4PM

9PM in London (GMT), 6AM in Tokyo (GMT+9)

Collective Intelligence of The Body

Moderator: Katy Börner, *Indiana University*

Presenter: Michael Levin, *Tufts University & Harvard University*

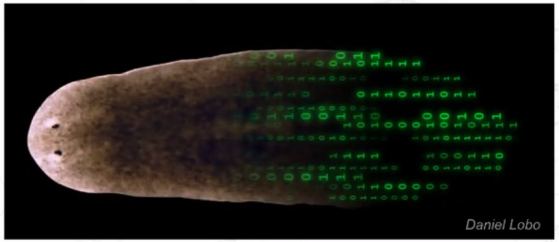
Michael Levin, *TUFTS University & Harvard University*

Collective Intelligence of the Body: The Multiscale Architecture of Selves

Michael Levin
Allen Discovery Center at Tufts

http://www.drmichaellevin.org/

http://thoughtforms.life/



ALLEN DISCOVERY CENTER at Tufts University

Computer-designed Organisms
TUFTS UNIVERSITY | UNIVERSITY OF VERMONT

WYSS INSTITUTE

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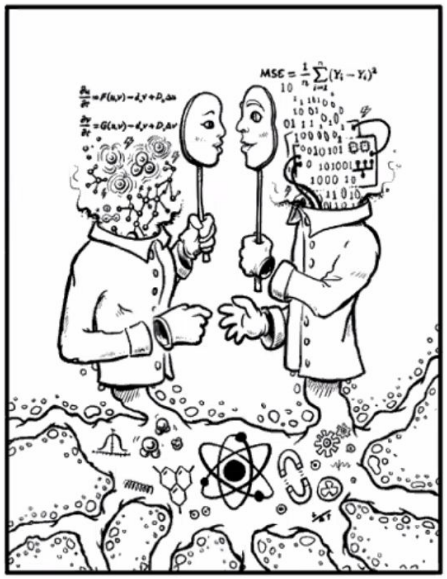
HARVARD

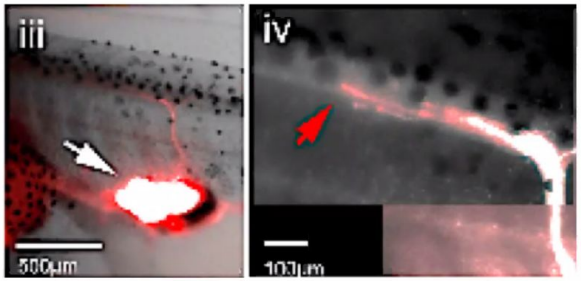
Adam Names the Animals in the GoE

Outline:

- What are you?
- What does it mean for biomedicine
- What next: beyond the standard human

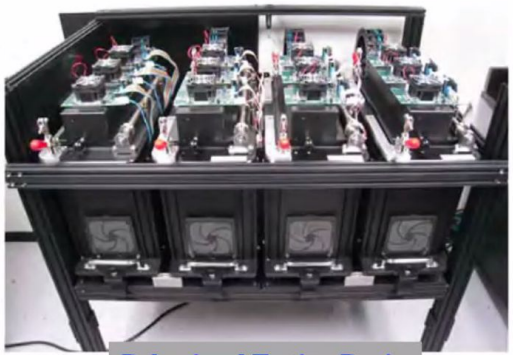


Play the Hand You're Dealt: functional plasticity



Ectopic eyes on tail provide vision!

Doug Blackiston



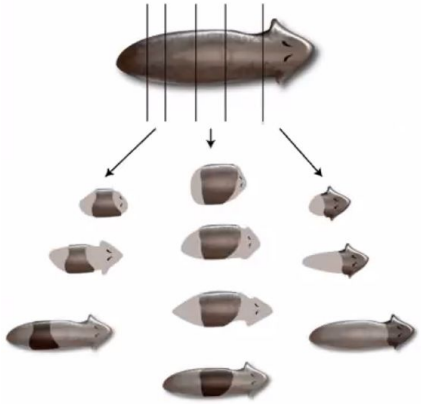
Behavioral Testing Device

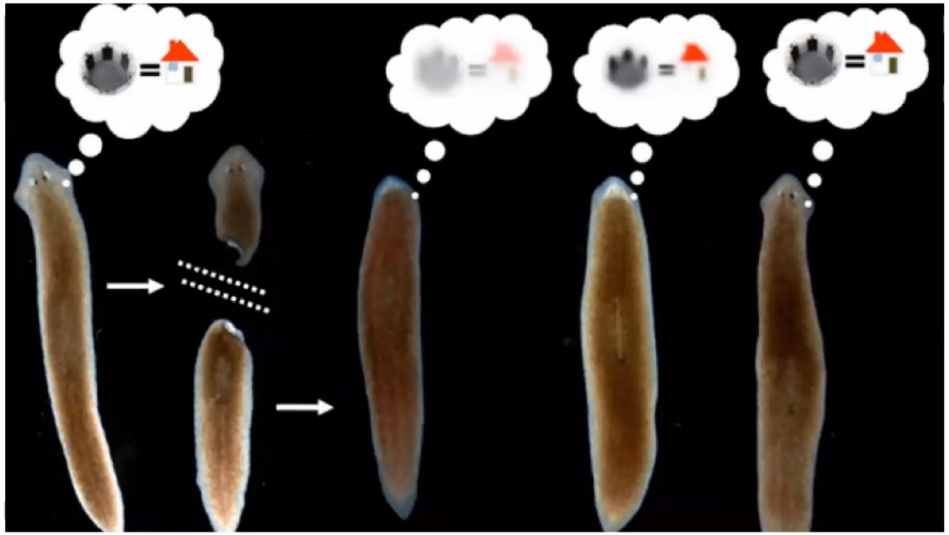
no evolutionary adaptation needed
(because embryos can't take much
for granted, have to solve on-the-fly:
evolution makes problem-solving
agents)! Why does this work?

Brain dynamically adjusts behavioral programs
to accommodate different body architectures

Memories can Move Around within Bodies

Memory stored outside the head, imprinted on regenerated brain





Tal Shomrat

© 2016. Published by The Company of Biologists Ltd | Biology Open (2016) 5, 1177-1188 doi:10.1242/bio.020149

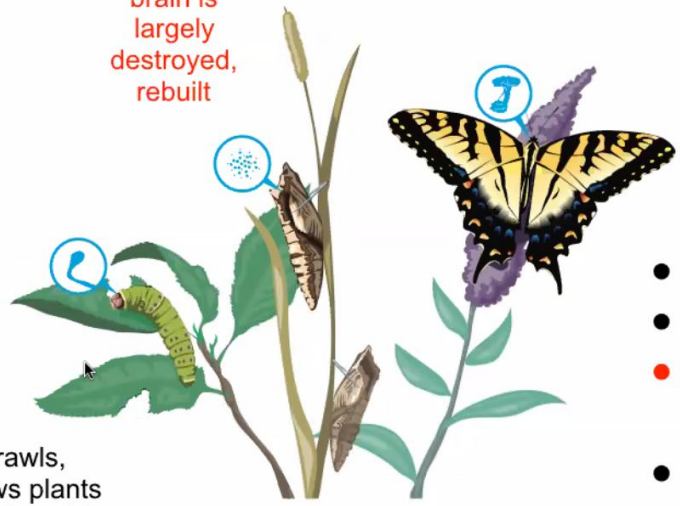
HYPOTHESIS

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

Moran Neuhof[1,*], Michael Levin[2,*] and Oded Rechavi[1,2,3,*]

Memories can Move Between Very Different Minds

memories can adapt to different environments;
can they do niche construction?



- minds are embodied
- bodies can change drastically
- memories are generalized and remapped onto new architecture
- what is it like to be a caterpillar changing into a butterfly?

Communicative & Integrative Biology 8:5, e1073424; September/October 2015; Published with license by Taylor and Francis Group, LLC

The stability of memories during brain remodeling: A perspective

Douglas J Blackiston[1], Tal Shomrat[2,3], and Michael Levin[1,*]

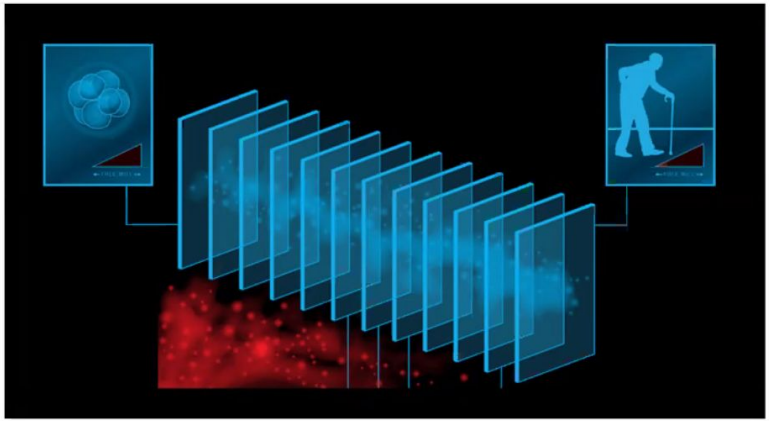
entropy

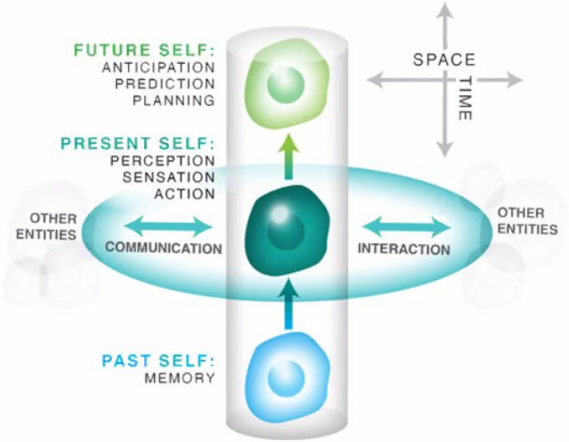
Perspective

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

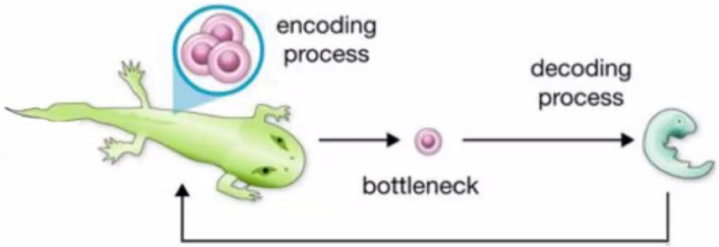
Michael Levin

You are a Dynamic, Self-constructing Story





creative, self-constructing process
is ancient!

