Introduction to Bioengineering
BIOE/ENGR.80
Stanford University

Spring 2020 Class Slides

Day 18
15 May 2020

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Week 6 look ahead

CONCEPT
SKILL

Diffusion of molecules (space, time, abundances)

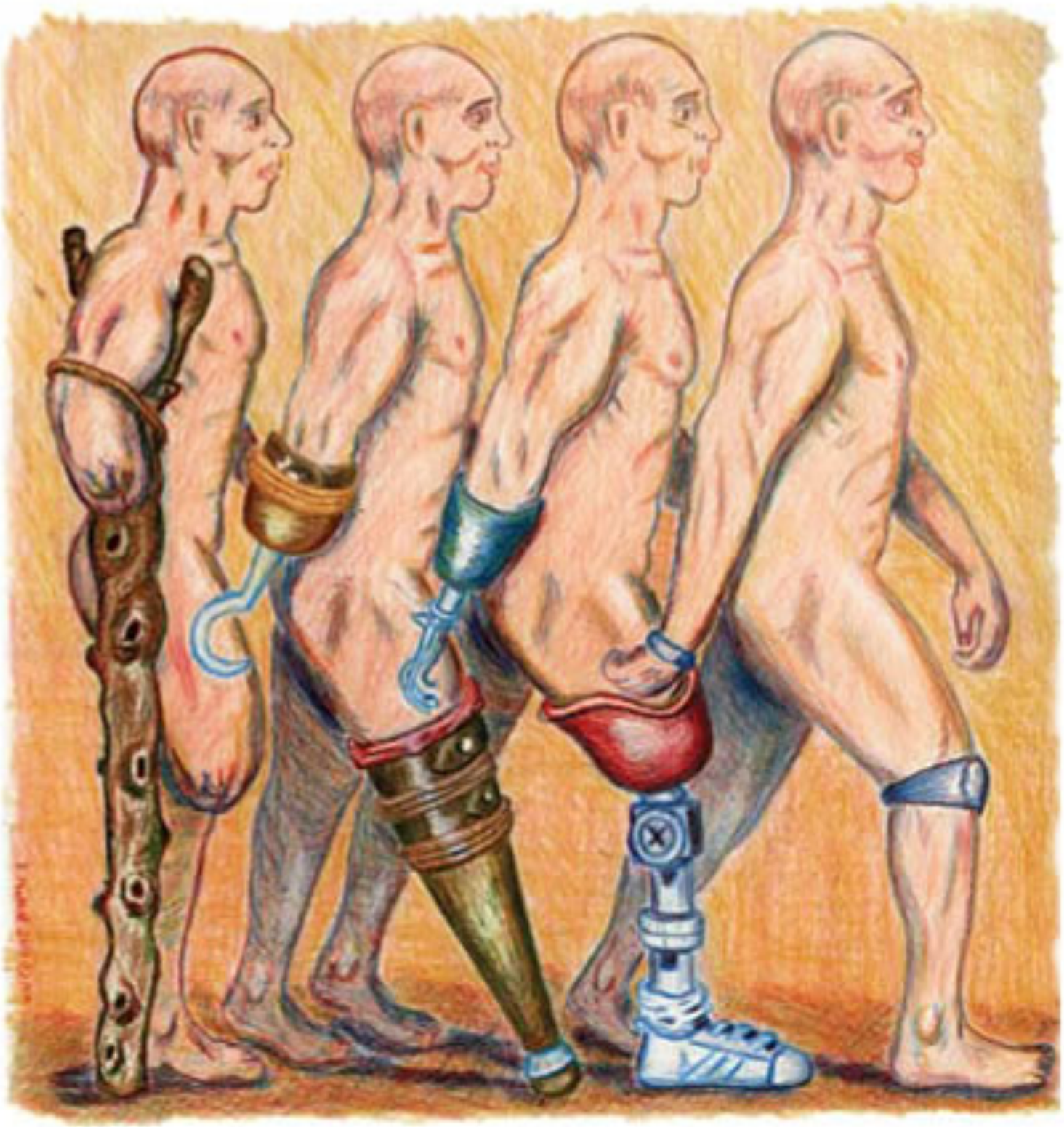
Programming patterns in autonomous systems

Programming patterns in living systems

WE ARE HERE

[Team Project]

- Brainstorms (three themes)
- Team Rules



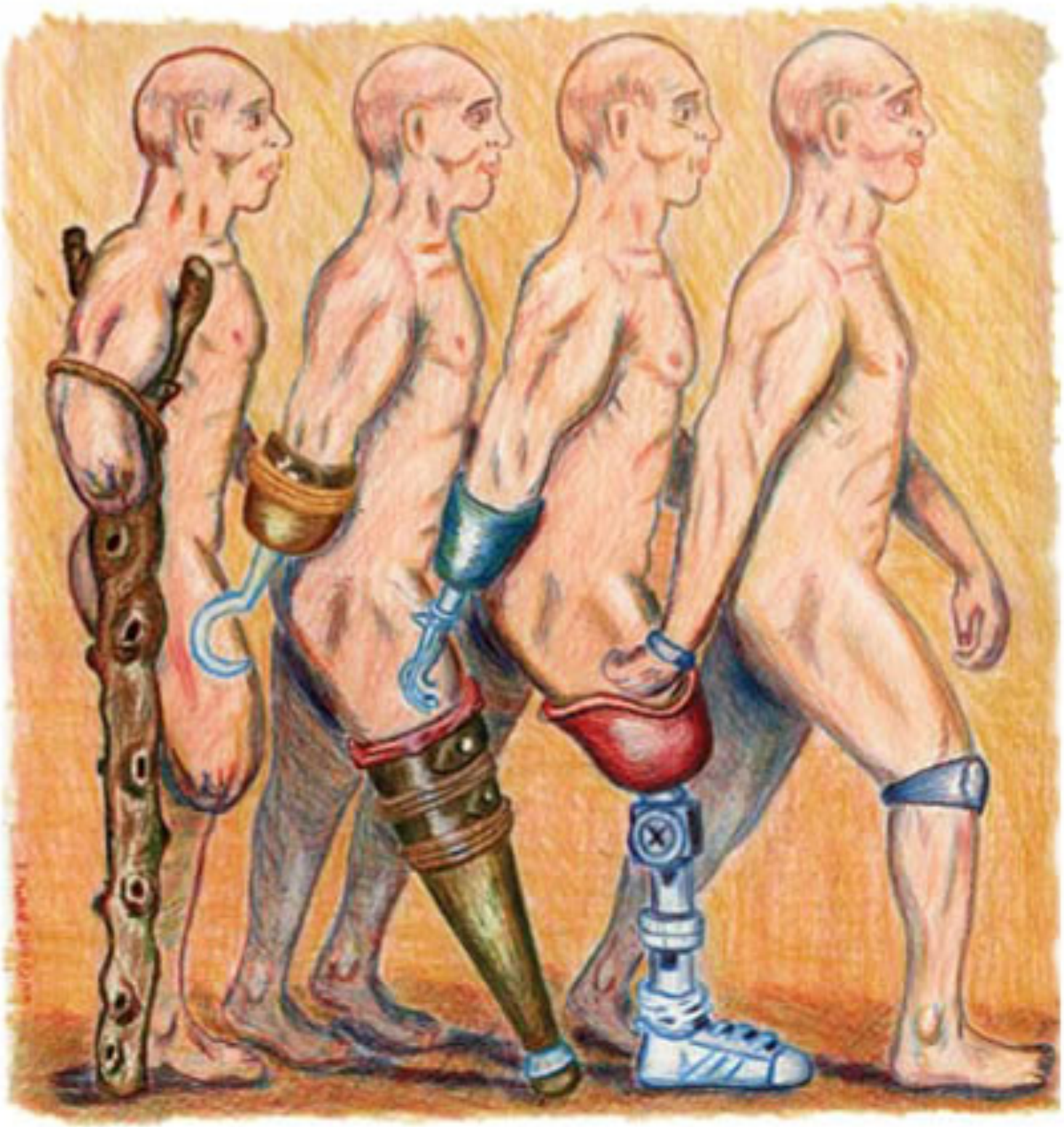
https://www.amputee-coalition.org/resources/a-brief-history-of-prosthetics/

Doing the "impossible"

How to decide what impossible things are actually possible?

