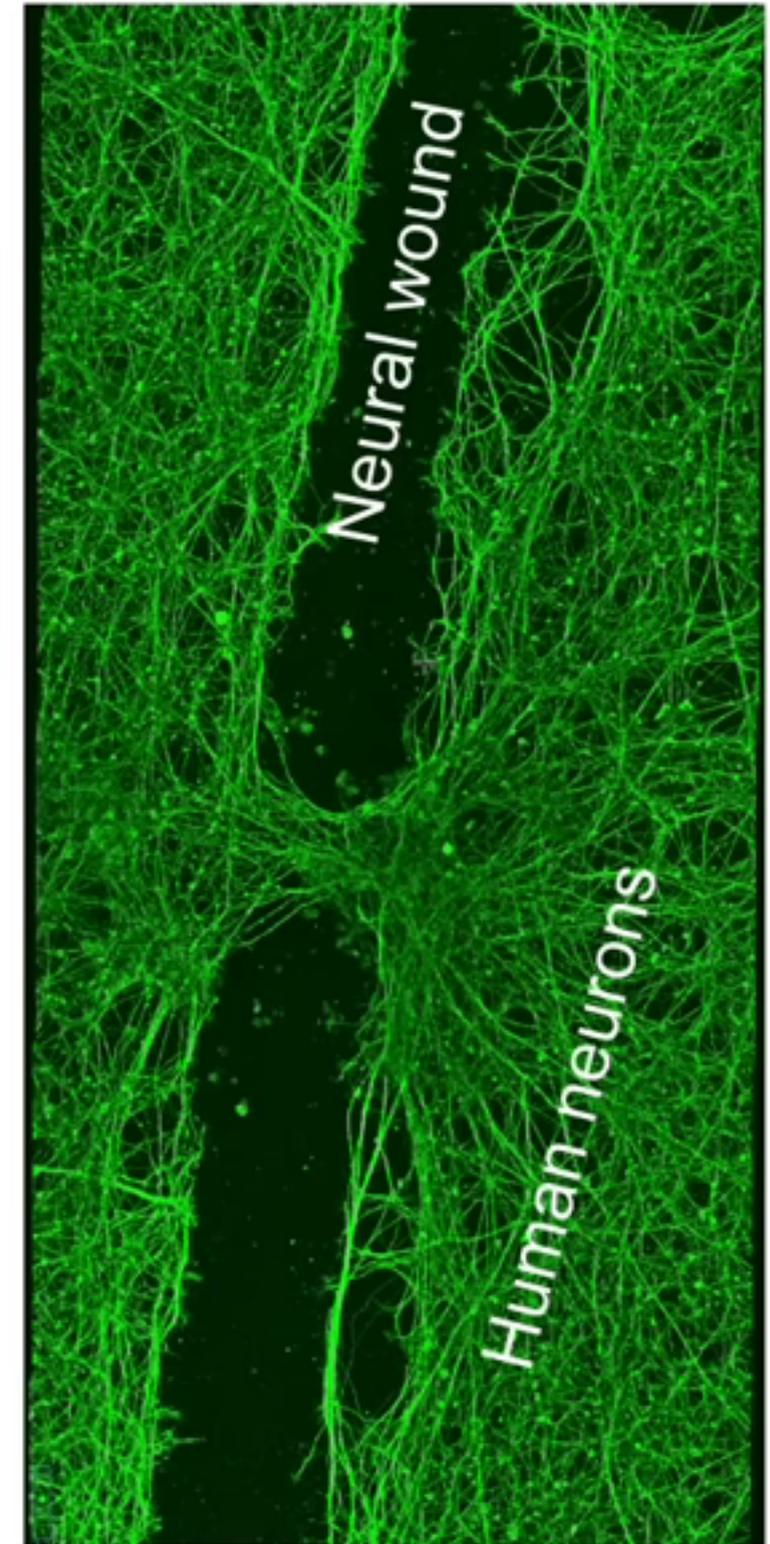
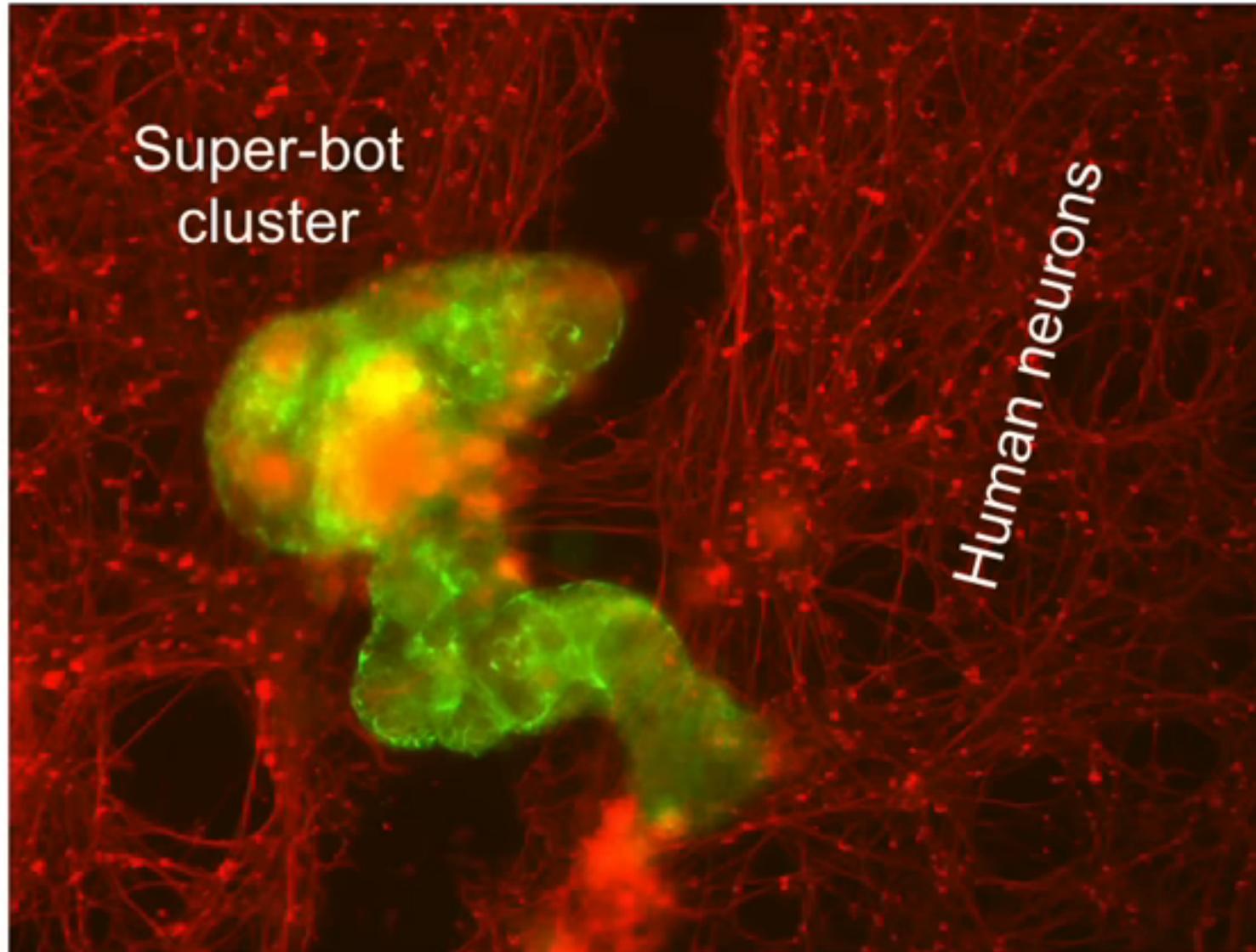
Could you guess the genome from these data?