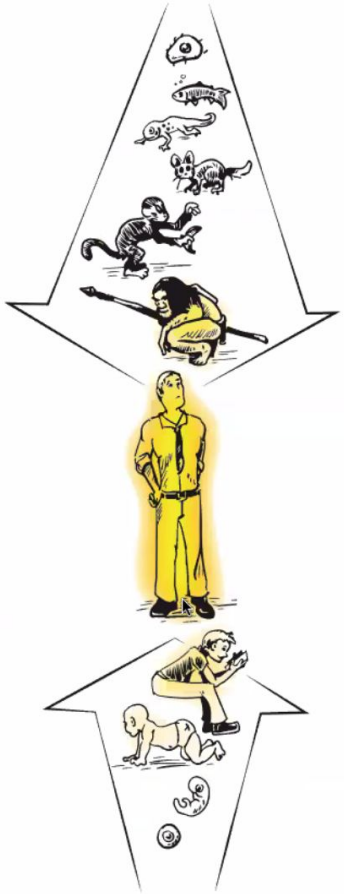


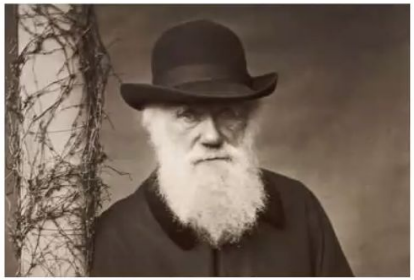
entropy

Perspective

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

A Continuum of Beings: scaling >> emergent levels

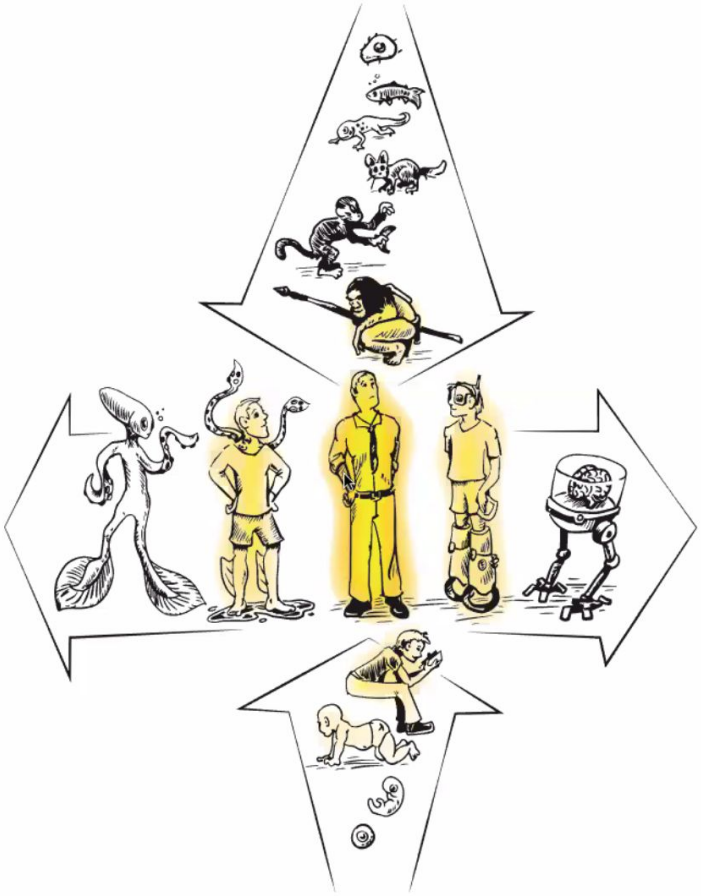




Darwin
1859

Karl Ernst
von Baer
1827

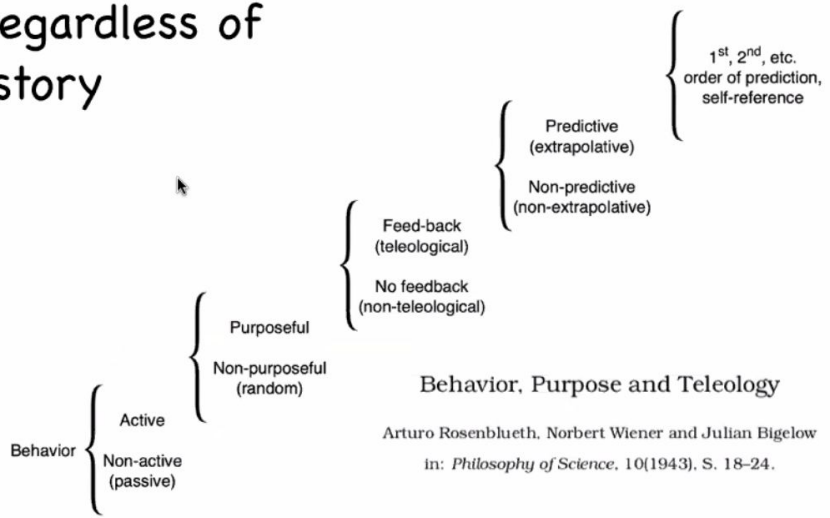
A Wider Continuum of Beings



My Framework Goal:

- Recognize, create, and relate to truly diverse intelligences regardless of composition or origin story

  - familiar creatures - us, apes, birds
  - weird creatures (colonial organisms, swarms)
  - synthetic biology - engineered new life forms
  - AI - software or robotic
  - exo-biological agents (Earth is N=1)



Behavior, Purpose and Teleology

Arturo Rosenblueth, Norbert Wiener and Julian Bigelow

in: *Philosophy of Science*, 10(1943), S. 18–24.

- moves experimental work forward - new capabilities, better ethical frameworks

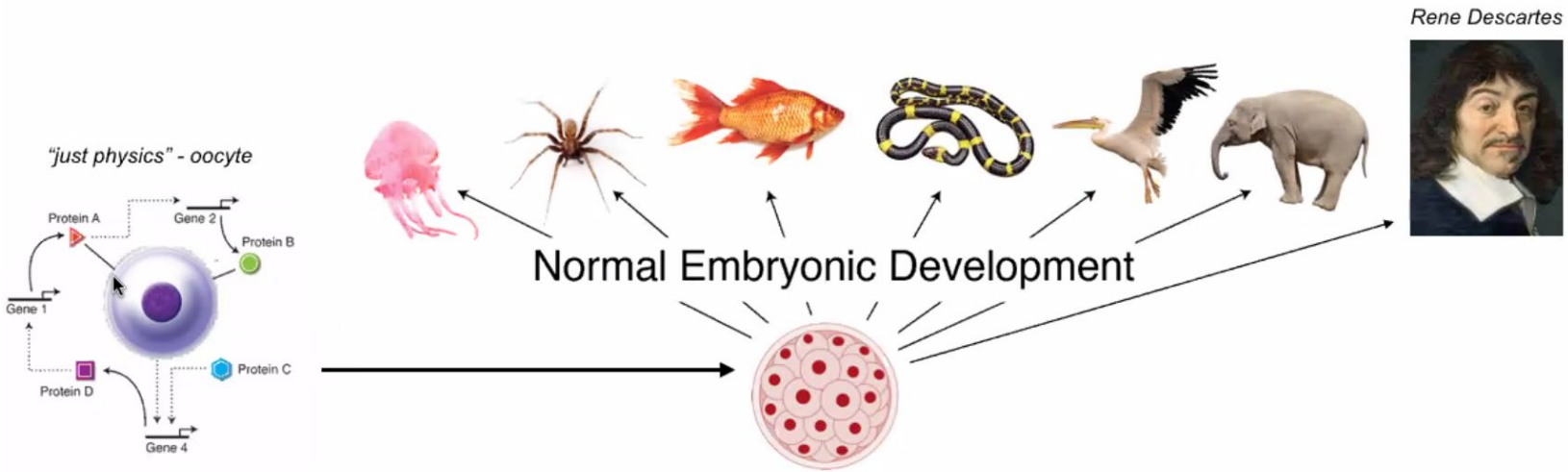
frontiers in Systems Neuroscience

HYPOTHESIS AND THEORY
published: 24 March 2022
doi: 10.3389/fnsys.2022.768201

Technological Approach to Mind Everywhere: An Experimentally-Grounded Framework for Understanding Diverse Bodies and Minds

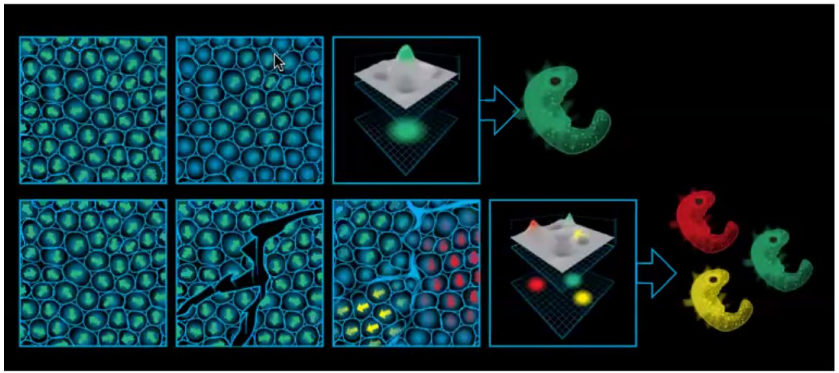
Michael Levin[1,2]*

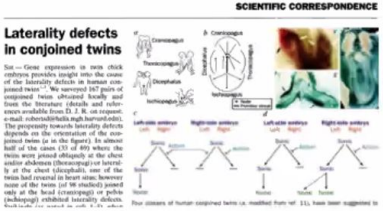
You Were Once "Just Physics"



we all make the journey across the "Cartesian cut"

Embryonic Origin of Selves from "Freudian Ocean" of a cellular blastoderm - alignment

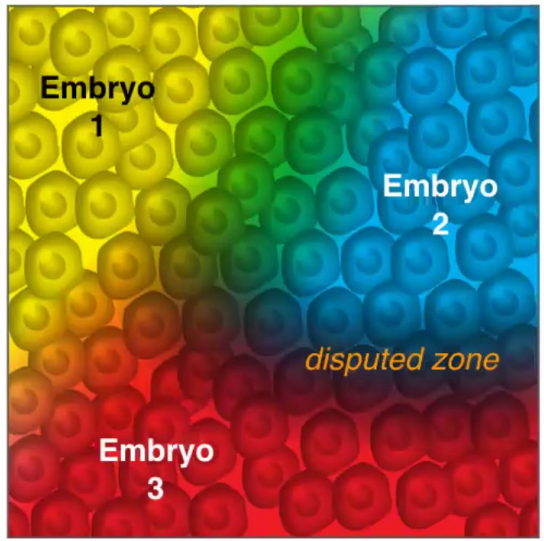




SCIENTIFIC CORRESPONDENCE

Laterality defects in conjoined twins

Sir — Gene expression in twin chick embryos provides insight into the cause of the laterality defects in human conjoined twins[1]. We surveyed 167 pairs of conjoined twins obtained locally and from the literature (details and references available from D. J. R. on request, e-mail: roberts@helix.mgh.harvard.edu). The propensity towards laterality defects depends on the orientation of the conjoined twins (a–c in the figure). In almost half of the cases (33 of 69) where the twins were joined obliquely at the chest and/or abdomen (thoracopagi) or laterally at the chest (dicephali), one of the twins had reversal in heart situs; however none of the twins (of 98 studied) joined only at the head (craniopagi) or pelvis (ischiopagi) exhibited laterality defects.

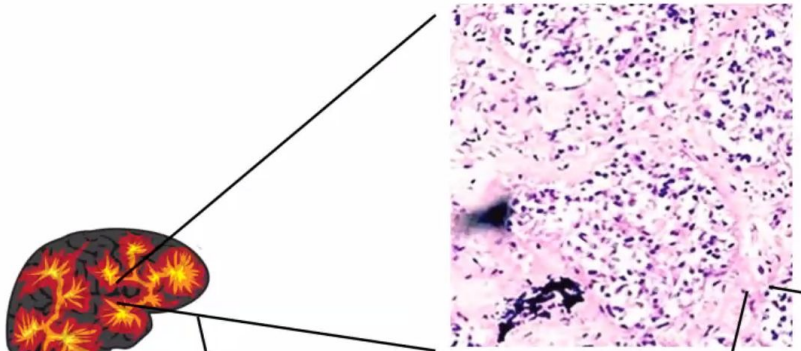


How many embryos are there?

Where is my border with "environment"?
every cell is some other cell's environment

Issue of **individuation** in cognition:
split brain patients, dissociative disorders, etc.

But at least, you're a true Unified Intelligence?



Jose Calvo, pineal gland histology

Gaël McGill

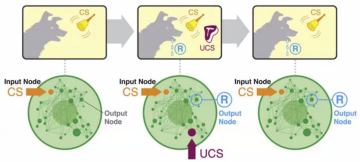
We are All Collective Intelligences!