How to organize people and resources to make the impossible true? I.e., how to plan and deliver?

Lessons learned?
How do you get started?
Ups and downs?
What happens after success?
Other?

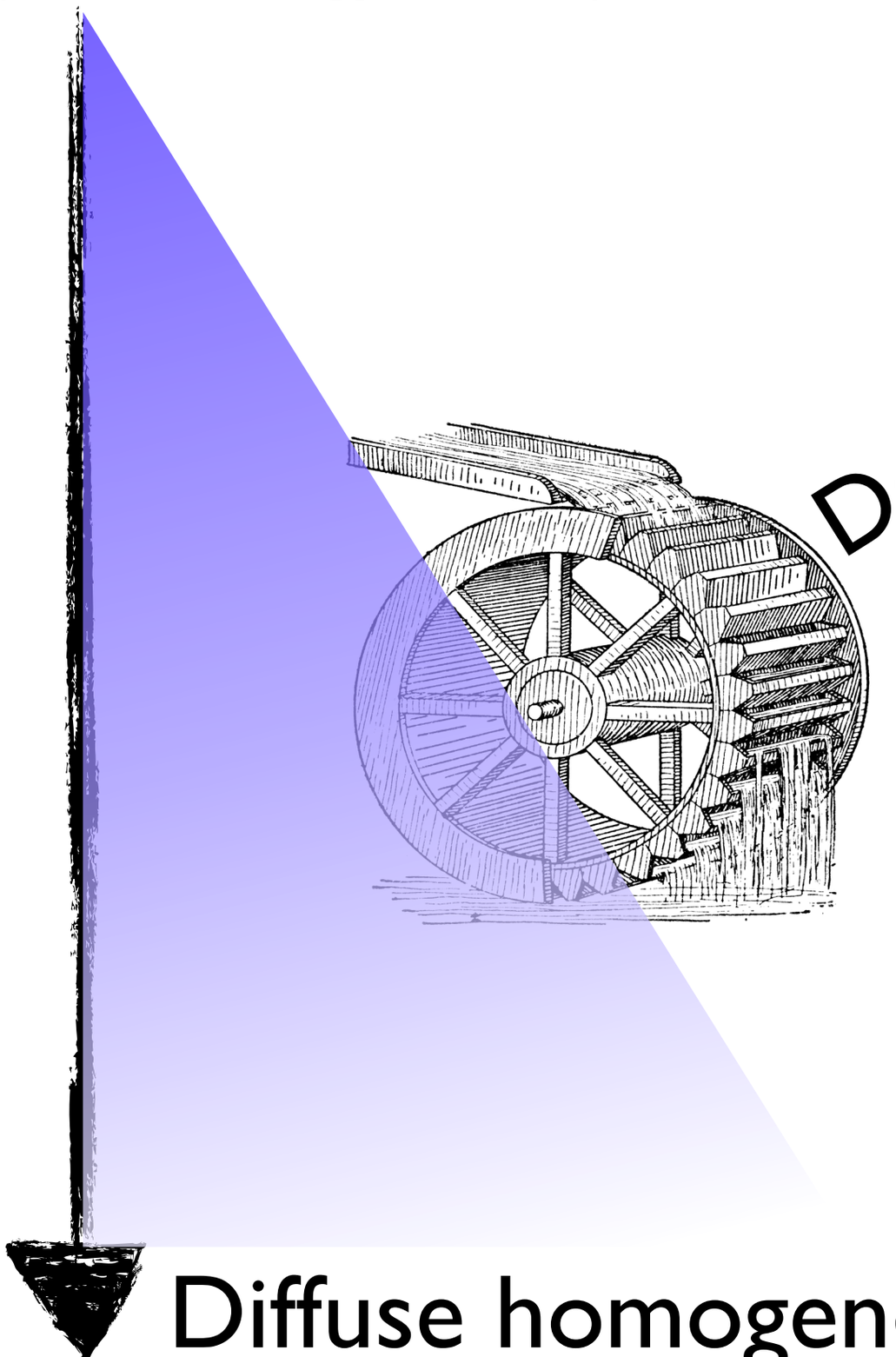


https://www.amputee-coalition.org/resources/a-brief-history-of-prosthetics/

http://www.hhmi.org/biointeractive/newt-limb-regeneration

Concentrated source

(stuff, energy, other)



Do something!