Could you guess behavior and form from the genome?

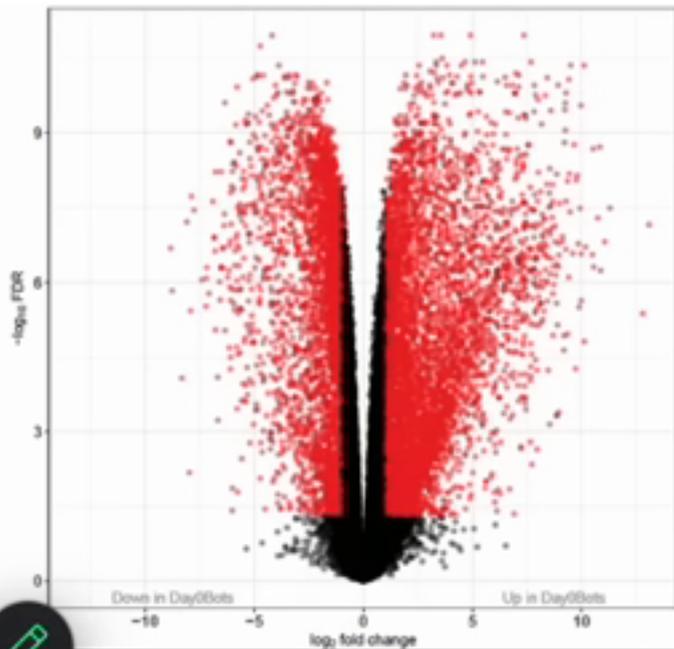
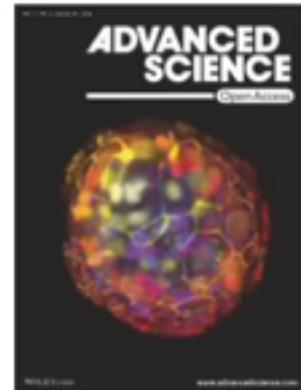
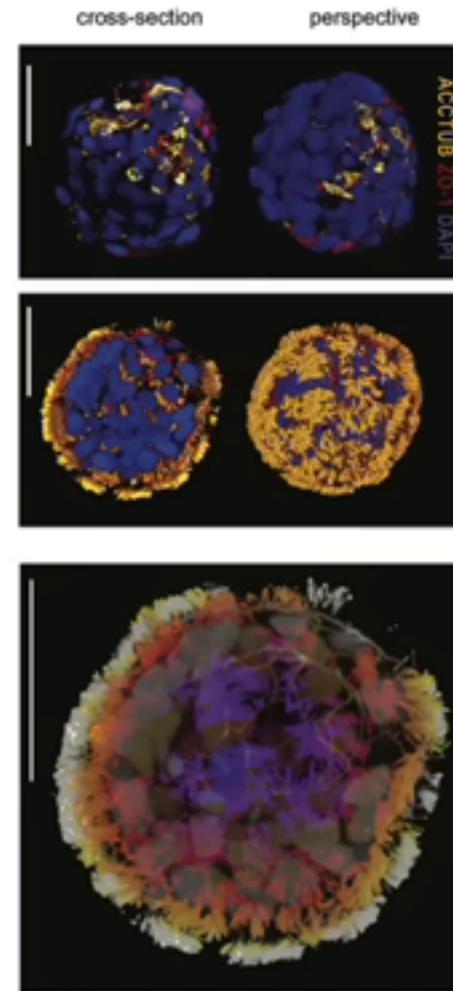
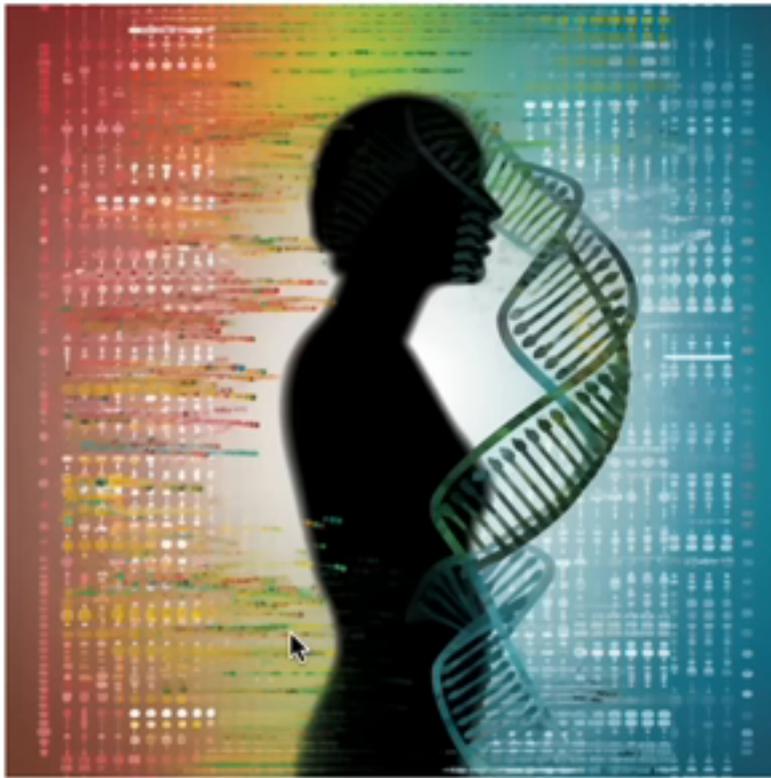
# Repairing Toward New Shape