Lacrymaria = 1 cell
no brain
no nervous system

high competency
at cell-level
agendas

We owe stories of **scaling** minds, and
the origins of their goals and competencies

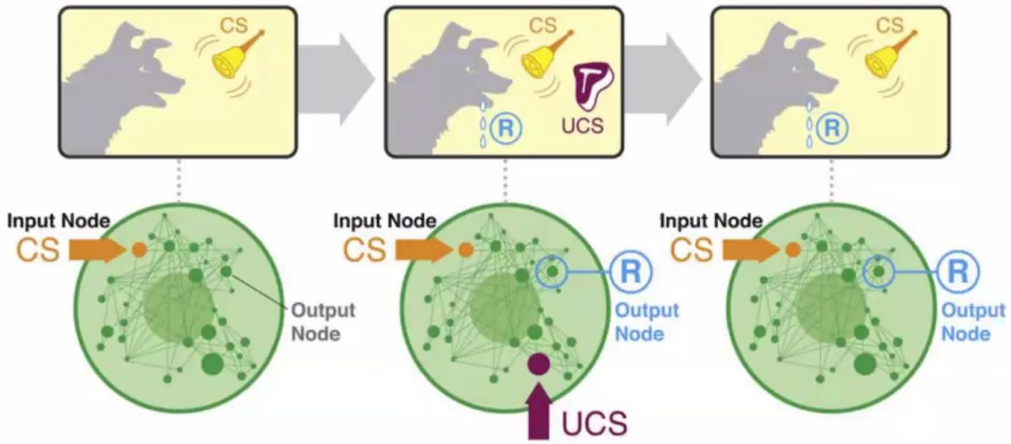
Collective Intelligence Below the Cell Level



Biomedicine:

- drug conditioning

Collective Intelligence Below the Cell Level



Biomedicine:

- drug conditioning

International Journal of Molecular Sciences
MDPI

Article

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

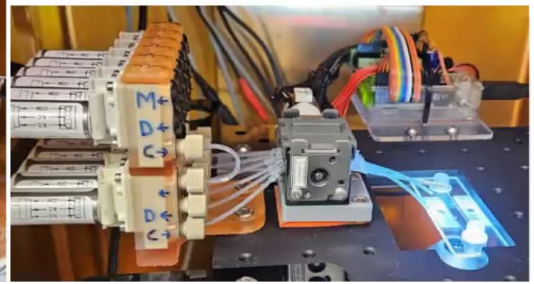
Surama Biswas [1,2,†], Wesley Clawson [1,†] and Michael Levin [1,3,*]

iScience
CellPress
OPEN ACCESS

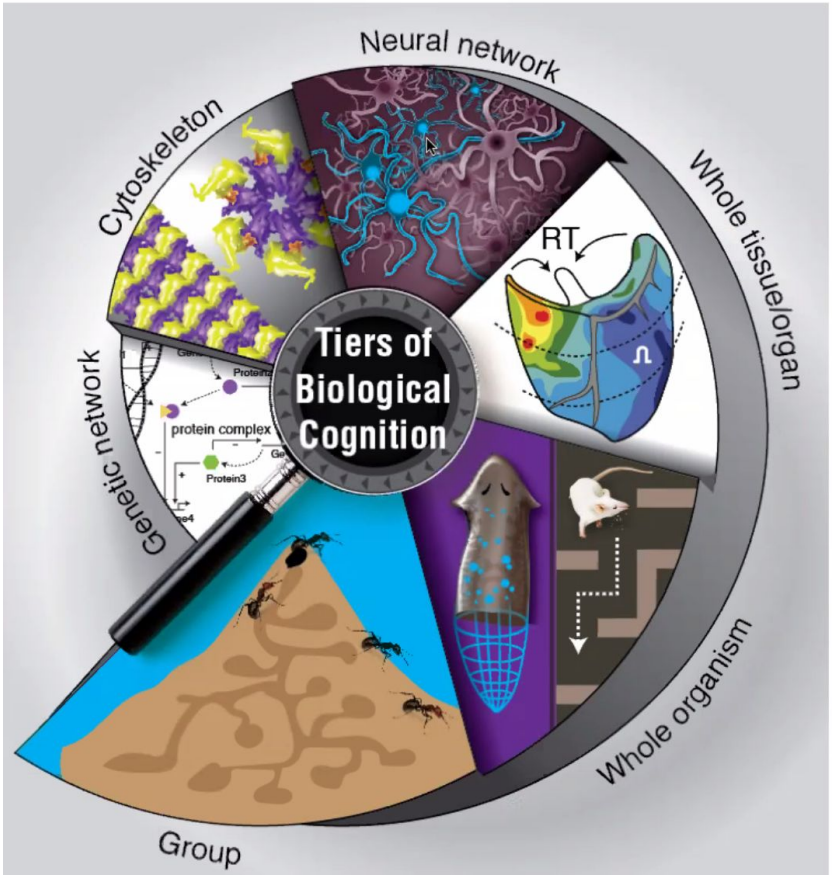
Article

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

Patrick Erickson



Nested Intelligence, not Merely Structure

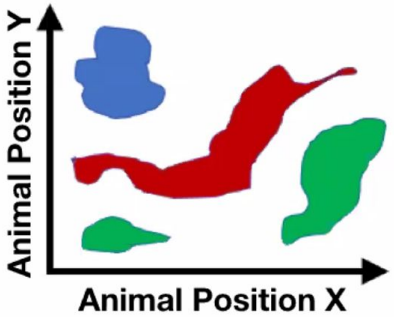


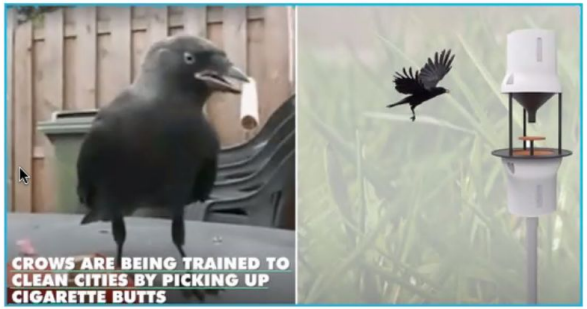
Multi-scale Competency Architecture

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

Collective Intelligence of Cell Groups: Competency and Embodiment in Diverse Spaces

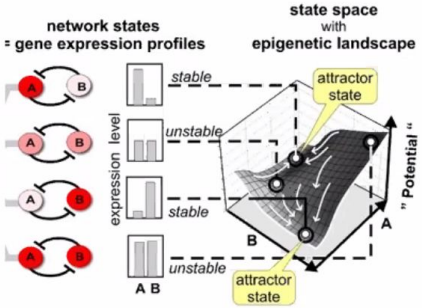
3D Space (behavior)





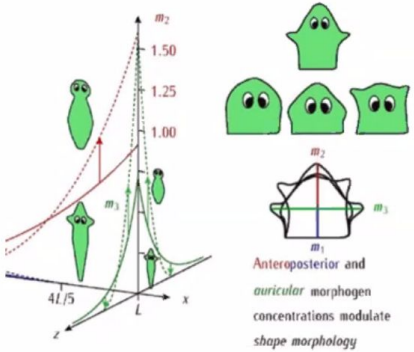
Transcriptional Space

Huang, S.; Ernberg, I.; Kauffman, S., Semin Cell Dev Biol 2009, 20, (7), 869-76.



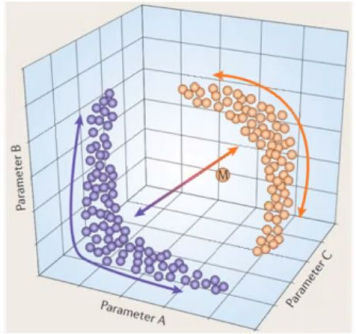
Morphospace

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



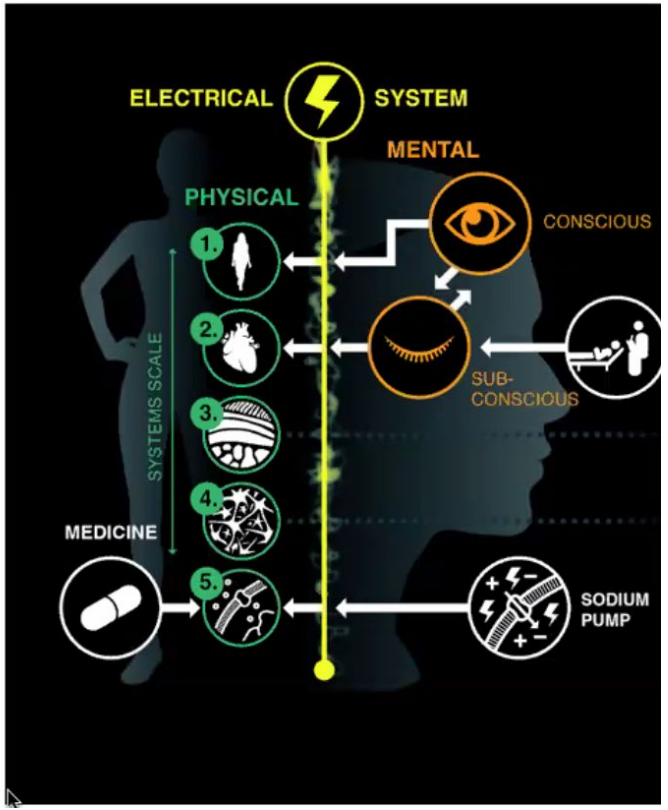
Physiological Space

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



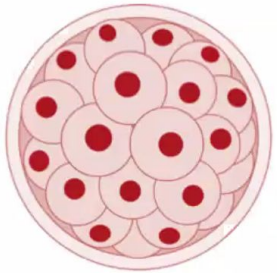
Outline:

- What are you?
- What does it mean for biomedicine
- What next: beyond the standard human

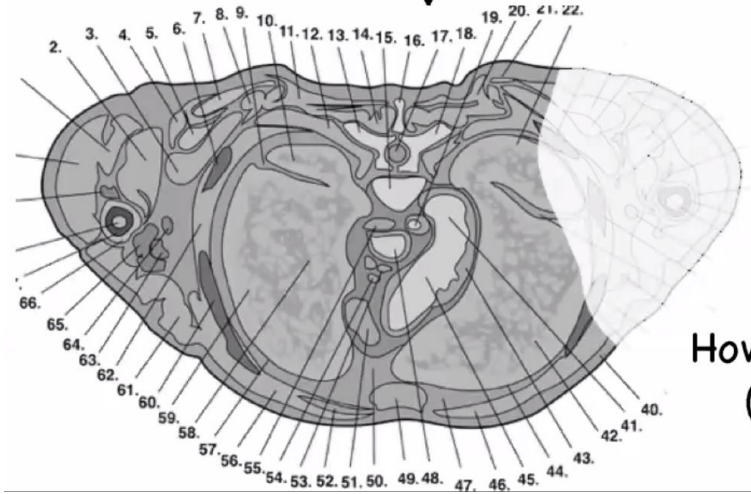


Where do Anatomies Come from?

stem cell
embryonic
blastomeres



self-assembly

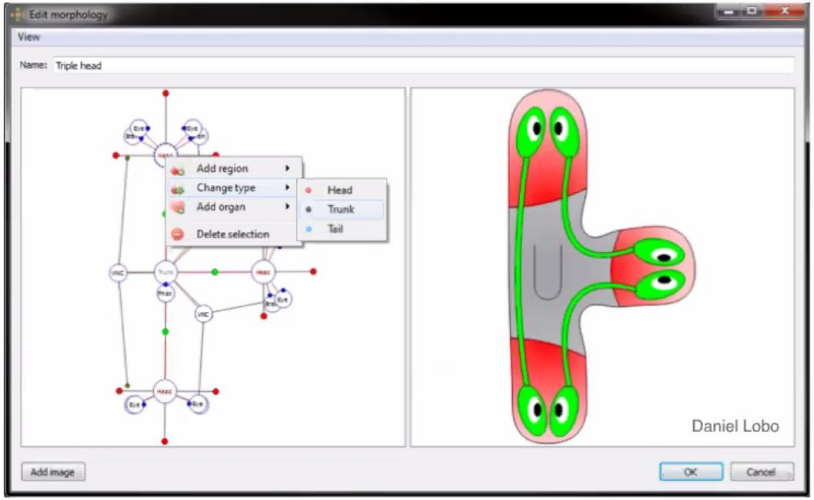


earthlymission.com

- 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?

Biomedical Endgame: Anatomical Compiler



Why we need it:

- Birth defects
- Traumatic injury
- Cancer
- Aging

Problems of information processing

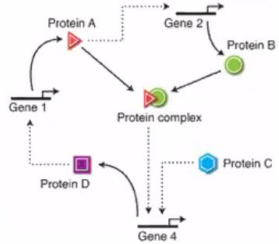
how to control emergence and scaling of cellular activity toward desirable complex, system-level outcomes?