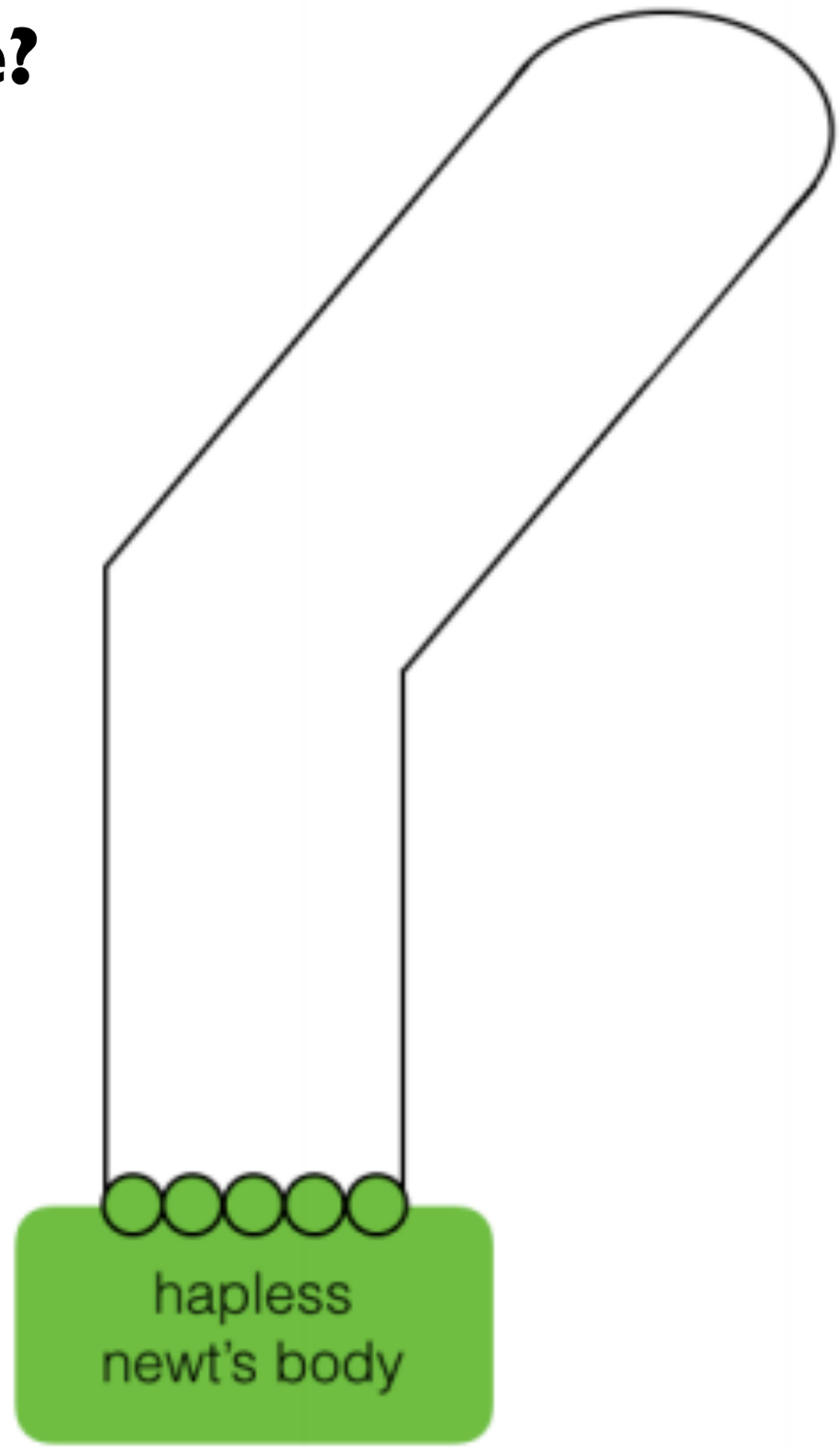
For cells, doing something can mean…

1. Grow & divide
2. Move
3. Communicate
4. Change state
5. Self destruct
6. Other

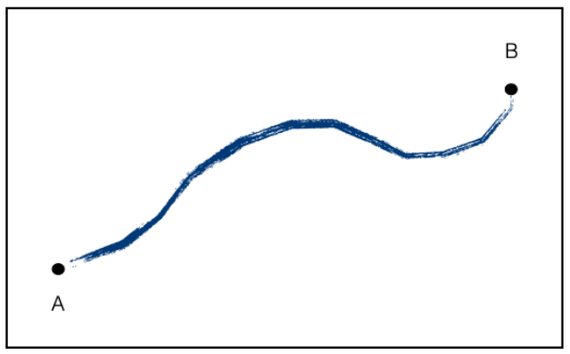
Diffuse homogeneity

(heat death, etc)

What's the simplest way you could grow a limb-like shape?

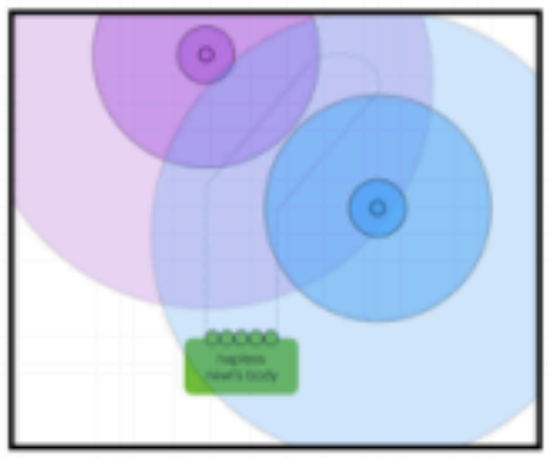


Challenge 1 — 'hand of god'

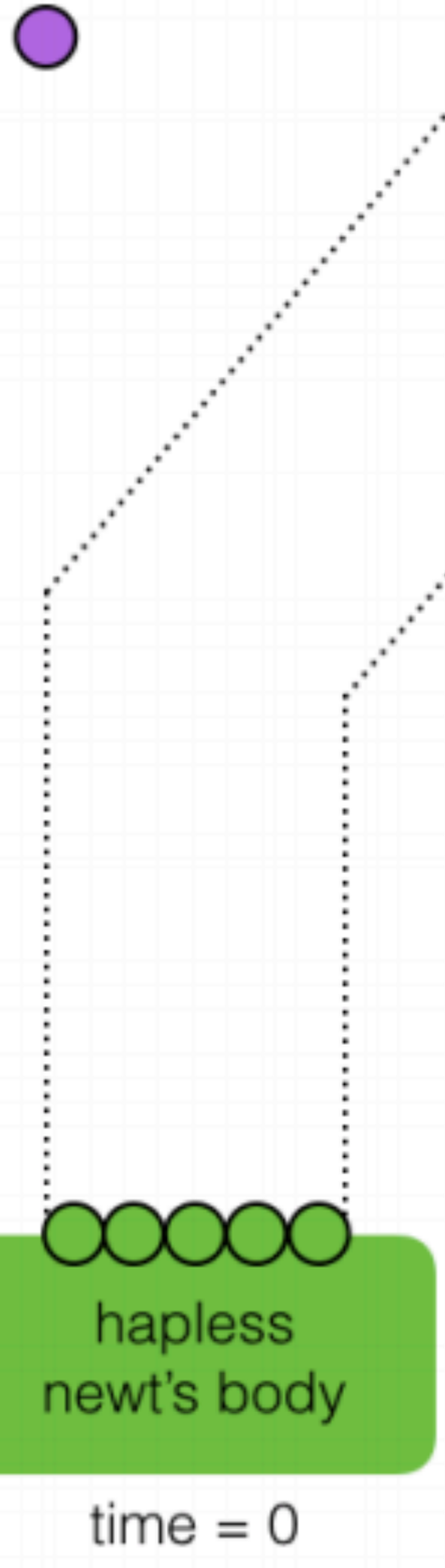


Draw a physical pattern on the slide that gets droplets to move from point A to point B (i.e., you are explicitly directing the behavior from outside the system)

What if there was no guiding hand, but there were external points of reference?