# Anthrobots Exert Neural Repair

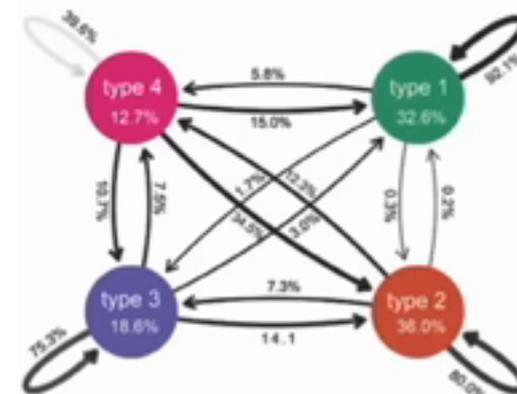


# No Evolutionary History Explains Form and Behavior:



drastically remodeled transcriptome

Ethogram of discrete behaviors

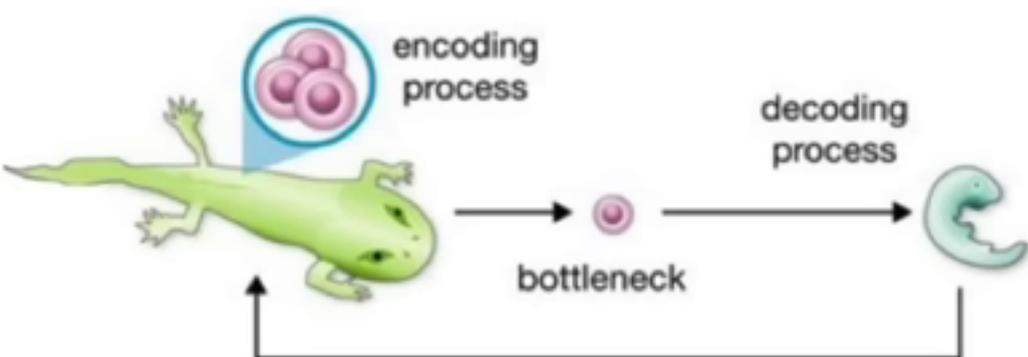
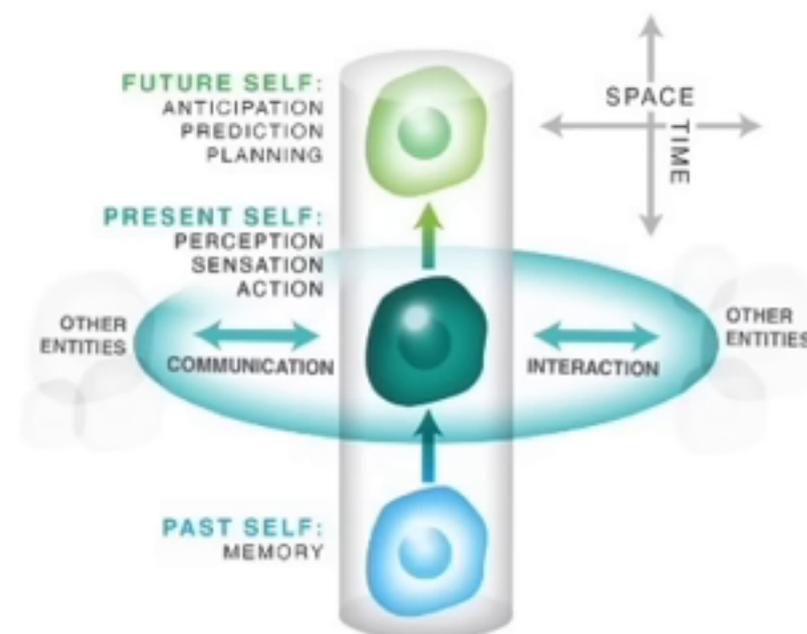
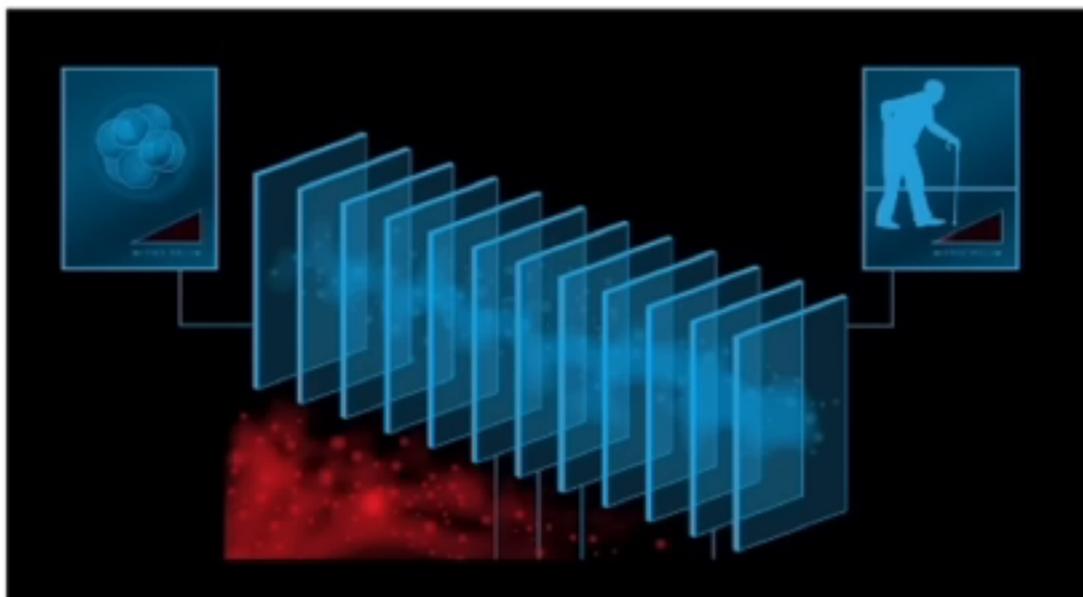