Why we don't have it:

this should *NOT be a 3D printer* - it should be a **communications** device (translator)

The State of the Art: biological information

We are very good at manipulating molecules and cells;

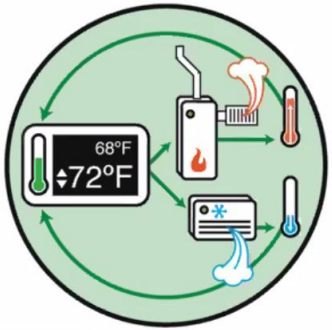


We are a long way from control of large-scale form and function

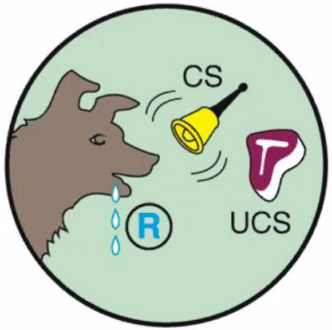
biomedicine has been largely at the hardware level of analysis and control, we have been assuming it's merely a complex machine. It's an agential material!

Axis of Persuadability: an Engineering Take on a Continuum of Agency

Hardware modification only

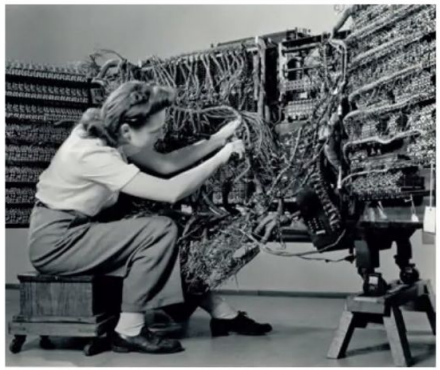


Modify the data encoding setpoint of goal-driven process



Training by rewards/ punishments

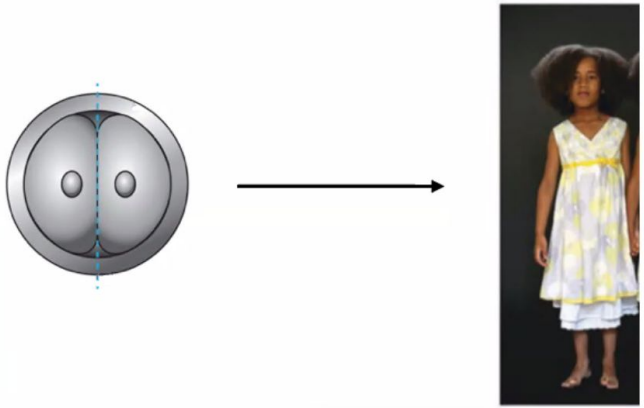
Communicate cogent reasons



Where do cell collectives fit?

Anatomical Goals = Regions of Morphospace

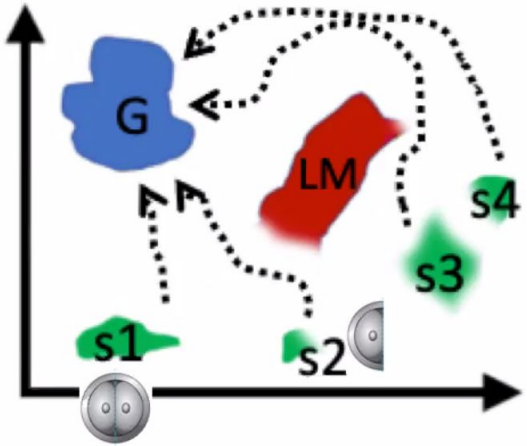
developmental self-assembly is very reliable:

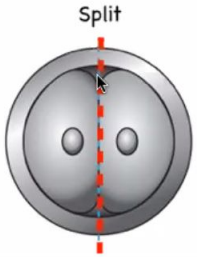


but emergent complexity is NOT why I call it intelligence
It's the problem-solving capacities (intelligent navigation of anatomical morphospace)

Same anatomy, from different starting states

- get to the same outcome
  - despite perturbations
  - **from diverse starting positions**
  - via different paths

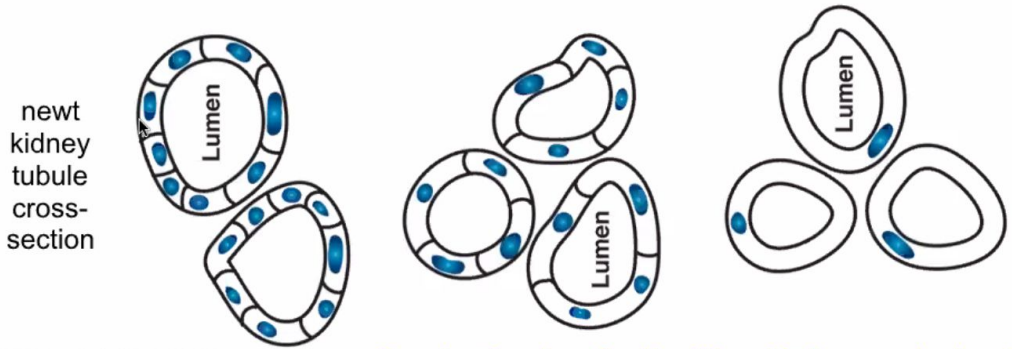




Splitting an embryo in half
makes 2 normal embryos

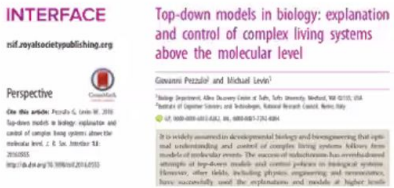
Problem-solving: creative use of parts

You Can't Rely on Evolutionary Priors



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

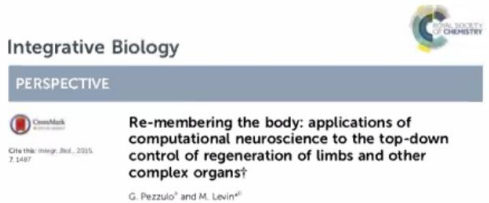

INTERFACE

rsif.royalsocietypublishing.org

Perspective

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

Giovanni Pezzulo and Michael Levin


Integrative Biology

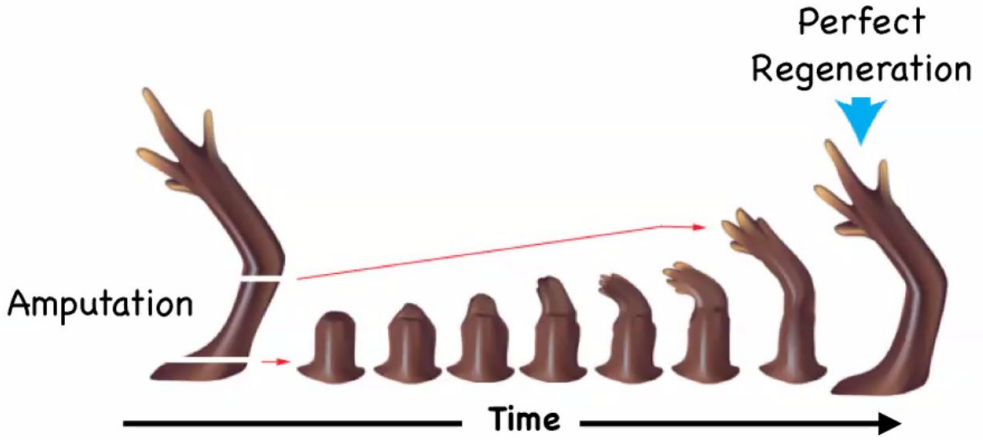
PERSPECTIVE

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

G. Pezzulo and M. Levin

Same anatomy, from different starting states

- get to the same outcome
  - despite perturbations
  - **from diverse starting positions**
  - via different paths

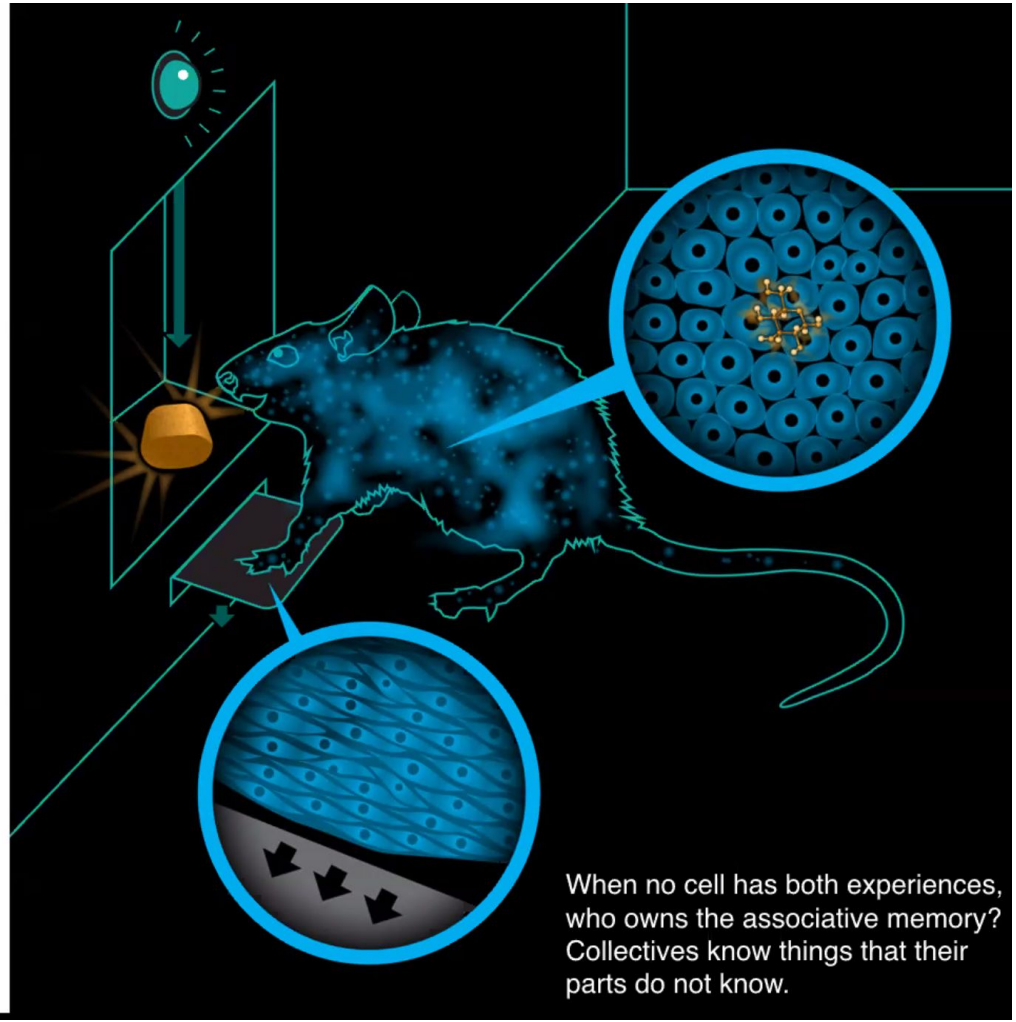


Anatomical homeostasis:

it stops when the correct large-scale setpoint (target morphology) has been reached

Cognitive Glue

(scaling problem)