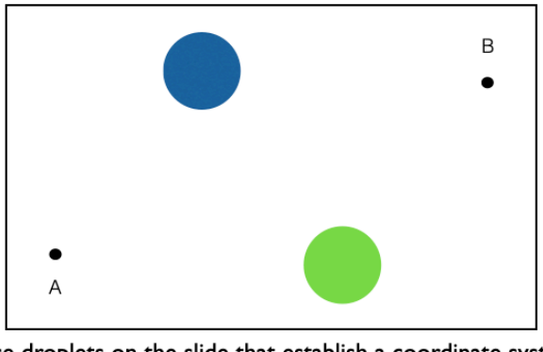


time > 0



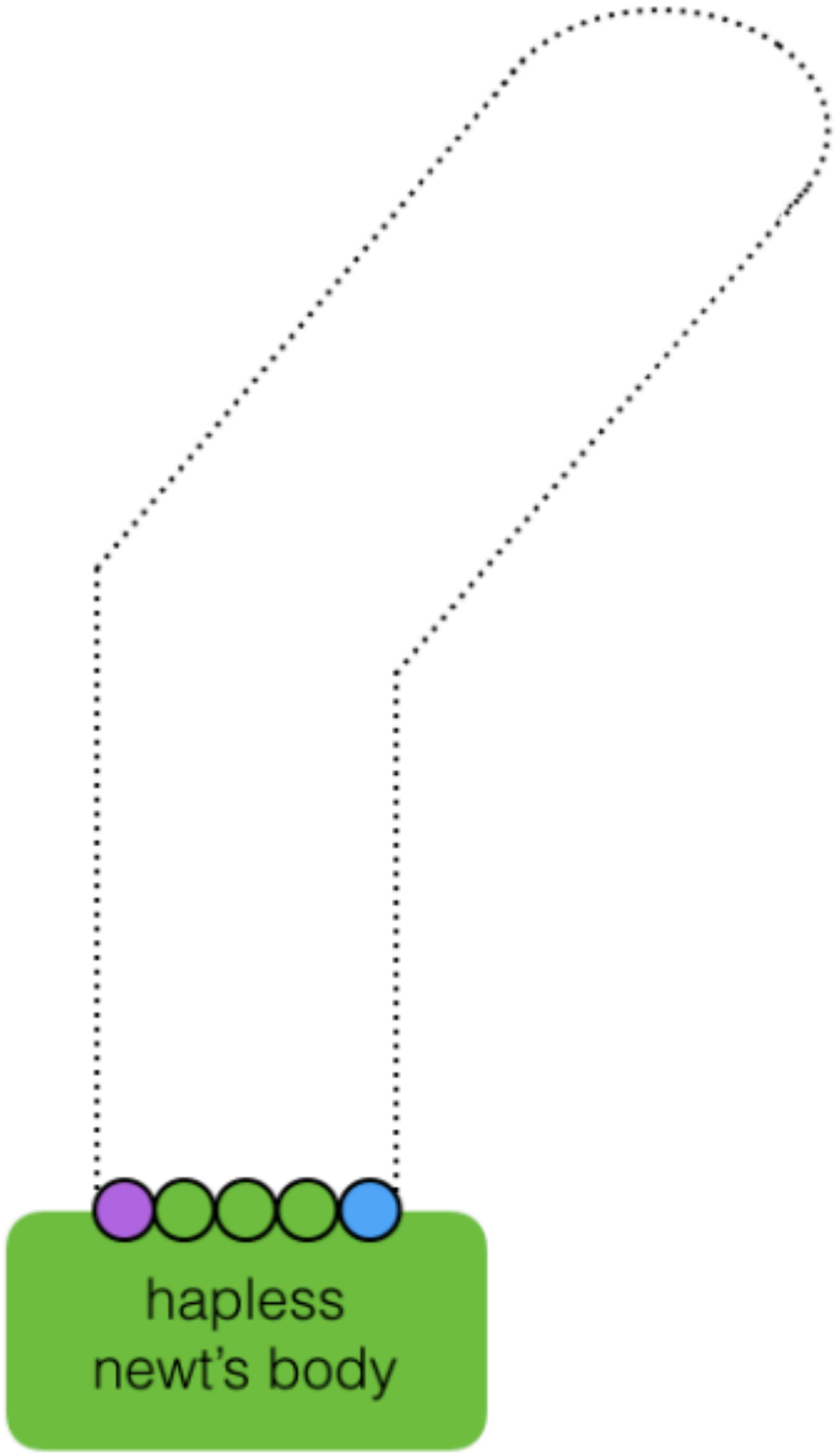
time = 0

Challenge 2 — ‘external coordinates’

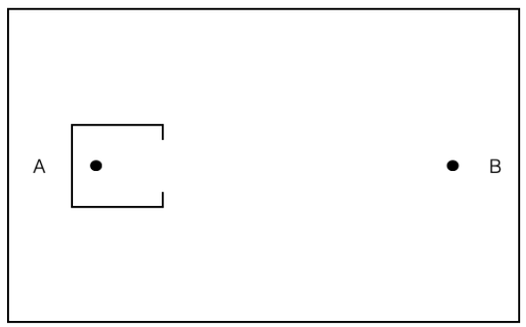


Place droplets on the slide that establish a coordinate system, causing another droplet to move from point A to point B (i.e., you make a coordinate system but droplets otherwise on their own).

What if there were no external points of reference?

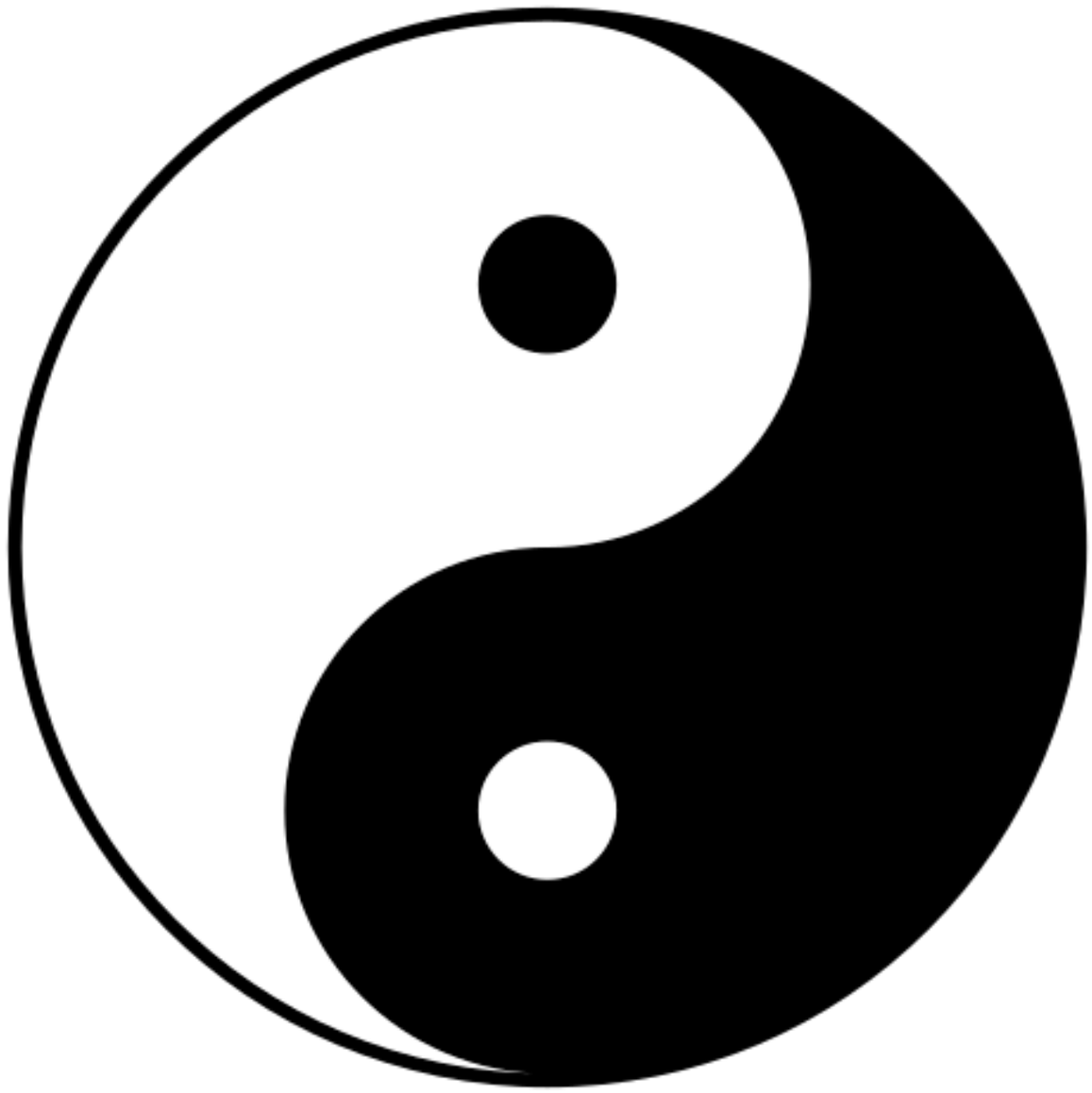


Challenge 3 — 'autonomous coordination'