# Conclusion:

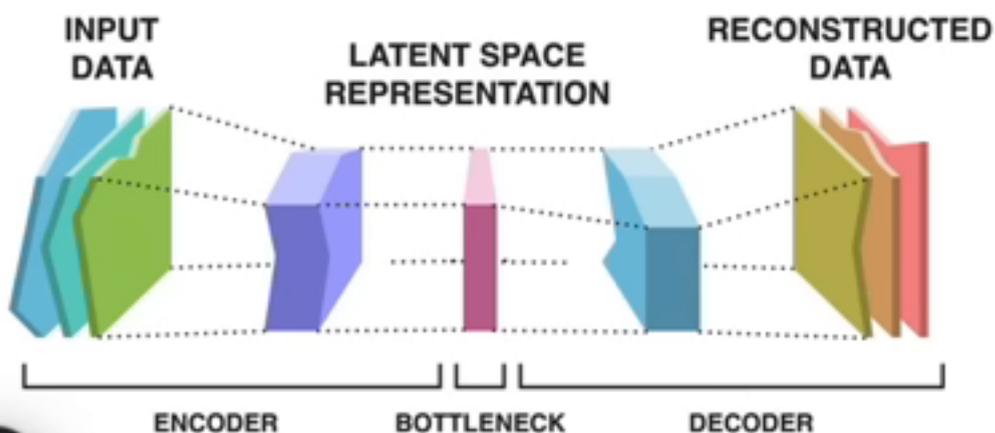
- Minds & bodies
- Future



# Memory Engrams and DNA - same paradox



Biology assumes the hardware is unreliable  
 Environment and your own parts will change, **don't over-train**  
 Little allegiance to past Self's meaning of engrams  
 Re-interpret on-the-fly - present/future is all that matters  
 Engram is highly compressed - creative remembering, not deduction  
 Undependable hardware and confabulation are a feature, not a bug  
 Consciousness = active, creative story-telling from own memory traces