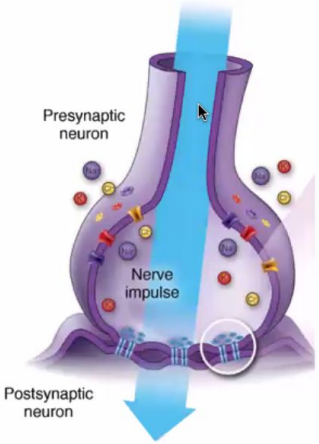
Hardware

gene products -> electric circuits

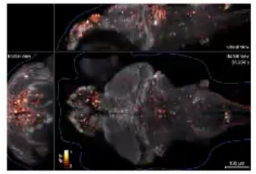
Software

electrical dynamics -> memory

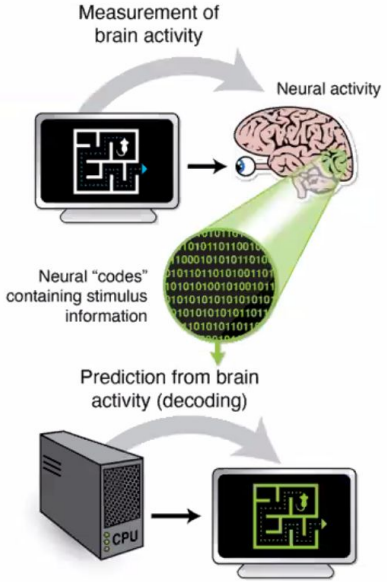
ion channels, electrical synapses



neural



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



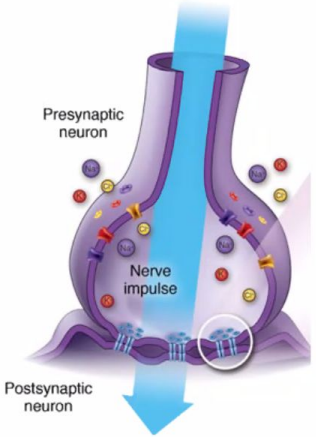
Hardware

gene products -> electric circuits

Software

electrical dynamics -> memory

ion channels, electrical synapses



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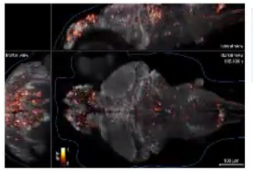
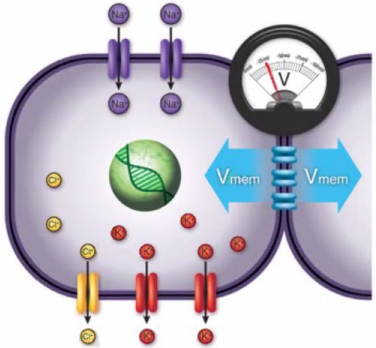
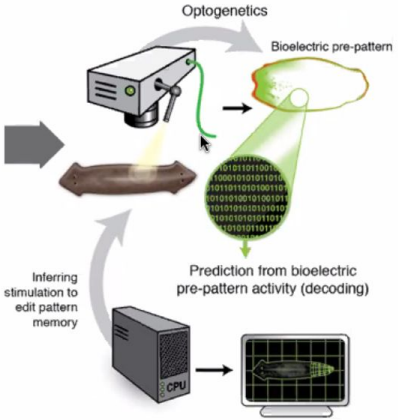


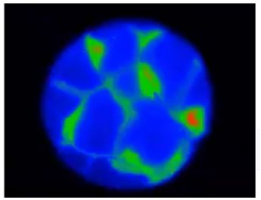
http://www.nature.com/nmeth/journal/v10/n5/full/nmeth.2434.html

developmental

ion channels, electrical synapses



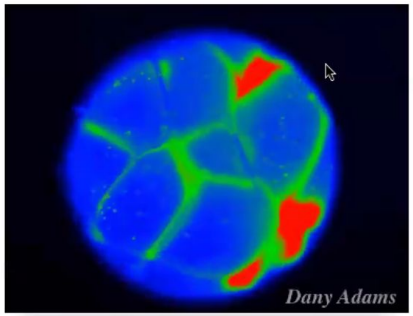




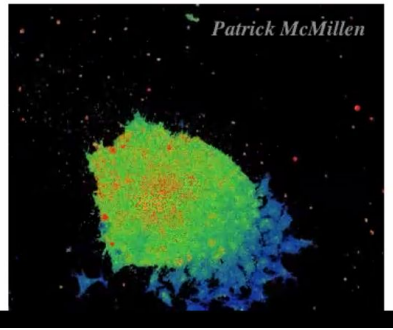
Dany Adams

How we detect and model bioelectric patterns:

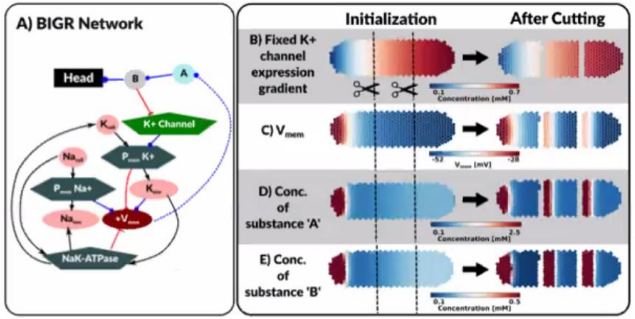
Characterization of endogenous voltage gradients - direct measurement and correlation with morphogenetic events

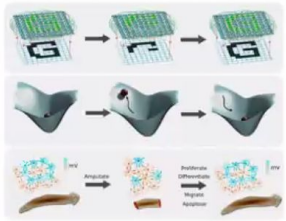


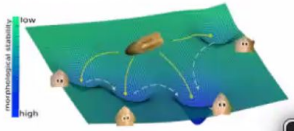
Voltage reporting fluorescent dye in time-lapse during *Xenopus development*

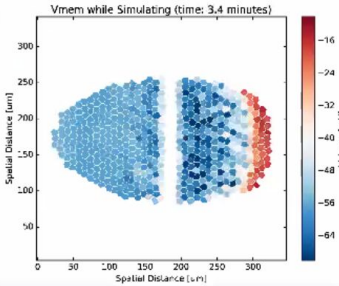


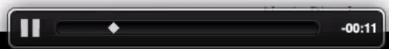
Quantitative computer simulation: synthesize biophysical and genetic data into predictive, quantitative, often non-linear models







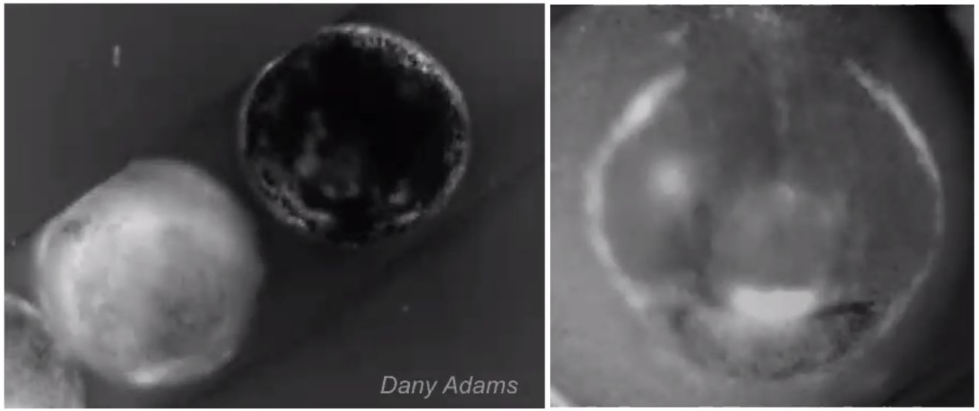




Endogenous Bioelectric Prepatterns = anatomical setpoint memories

reading the mind of the body

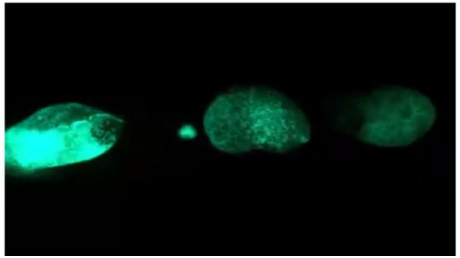
craniofacial development "electric face" prepattern required for normal face



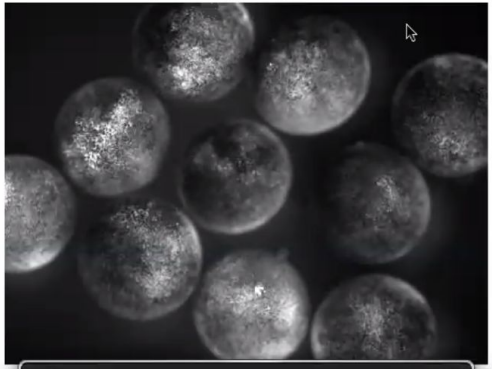
hyperpolarized — depolarized

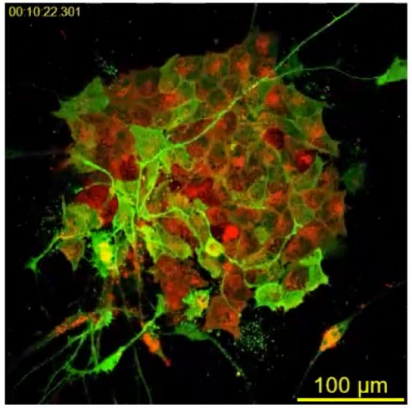
monitoring defects, multiscale cognitive glue

Patrick McMillen

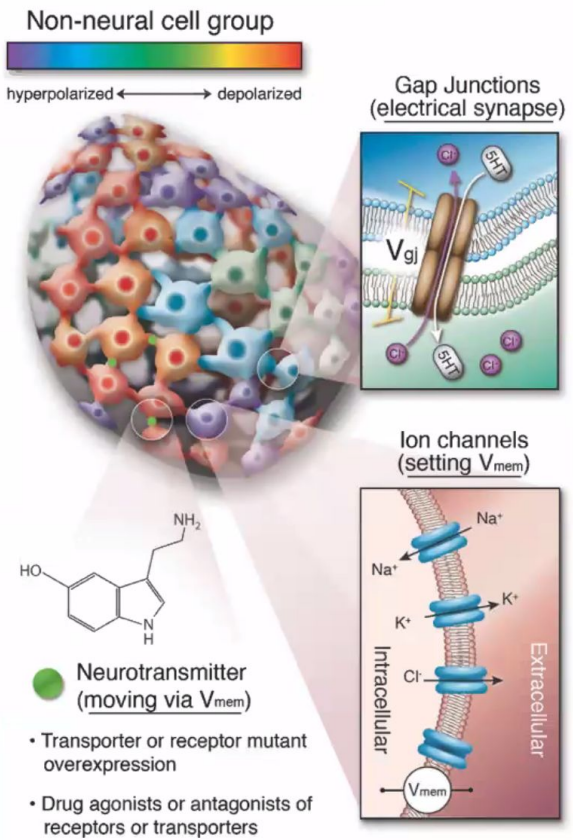


Angela Tung, Megan Sperry





Hacking the Bioelectric Interface to Communicate with Cellular Collective



Tools we developed
(no applied fields!)