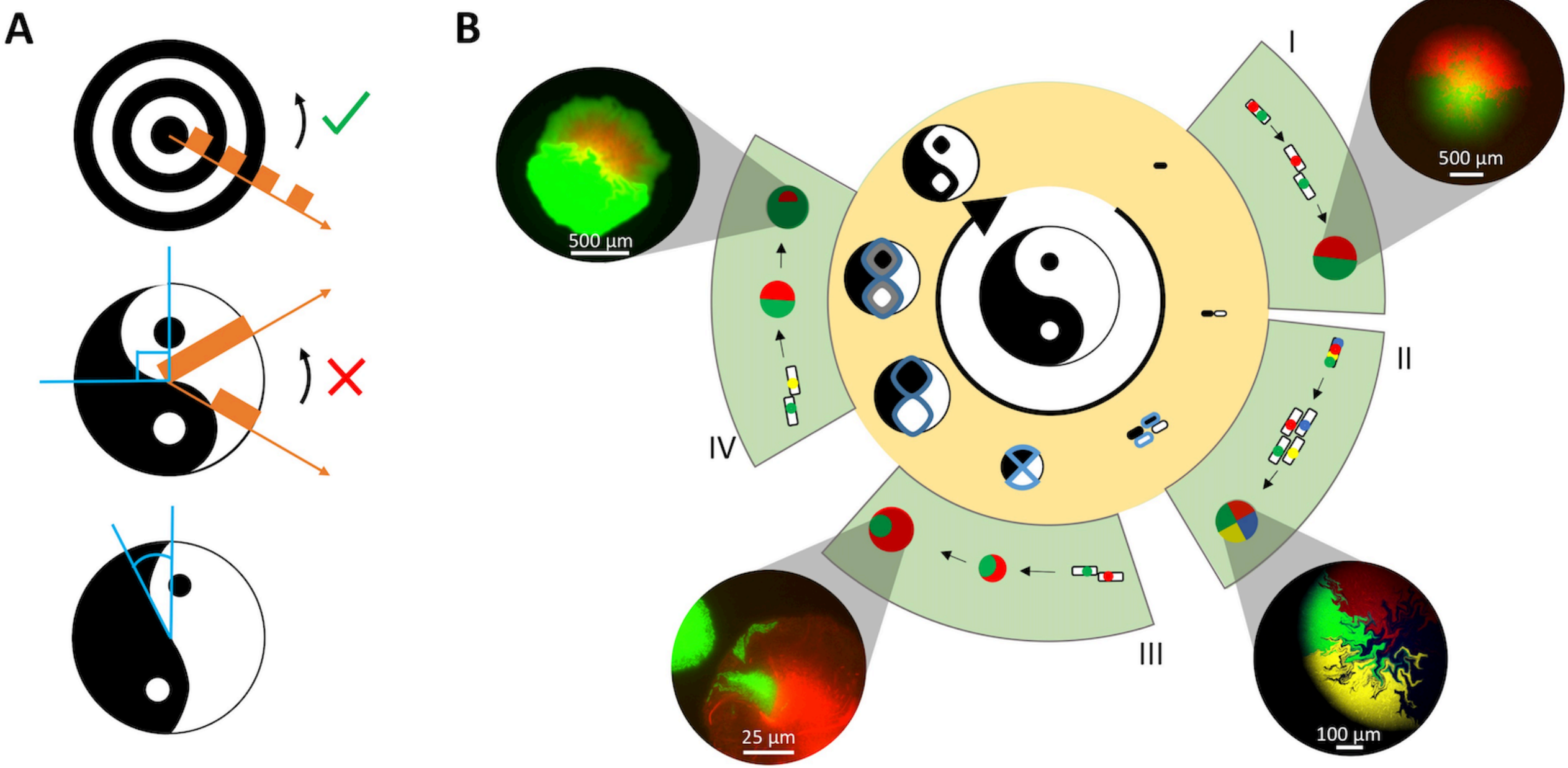
Place droplets only in the seed box that causes a droplet to move from point A to point B (i.e., seed a system that autonomously controls its own behavior).

OK. So, how would you grow a yin yang from a single seed cell?



https://www.biorxiv.org/content/10.1101/549352v1

Take a complicated problem and break it down into a set of simpler problems…



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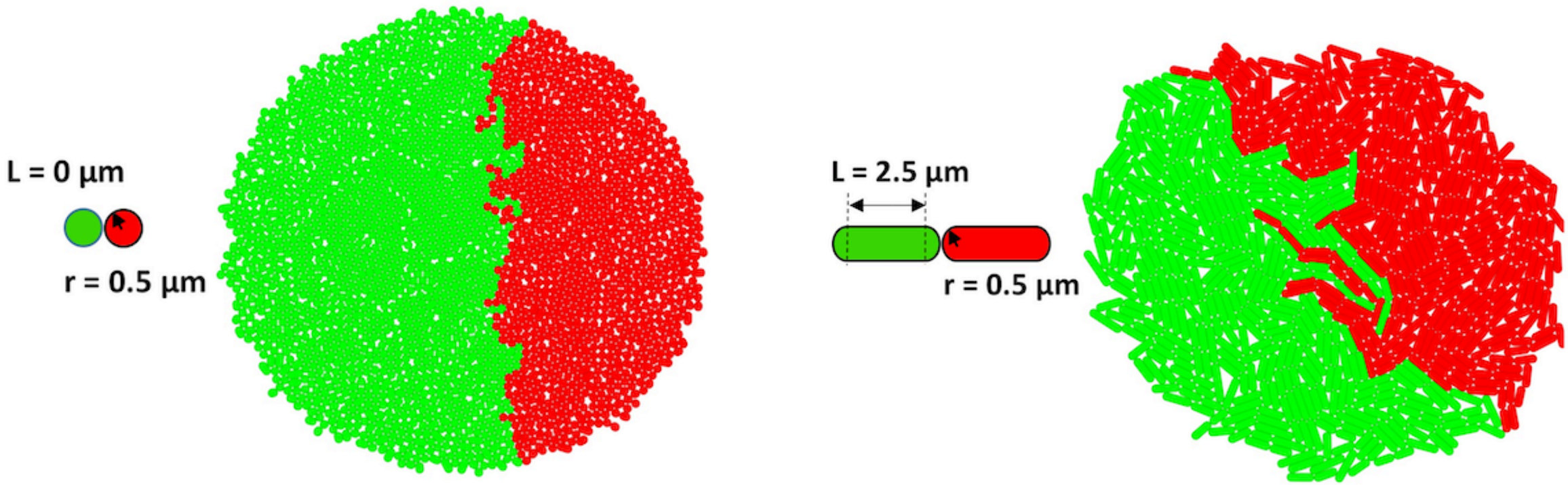
One interesting aspect is how the mechanical, chemical, and biological realms are coupled… how can we leverage such couplings as bioengineers?