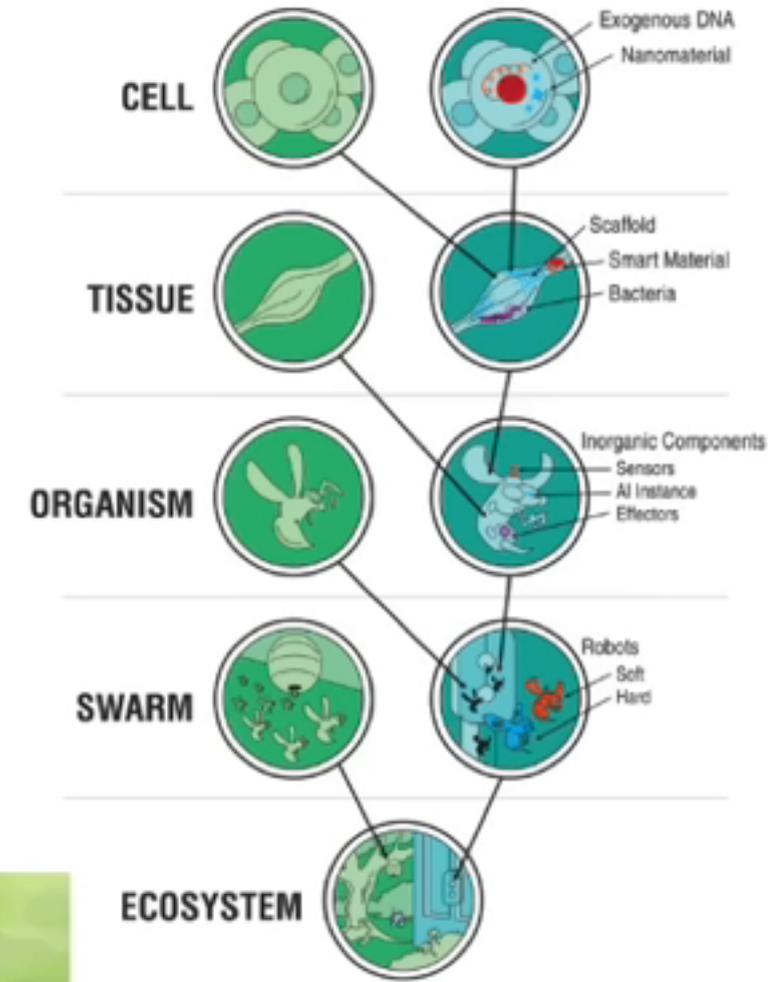
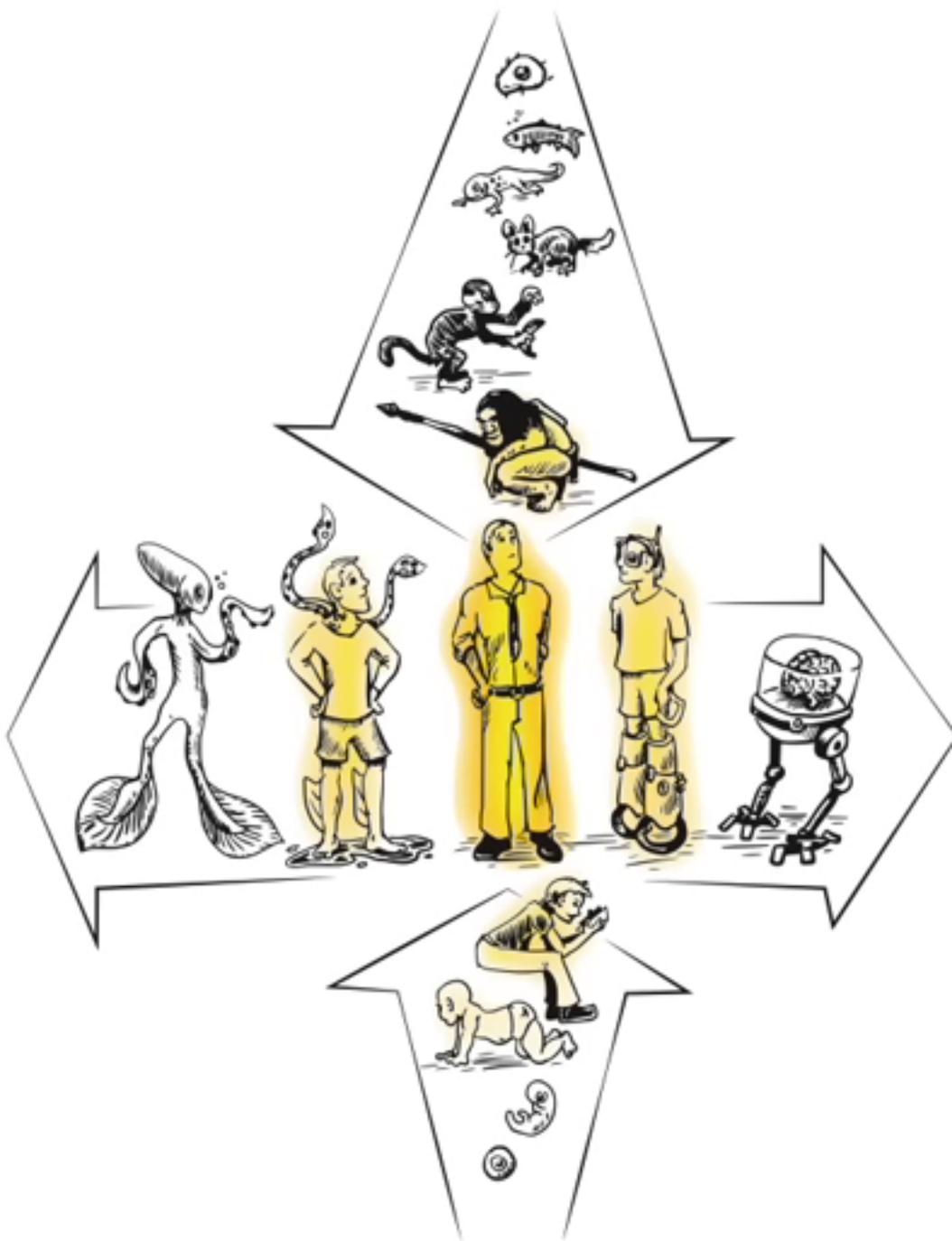