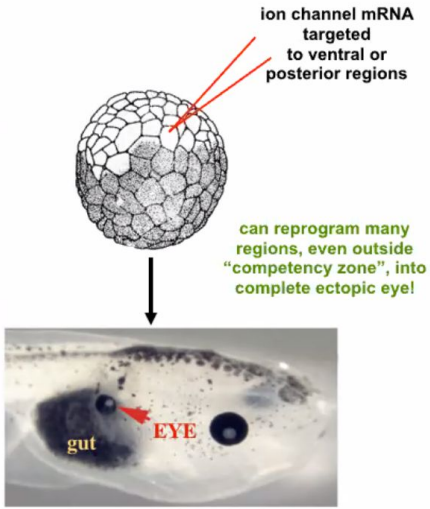
- Dominant negative Connexin protein
- GJC drug blocker
- Cx mutant with altered gating or permeability

Synaptic plasticity

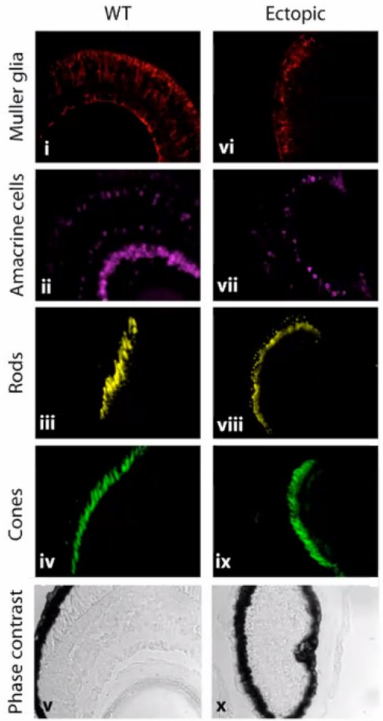
- Dominant ion channel over-expression (depolarizing or hyperpolarizing, light-gated, drug-gated)
- Drug blocker of native channel
- Drug opener of native channel

Intrinsic plasticity

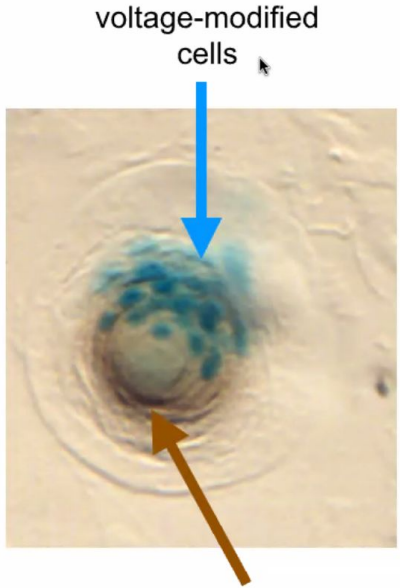
Cracking the Bioelectric Code: communicate goals, not force micro states; exploit competencies



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



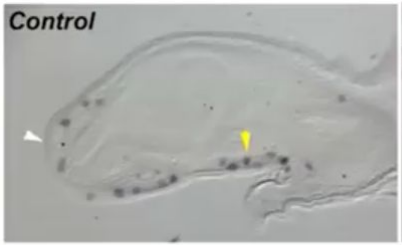
Sherry Aw, Vaibhav Pai

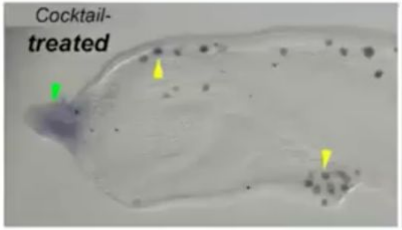


Brief bioelectric signals trigger long-term, self-limiting behavioral cascades (simple stimulus, complex response)

Hind-leg amputation
+
designed ionophore
cocktail regimen

The regenerated leg has both sensation and mobility:



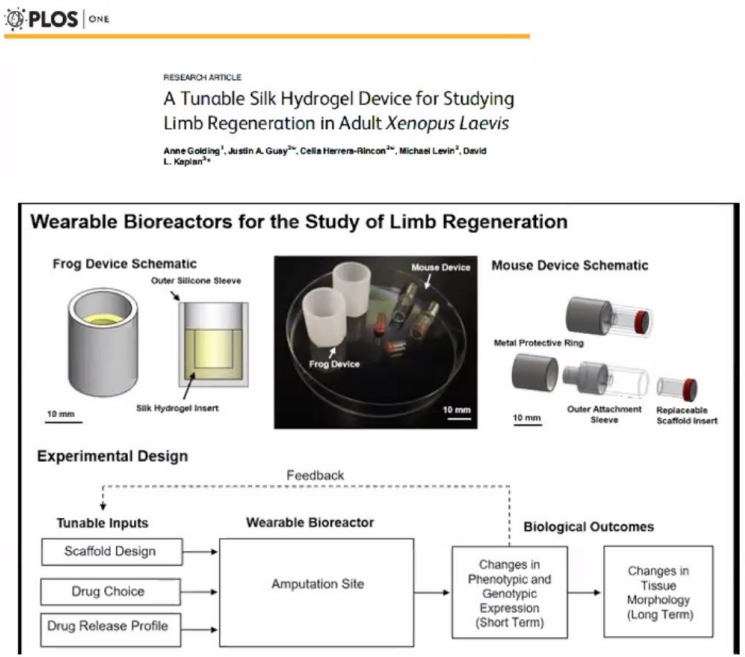


MSX1 marker - blastema induced

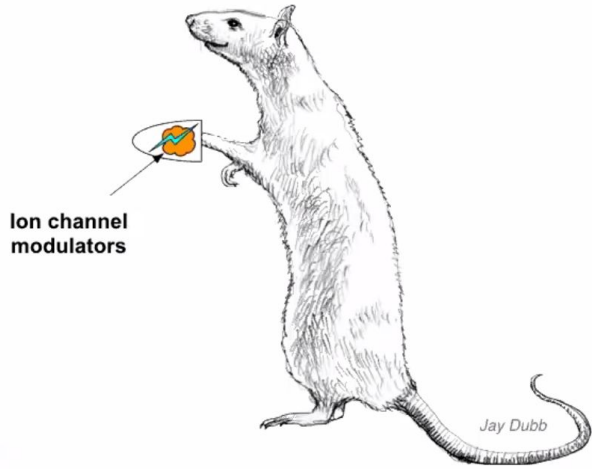
Outgrowth with distal patterning induced (and still growing)

Practical Applications for Regenerative Medicine

- Wearable bioreactors to deliver bioelectric prompt in vivo: a path to mammalian limb regeneration:

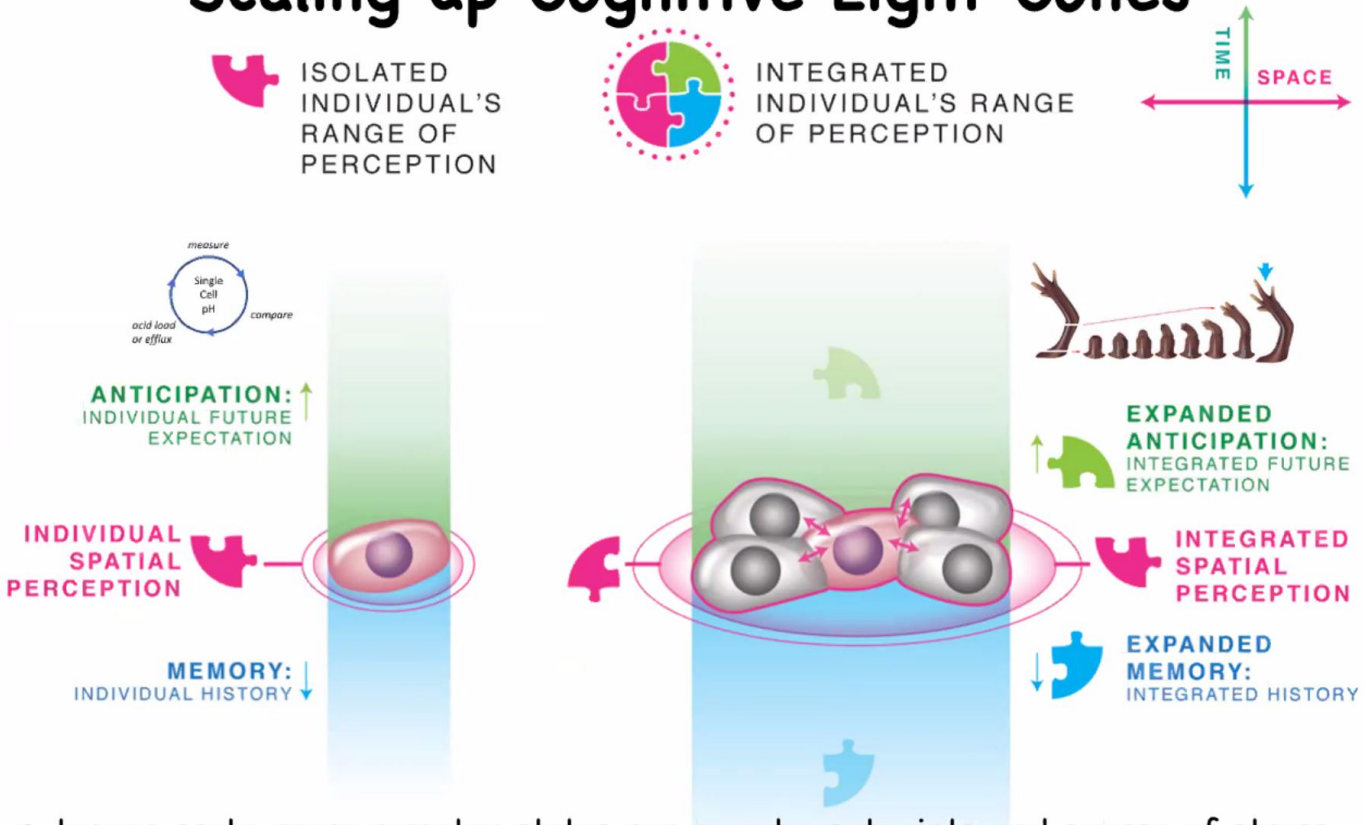


David Kaplan's lab, Tufts BME



Disclosure:
Morphoceuticals Inc.

Scaling up Cognitive Light Cones



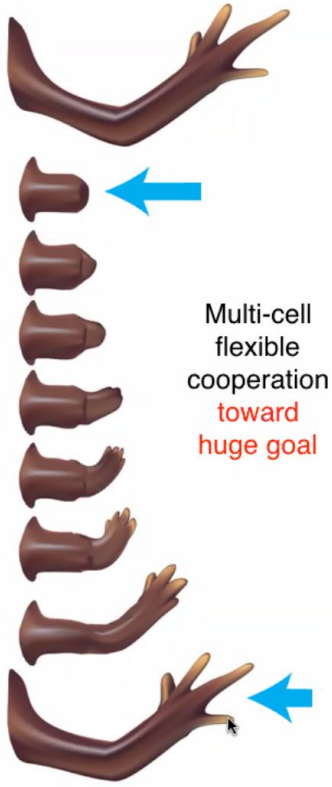
- larger-scale, more complex states can now be setpoints and source of stress
- increase cognitive light cone & **project it into other problem spaces (create new problem spaces! intelligence = search for problems, not just solutions)**

Scaling Goals, Changing Problem Space

Single cell goals

video by Charles Krebs

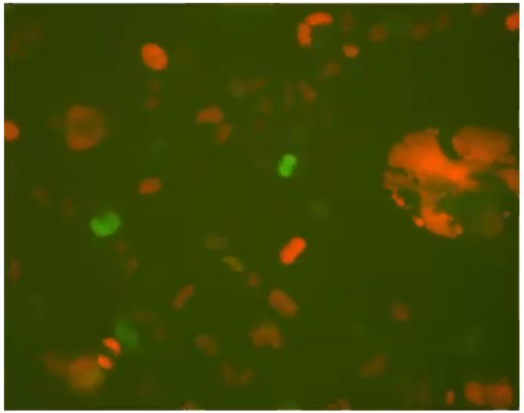
goal size scales UP



Multi-cell flexible cooperation toward huge goal

goal size scales DOWN

Cancer = defection, reversion to local (unicellular-scale) goals

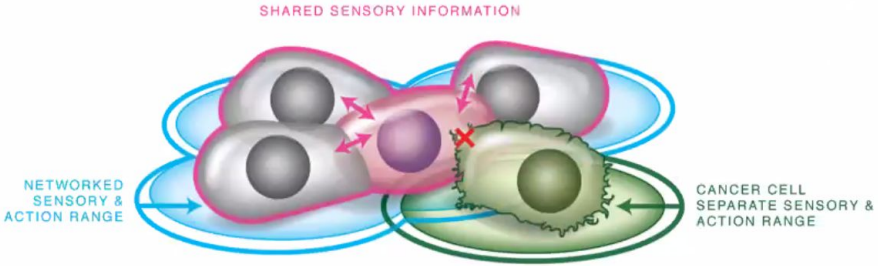


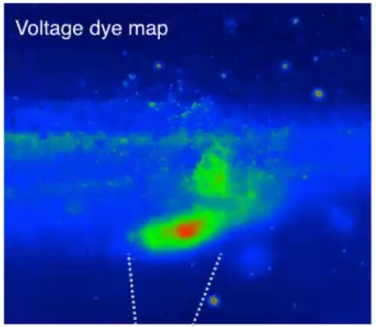
video by Juanita Mathews

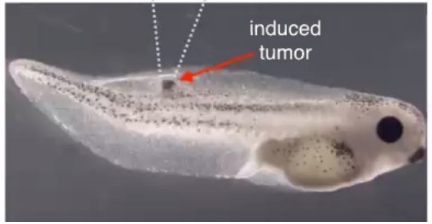
Cancer cells are *not* more selfish
They just have *smaller Selves*