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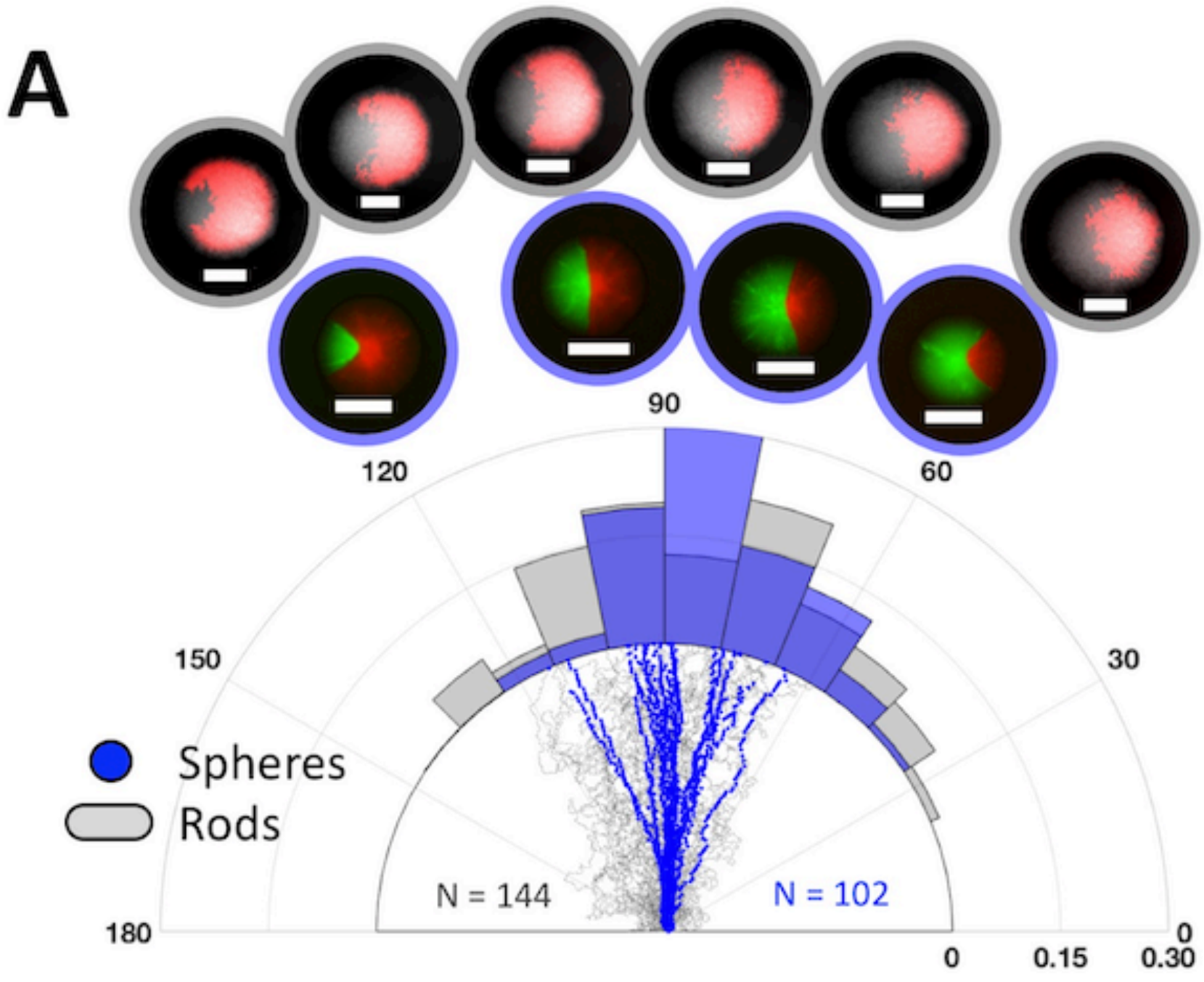
Just changing two simple variables (relative growth rates and cell lengths) can produce all of the below…



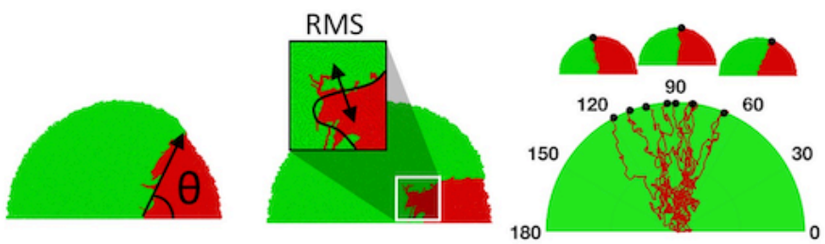
https://www.biorxiv.org/content/10.1101/549352v1

Abstraction again appears as a tool for managing biocompleixty…

Morphogenesis

Composition of tissue properties and form

I need a set of pattern borders with these curvatures



Patterns

Tissue formations after growth of cell lineages

Here you go

Grow me a border with this curvature and texture

$$\textbf{Curvature} \quad [\theta] \quad f(\mu_1, \mu_2) \propto {}^{\mu_1}/_{\mu_2}$$

$$\textbf{Texture} \quad [RMS] \quad f(k) \propto k^{0.4}$$

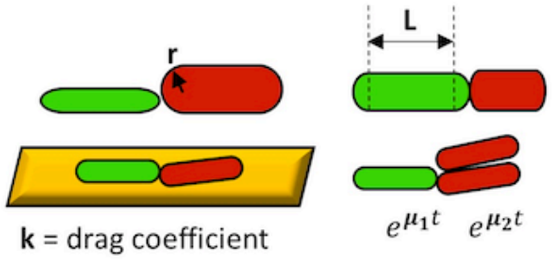
$$\textbf{Reliability} \quad \left[\frac{1}{STD}\right] \quad f(L, r) \propto \frac{-2r}{L\left(\frac{L}{2r} - 4\right)^2}$$