Perspective

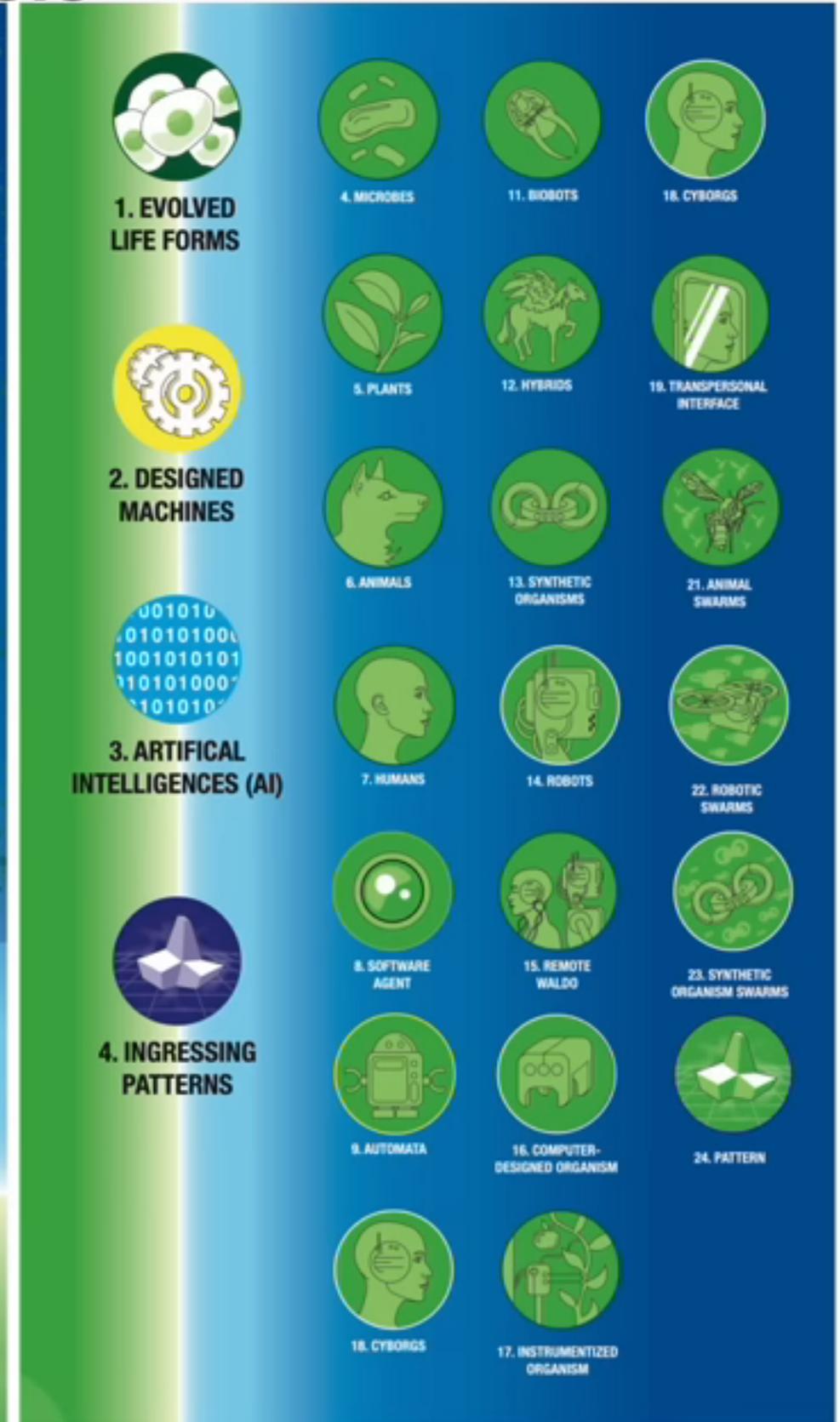
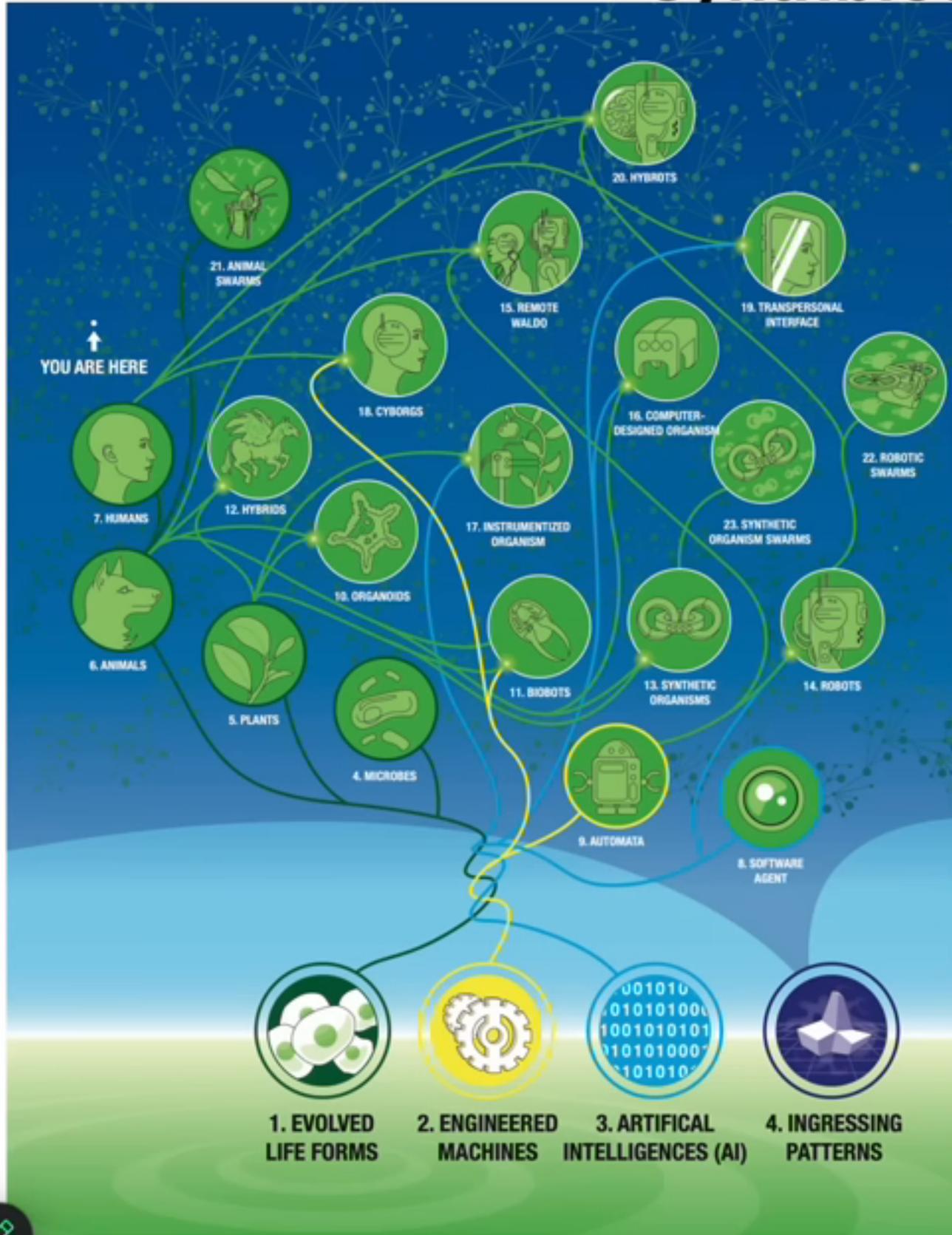
**Self-Improving Memory: A Perspective on Memories as Agential, Dynamically Reinterpreting Cognitive Glue**

