

5. Clonal multicellular and its evolutionary origin

Tuesday, 7 September 2021

Remember to turn on zoom



confusions / clarifications / questions?

Portfolio report Zach, Brian and Chavvinder

What is "cheating" under these conditions, and how might it arise? →

Is it a mistake to call it "cheating"?
Cheating is not contributing to the quorum by not producing the signal being produced by the rest of the cell density. This could arise due to mutations in all parts of the mechanism related to this particular signal

What else might a "good" answer mention?
What is to stop everyone from "cheating" →
how can (limited) selflessness survive?
?

Differentiation in bacteria

The response of *E. coli* to lactose is an example of an adaptive (easily reversible) response. Bacteria can also undergo more dramatic and stable (irreversible) phenotypic changes. One of these is spore formation, which involves complex changes in cell structure. Spores do not divide, but can survive harsh conditions. (1).

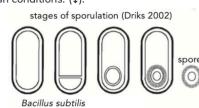
Such processes are examples of how a single genotype can generate multiple, stable, and often mutually incompatible, phenotypes - a process similar to that involved in cellular differentiation in multicellular organisms.

The sporulation switch involves a cascade of regulatory switches. How might you expect the behavior of the sporulation switch to differ from the switch that activates the lac operon? (1)

e.g. would it be noisy or hard to activate?

The sporulation switch would differ from the switch that activates the lac operon as it is a very intensive process, so for it to happen with some random noise (like the very noisy lac operon) it would be, in a way, wasteful.

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Here is a simplified diagram of the *B. subtilis* spore formation molecular decision network. A standard arrow (\rightarrow) indicates a positive or activating effect, a barred arrow ($\overline{\rightarrow}$) indicates a negative or inhibitory effect. In this pathway phosphate groups are transferred from different Spo proteins. The $-P$ symbol indicates that a protein has been phosphorylated.

Q1:(1) How might phosphorylation alter a protein's structure & activity?

Phosphorylation can turn a protein on and take it from a deactivate state to an active state

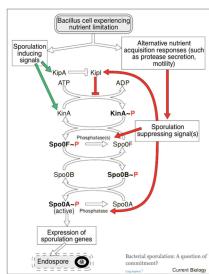
It would decrease the level of phospho-SpoOF in a cell because the activator phosphatase would not be present

Q2:(-) Nutrient levels influence the activity of the phosphotase that acts on SpoOF. Predict how a mutation that inactivates this phosphatase will influence the level of phospho-SpoOF in a cell?

It allows the SpoOA to be activated without everything else being activated, so you can just activate the SpoOA and get an endospore.

Q3: How might activating of the phosphatase that on SpoOA influence the response of the system to nutrient starvation? (\rightarrow)

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We can use the sporulation network to reveal some common features of signaling pathways. Assuming that nutrients are exhausted at $t=5$; plot how the concentration of phosphorylated KinA [KinA-P] in a typical cell changes as a function of time (1).

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generating your prediction (your graph)?

groupQ: how would you draw it (and why)?

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Cooperative behaviors: There are behaviors that make no sense for a single isolated cell to do, but do "make sense" when cells are at high density, e.g. the synthesis and secretion of digestive enzymes and toxins, the import of DNA, and behaviors such as programmed or altruistic cell death and the generation of persister phenotypes.

Transient metazoans There are other types of behavior that cannot be carried out by unicellular organisms because they are just not big enough. Many involve forming structures that enable individuals to escape a hostile environments (Du et al 2016). To build these structures, individual organisms (cells) aggregate, often migrate as a group, form macroscopic multicellular structures, and produce differentiated cells that can disperse to more hospitable environments.

To determine whether such cooperative behaviors "makes sense" the organisms involved need to know whether there are enough cells around; how might a cell monitor cell density? (1)

How does a unicellular organism sense aspects of its environment?