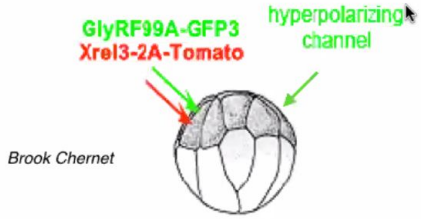
Flexible Boundary Between Self and World:
shifting scale of cognitive agent -> biomedical roadmap

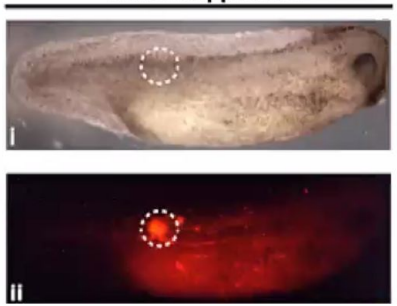
Cells Coupled by Gap Junctions, Disconnected Cancerous Cells









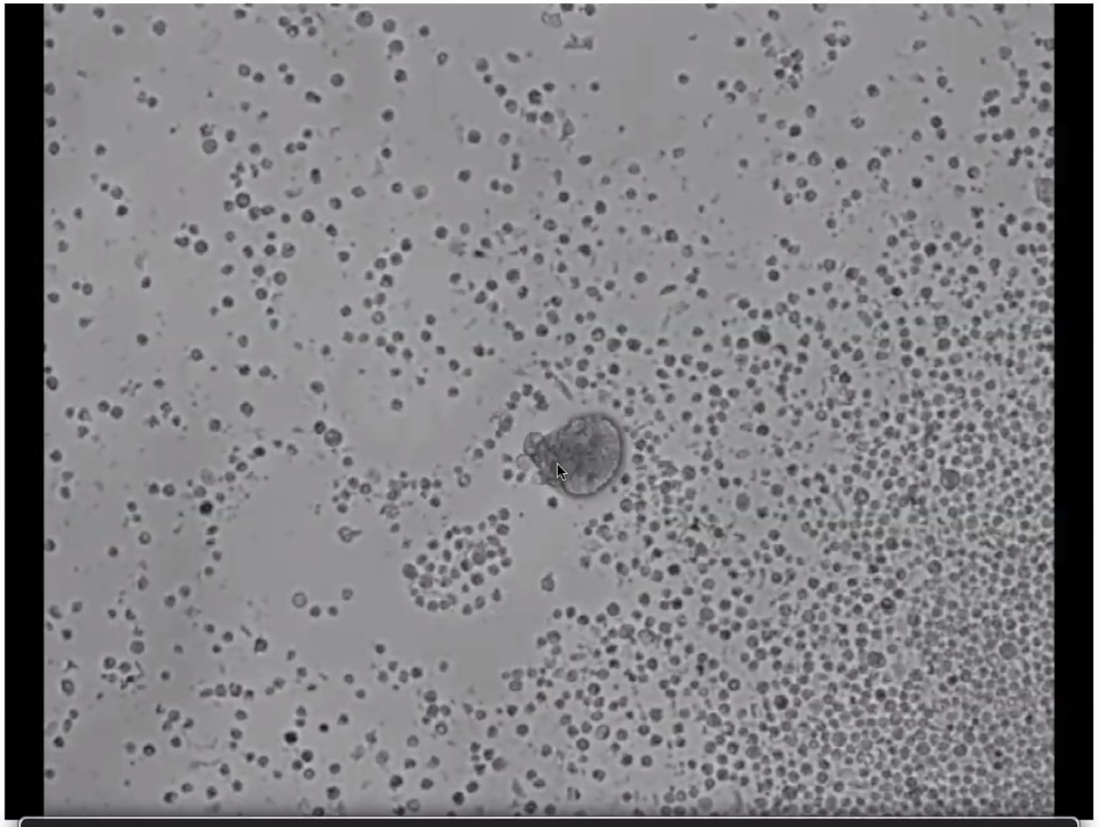


Cancer = dissociative identity disorder of the morphogenetic intelligence

Reintegration therapy - plasticity

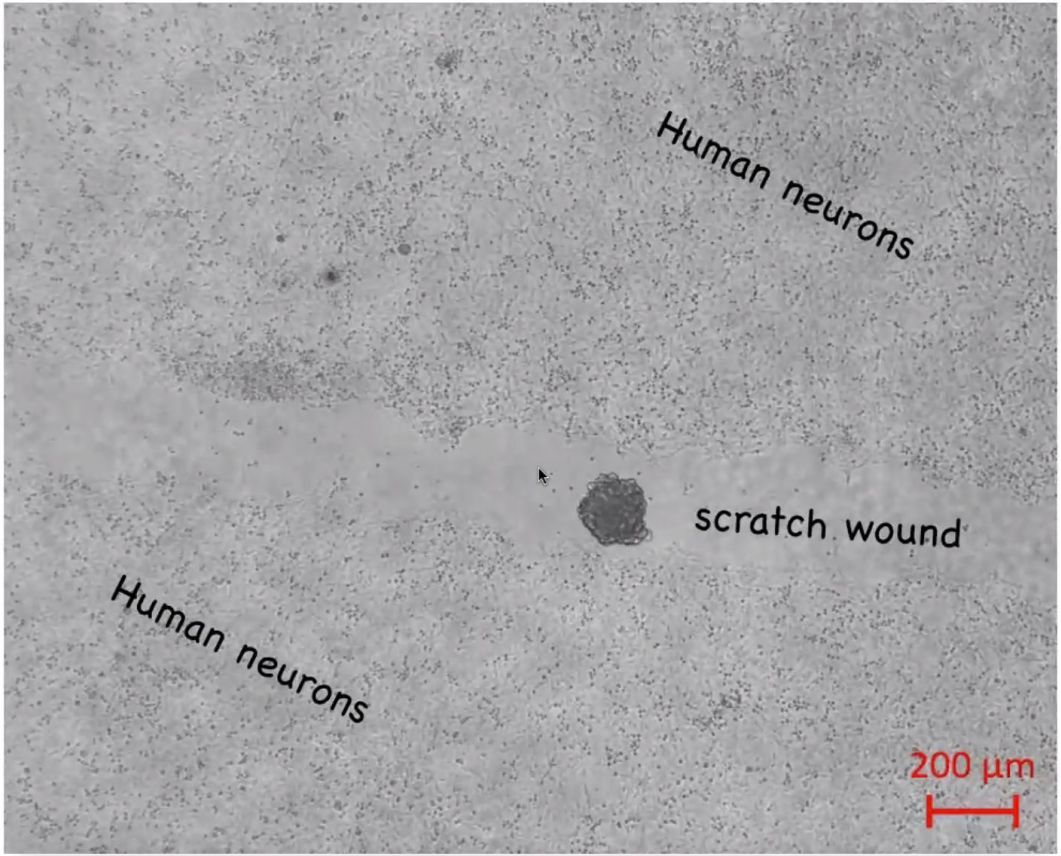
Where do Selves' goals come from?

Can You Guess What This Is?
can you guess its goals and competencies?



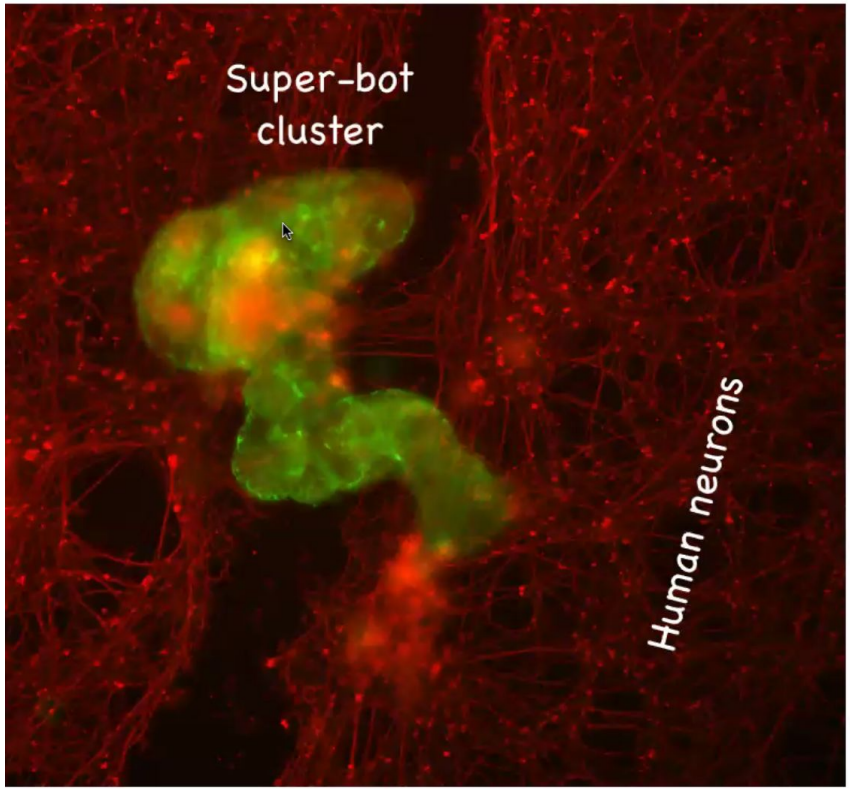
Gizem Gumuskaya

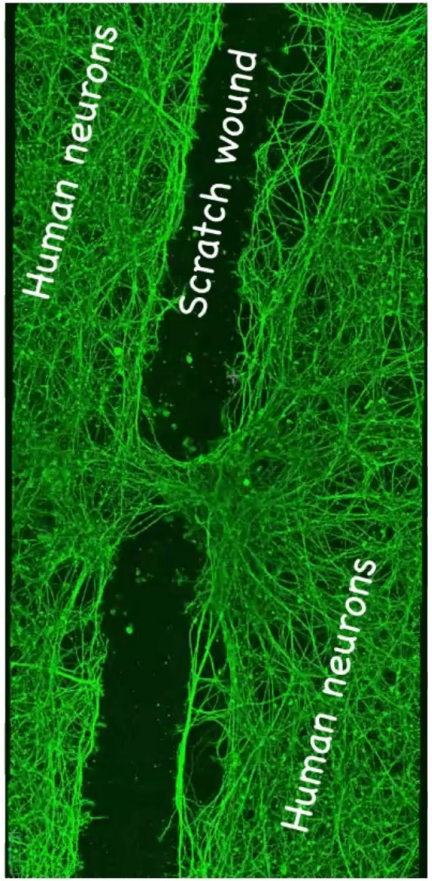
Anthrobots Traverse Wounds in vitro:



Gizem Gumuskaya

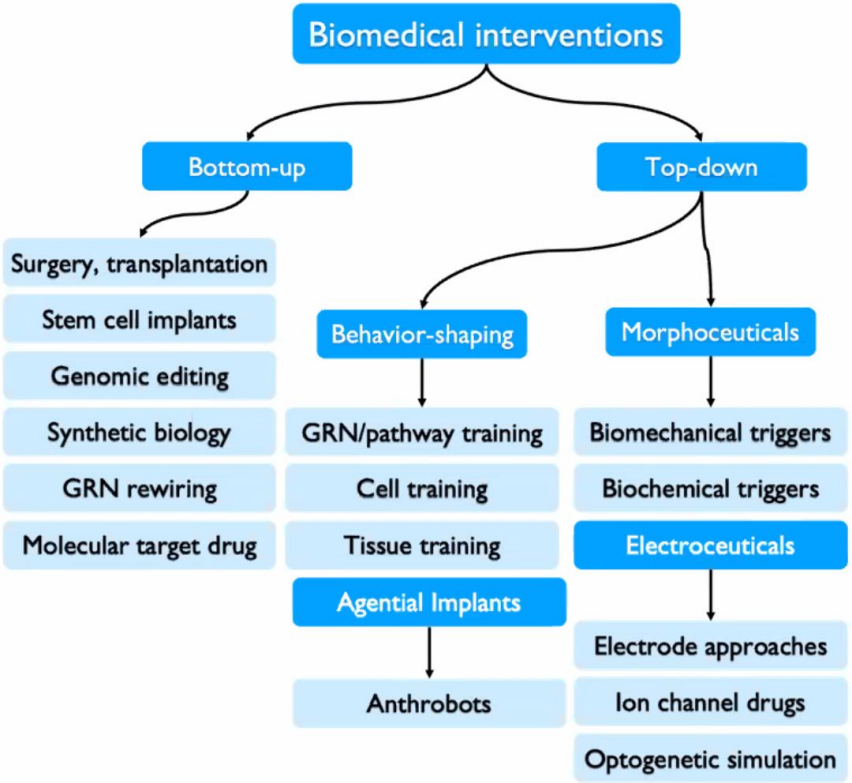
Anthrobots Exert Neural Repair:
Toward Agential Interventions