Michael Levin

# Plasticity of Life: beyond standard forms



# ENDLESS FORMS MOST BEAUTIFUL ~~ARTIFICIAL~~ synthbiosis



# Thank you to:

## Post-docs and staff scientists in the Levin lab:

**Douglas Blackiston** - brain-body interface plasticity, synthetic living bodies

**Laura Vandenberg** - craniofacial remodeling

Léo Pio-Lopez - bioinformatics of cognitive scaling, aging, and bioelectricity

Devon Davidian, Evgenia Shmeleva, Nirosha Murugan, Celia Herrera-Rincon, AiSun Tseng - limb regeneration

**Vaibhav Pai** - voltage gradients in eye/brain induction and repair

Juanita Mathews - bioelectricity of cancer

Patrick Erickson - cellular learning

**Patrick McMillen** - bioelectric imaging and transitions to multicellularity

## Ph.D. Students:

Franz Kuchling - cognitive neuroscience modeling applied to pattern homeostasis, Volvox surprise minimization

**Gizem Gumuskaya, Nikolay Davey** - Anthrobots

**Angela Tung** - cross-embryo communication

## Undergraduate Students:

**Maya Emmons-Bell** - planarian head plasticity, barium adaptation

**Pranjal Srivastava, Ben G. Cooper, Hannah Lesser, Ben Semegran, Andrew Bender, Douglas Hazel** - Anthrobots

+ many other undergraduate students working in our lab over the years

## Technical support:

Rakela Colon, Jayati Mandal - lab management

Erin Switzer - vertebrate animal husbandry

Emma Lederer - Xenobot behavior

Joan Lemire - molecular biology

## Collaborators: Allen Center members +

Dany Adams - bioelectric face prepattern

Alexis Pietak, Marcel Blattner, Salvador Mafe, Javier Cervera - computational modeling of bioelectrics

Joshua Bongard - Xenobot simulations and AI

David Kaplan -  $V_{mem}$  and human MSC differentiation, regenerative sleeves

Fiorenzo Omenetto - optical approaches to bioelectric modulation

**Giovanni Pezzulo** - cognitive science models of pattern regulation

Vitaly Volpert, **Chris Fields** - mathematical models of pattern regulation

**Richard Watson** - computational models of cognitive scaling and evolutionary learning

Don Ingber, Richard Novak, V. J. Koomson, J. H. Dungan - mammalian bioengineering

Jack Tuszynski - cell biophysics and drug discovery

Model systems: tadpoles, planaria, zebrafish, slime molds, human cells, and chick embryos

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Illustrations: Jeremy Guay @ Peregrine Creative

Closures: Morphochemicals, Fauna Systems, Astonishing Labs