Border Functions

Composition of operators to define border growth

Here is your desired border grown with 75% reliability

Give me spherical cells with growth rates μ_1, μ_2



Operators

Physical properties of cells that can be used to program borders

Here are spherical cells with growth rates μ_1 and μ_2

Get the DNA that allows control over cell growth rates

AGTCATGGTGTTAATCCT…

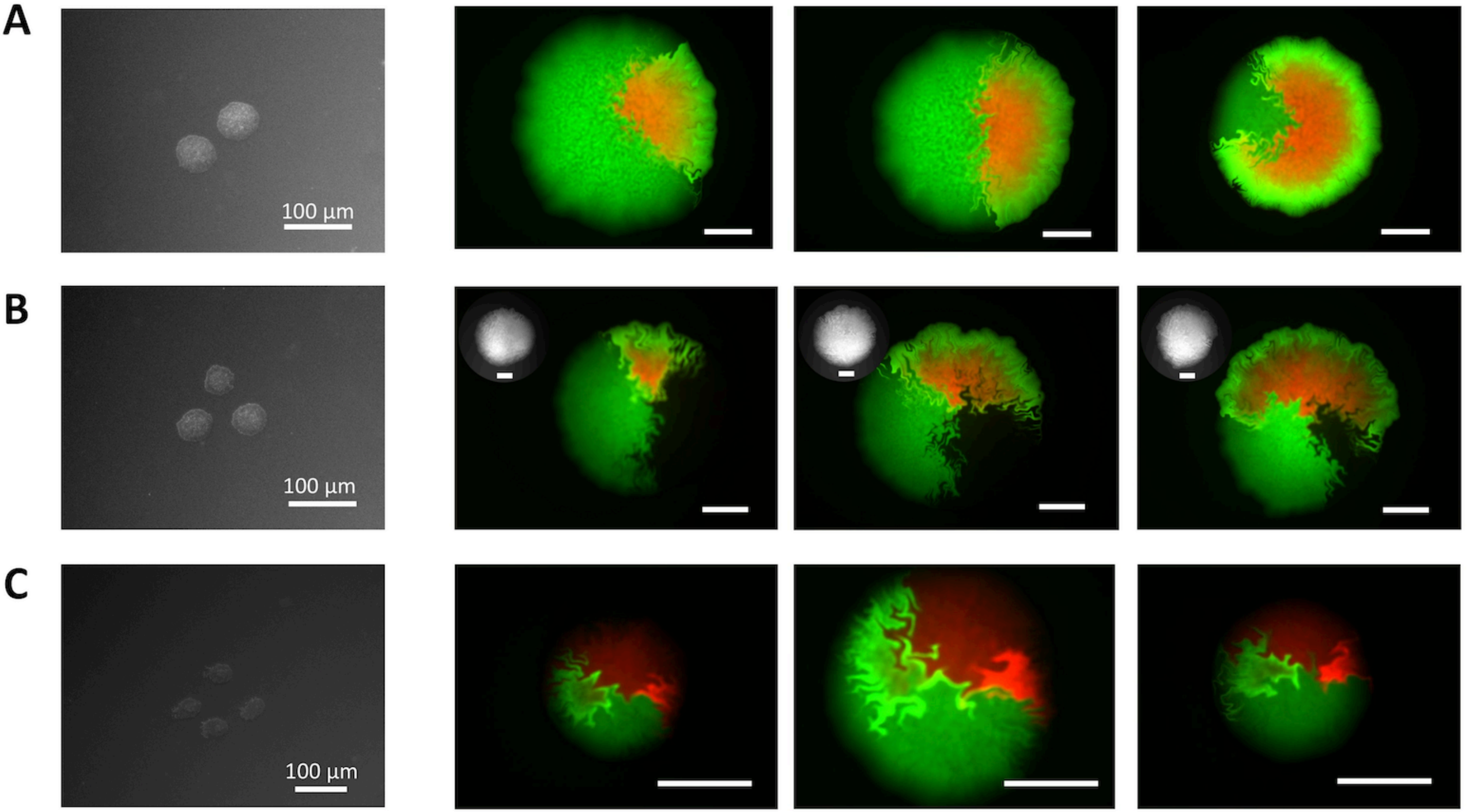
DNA

Genetic encoding of operators that can be used to shape borders

Here are bacteriostatic antibiotic resistance markers

https://www.biorxiv.org/content/10.1101/549352v1

So, can bioengineers grow arbitrary patterns from living cells, from scratch?



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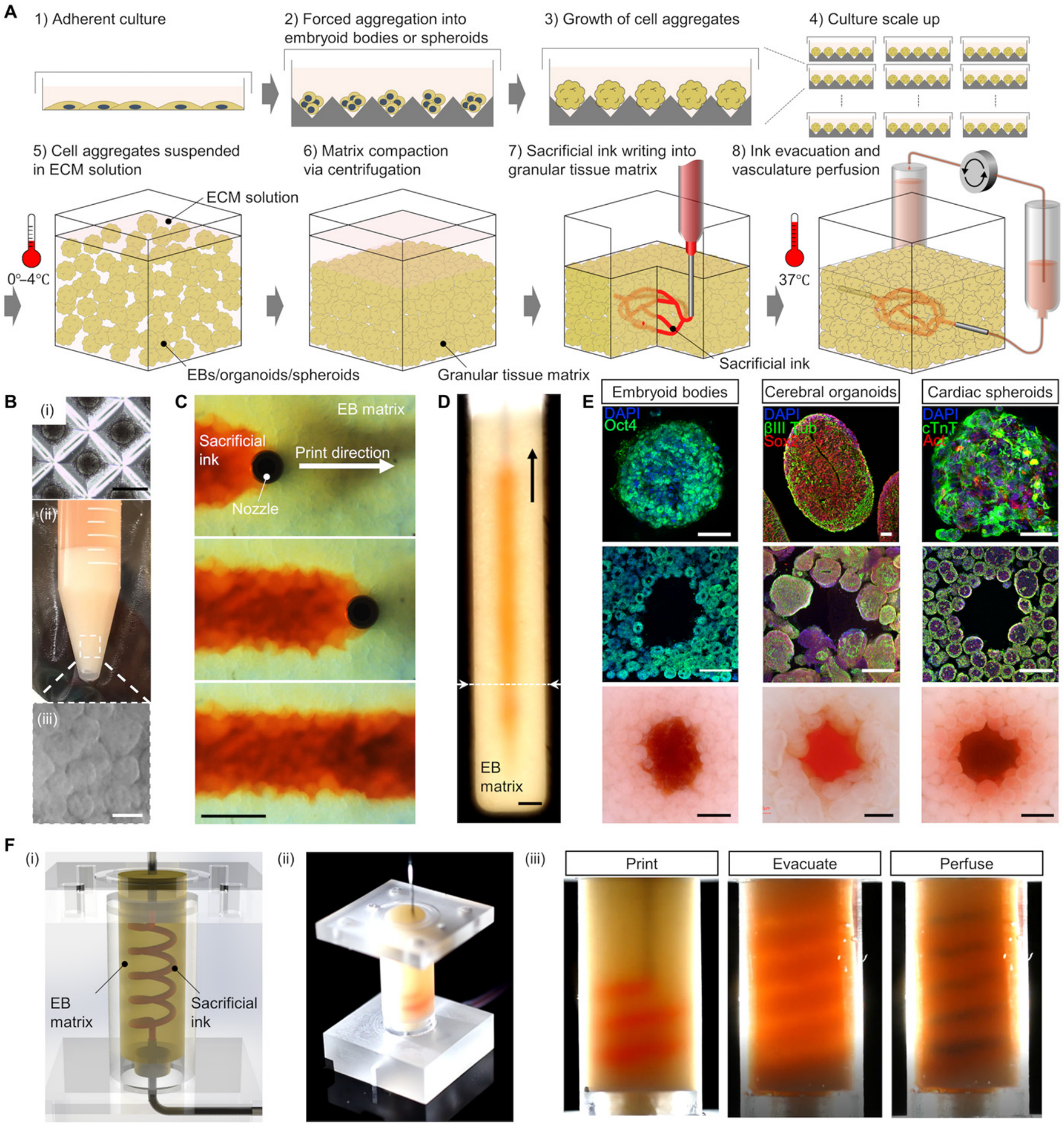


https://advances.sciencemag.org/content/5/9/eaaw2459

What about a hybrid approach?