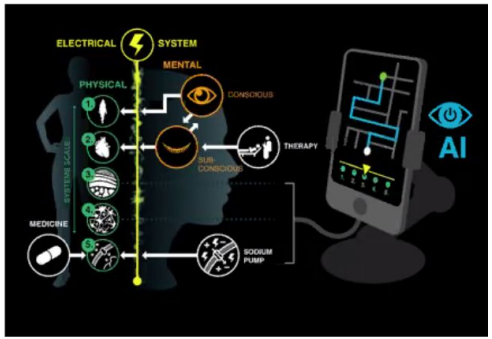


Gizem Gumuskaya

Future Medicine: communication, training (molecular pathways, cells, tissue)

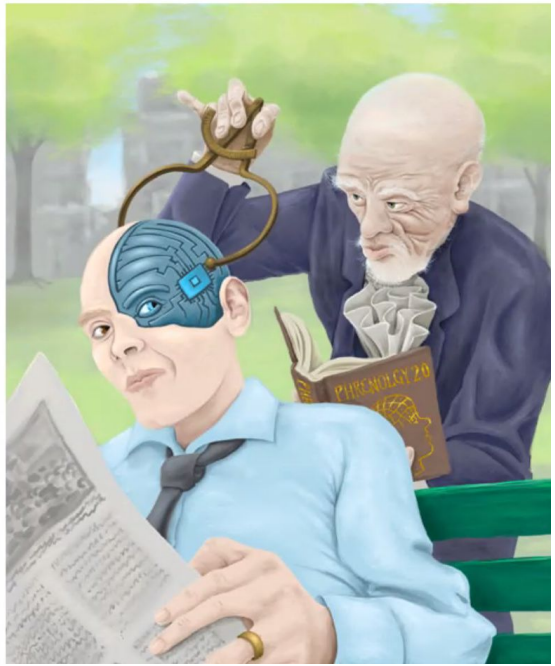


bioelectricity is not yet another piece of biophysics to be micromanaged;
it is a communication interface to the root of the problem - boundary of active agents between self and world

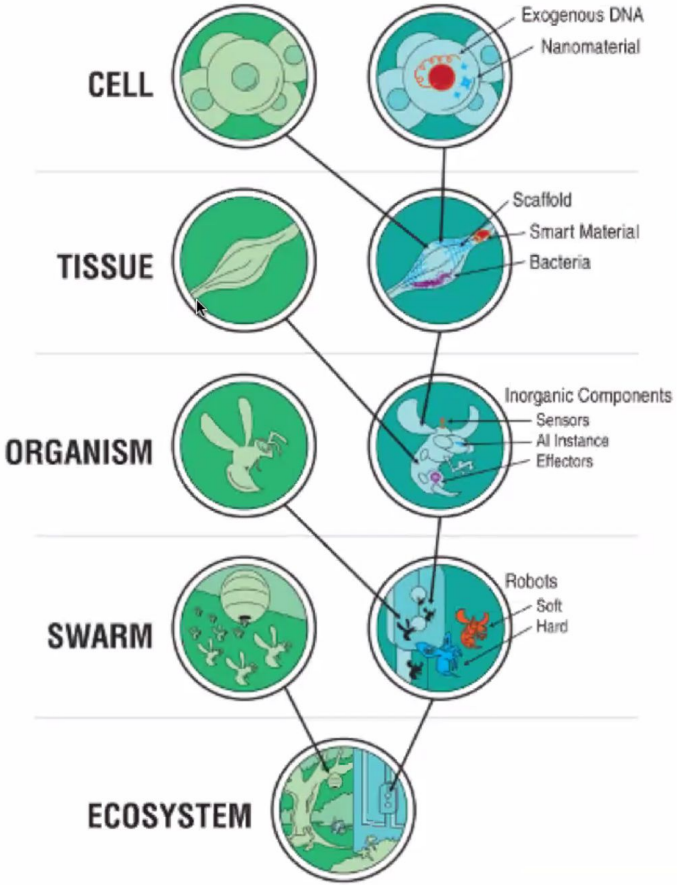


Outline:

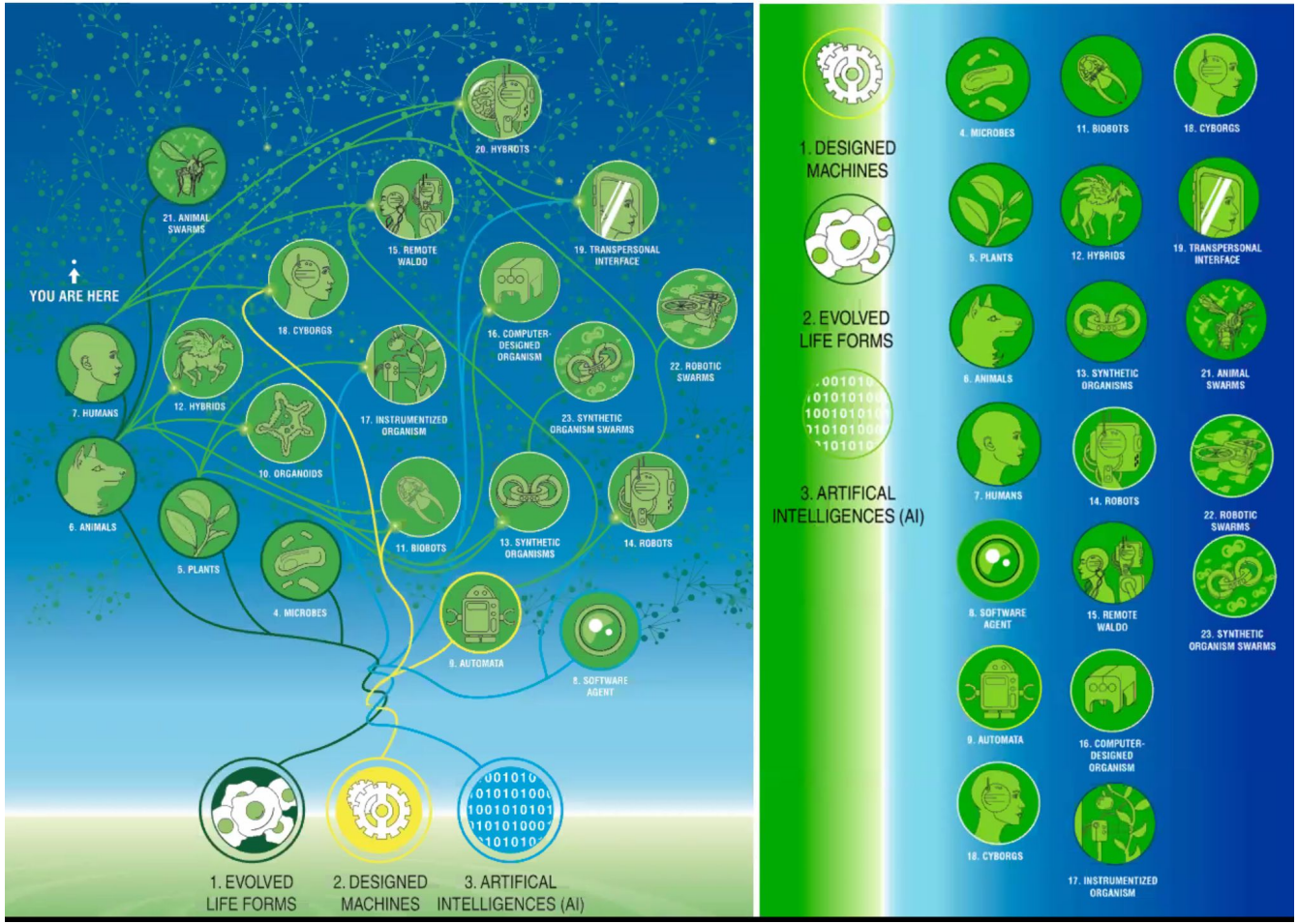
- What are you?
- What does it mean for biomedicine
- What next: beyond the standard human



Life is Highly Interoperable



"Endless Forms Most Beautiful"<—>ethical synthbiosis



Garden of Eden v2.0

Summary:

- Intelligence is everywhere; learning to rise above our limitations and recognize it in unfamiliar guises is essential for biomedical progress and ethical flourishing of sentient beings

- You are a self-constructing story continuously told by a collective intelligence of organs, cells, and molecules. Transformative regenerative medicine awaits tools to communicate with, and collaborate with, this intelligence

- The future:
  - ~~Anthropomorphism ; binary categories of man, machine, life~~
  - Continuum of agency
  - AI tools as universal translators to Diverse Intelligences

More Details Here:


frontiers in Ecology and Evolution

HYPOTHESIS AND THEORY

Living Things Are Not (20th Century) Machines: Updating Mechanism Metaphors in Light of the Modern Science of Machine Behavior

Joshua Bongard and Michael Levin


Cognition all the way down

Biology's next great horizon is to understand cells, tissues and organisms as agents with agendas (even if unthinking ones)

Michael Levin & Daniel C Dennett

https://aeon.co/essays/how-to-understand-cells-tissues-and-organisms-as-agents-with-agendas


NOEMA

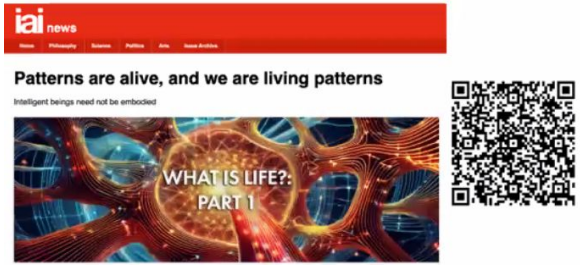
The Space Of Possible Minds

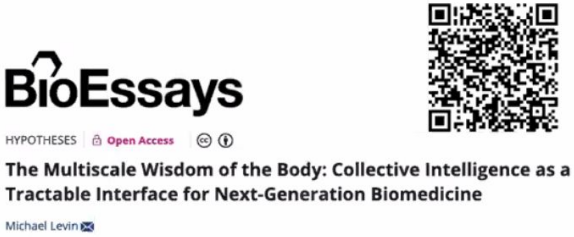
Today's debates about artificial intelligence fail to grapple with deeper questions about who we are and what kind of future we want to build.


NOEMA

Why We Fear Diverse Intelligence Like AI

Our fear of AI's potential is emblematic of humanity's larger difficulty recognizing intelligence in unfamiliar guises.




BioEssays

HYPOTHESES | Open Access

The Multiscale Wisdom of the Body: Collective Intelligence as a Tractable Interface for Next-Generation Biomedicine

Michael Levin

Thank you to:

Post-docs and staff scientists in the Levin lab:
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Brook Chernet, Maria Lobikin - bioelectrics of cancer

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Joan Lemire - molecular biology

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Alexis Pietak - computational modeling of bioelectrics
Josh Bongard - AI-designed organism
David Kaplan - V_{mem} and human MSC differentiation, regenerative sleeves
Simon Garnier - computational analysis of Anthrobot form and function
Chris Fields - physics of sentience and sentience of physics
Richard Watson - computational models of cognitive scaling and evolutionary learning
Giovanni Pezzulo - cognitive science applied to morphogenesis
Don Ingber - mammalian bioengineering

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

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Disclosures: Morphoceuticals, Fauna Systems, Astonishing Labs

Q&A

https://humanatlas.io/events/2024-24h

Questions

How do we define a Multiscale Human?

How do we map a Multiscale Human?

How do we model a Multiscale Human?

How can LLMs or RAGs be used to advance science and clinical practice?

Thank you