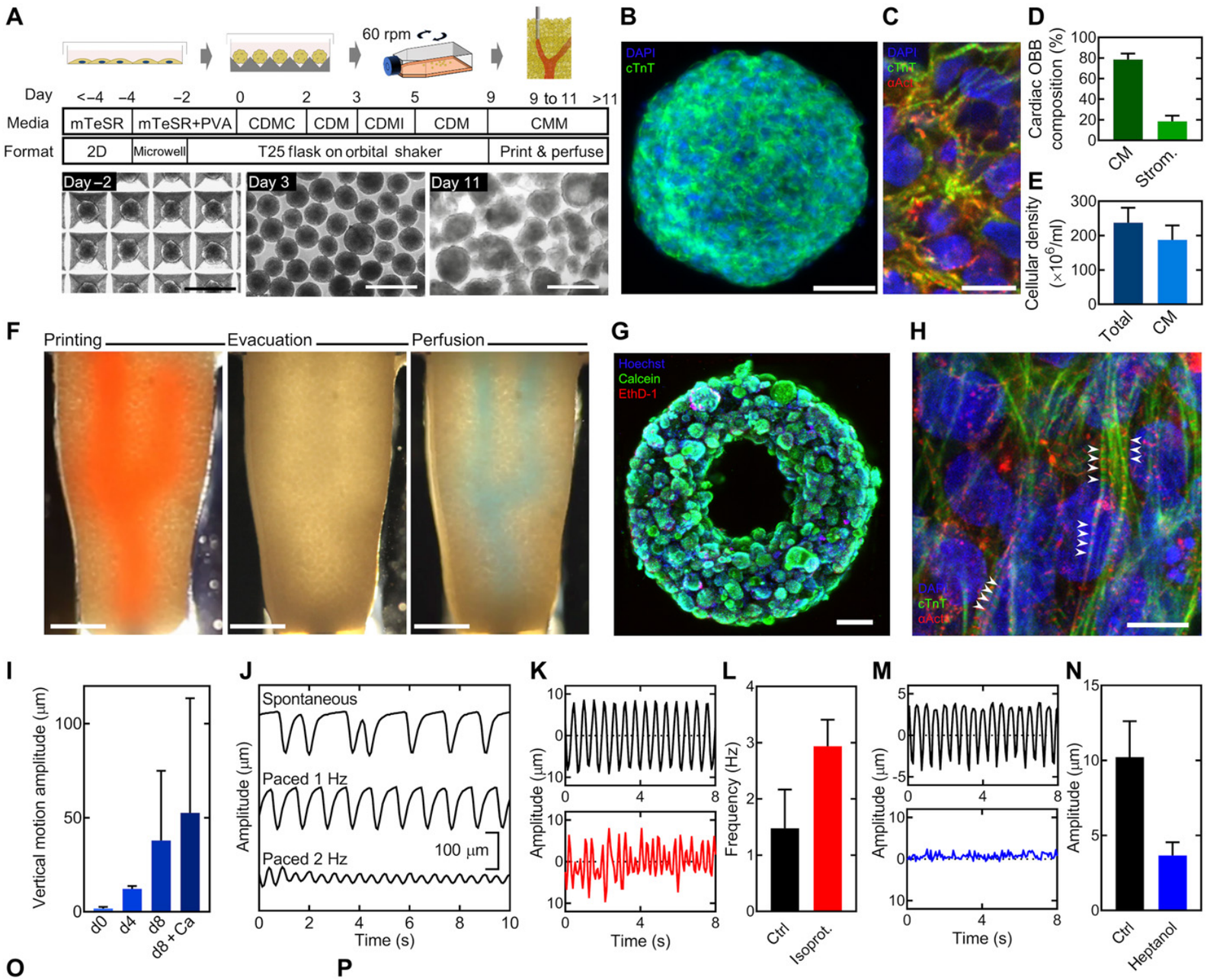
Use the biology for what the biology is good at, combined with what we can control from outside!

Vascular system on demand?

What about a hybrid approach?

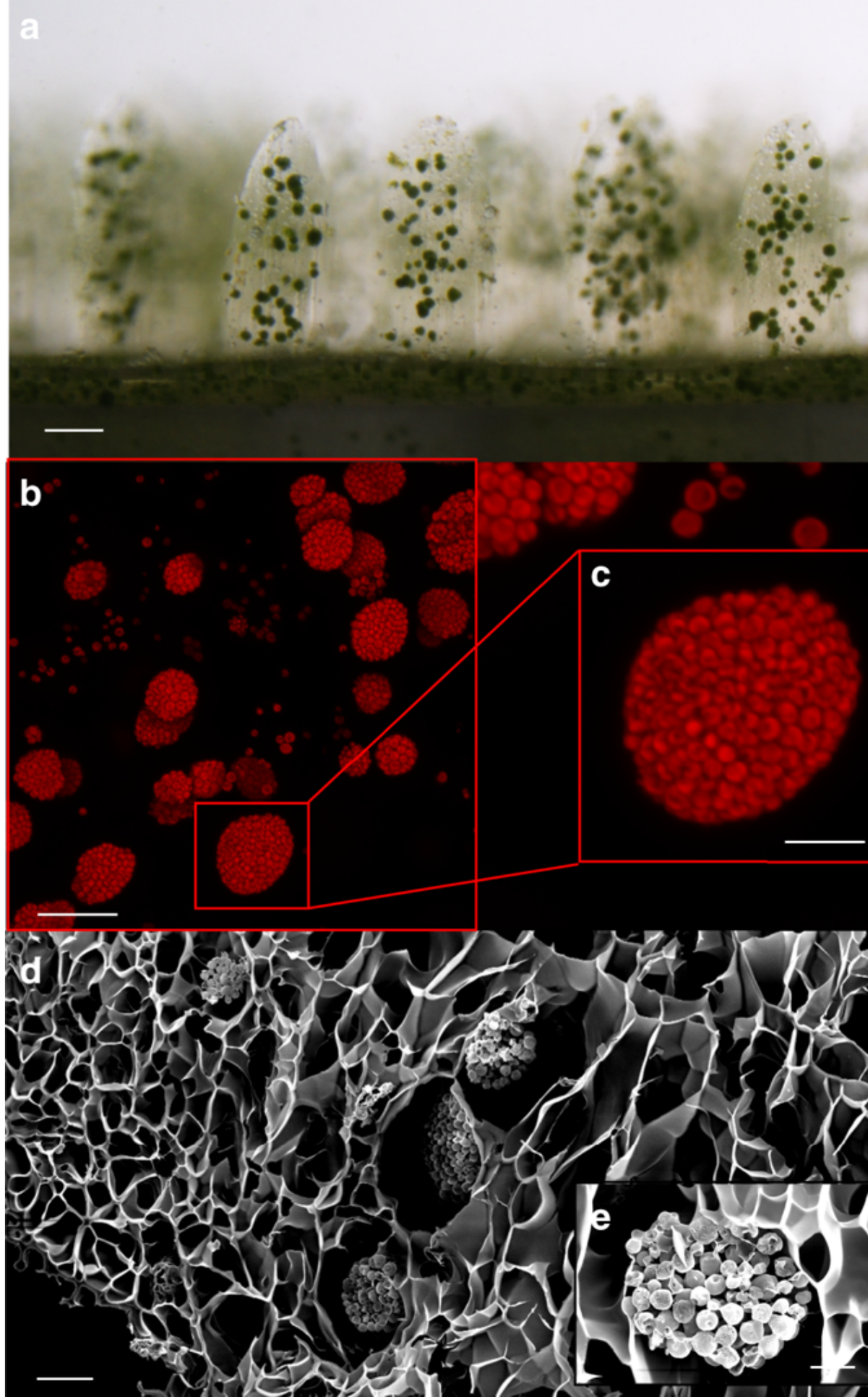
Use the biology for what the biology is good at, combined with what we can control from outside!

Cardiac vascular system on demand?



https://advances.sciencemag.org/content/5/9/eaaw2459

Same hybrid approach…
Living 3D printed bionic coral



https://www.nature.com/articles/s41467-020-15486-4