Quorum sensing

from Du et al 2016 The Evolution of Aggregative Multicellularity and Cell-Cell Communication in the Discobionts

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The best studied of these systems is the cellular slime mold *Dictyostelium discoideum*. Dicty is "normally" unicellular - crawling around in soil, eating bacteria, growing, and dividing. When conditions become hostile, however, it changes its strategy; it becomes transiently multicellular. Individual organisms (cells) cooperate (and some sacrifice themselves) to generate a structure that lifts related cells out of the soil and allows for the formation and dispersal of spores.

This strategy makes little sense if there are few cells around, so Dicty uses quorum sensing to monitor cell density. Cells secrete the preservation factor (PSF) protein.

What factors control the concentration of PSF around the cell that secretes it? (1)?

what factors control the local [PSF]?

?

Then, draw a graph (1) of your prediction of the relationship between [PSF] (y-axis) and cell density (x-axis).

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There is no reason to migrate and differentiate if life is good, so Dicty uses a second signaling system to monitor the availability of food. If the local population density is sufficiently high (above a threshold), starving cells secrete cyclic AMP. As extracellular [cAMP] increases cells migrate towards one another, aggregating to form a "slug" that migrates, finds a good location and differentiates.

Q1: If [PSF] is below threshold, is PKA active or not? Explain the thinking behind your answer (1)

What assumptions are involved in building the model you use to answer the question?

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Approximately 20% of the cells in the slug differentiate to form the holdfast and stalk, and die. The remaining cells form the spores that are lifted up out of the soil and released. Which cells become stalk (and die) and which spores (and may survive) is a stochastic process that involves different gene expression programs.

Dictyostelium (amoeba)

Du et al., 2019

Remembering that single Dicty cells are independent organisms, why is it important that the process of cell fate determination be stochastic, what might you expect to happen if it weren't. Start by considering what the term stochastic means. (-).

Stochastic means that the process is essentially random on a micro scale, but when looking at the overall (like the whole slug) we can see a trend of 80/20. But for a given cell you can't know the odds of it becoming head or stalk. It is important that cell fate determination be stochastic because if it weren't then there would be an evolutionary bias that would arise towards one side. For example evolutionarily there could be a single event where spore formation is selected for but then in the event where a slug has to form, if everyone could only be spores then there is an issue. So it is important to possess the ability to do both and not have it be predetermined as a population would not be as able to survive a variety of conditions.

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D. discoideum also has a sexual cycle (→) with distinct mating types. Two cells of different mating types fuse. The resulting diploid cell attracts haploid cells and induces them to die. The dead cells are either consumed or used to form a wall around the resulting giant diploid cell that then enters meiosis, forming and releasing recombinant haploid cells.

As a quick background check, what is the "purpose" of meiosis, why might it be beneficial under stressful conditions (1).

The purpose of meiosis is to lead to ^{various} sexual reproduction. Meiosis could be beneficial under stressful conditions by generating diversity by allowing new combinations of the recombinant chromosomes. Thus, increased genetic variation could arise in offspring which could aid in natural selection.

Flowers et al., 2010

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Clonal multicellularity

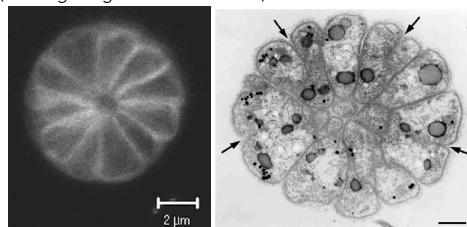
- What is clonal multicellularity (versus colony formation)?
- Origins & advantages
- Why is there a somatic/germ layer divide?

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Most prokaryotes are unicellular

(may be part of multi-species biofilms)

Multicellular motile magnetotactic (Gram-negative) prokaryote
(Ca. *Magnetoglobus multicellularis*)



magnetosomes: membrane-bound, nanocrystals of magnetite (Fe_3O_4) or greigite (Fe_3S_4)

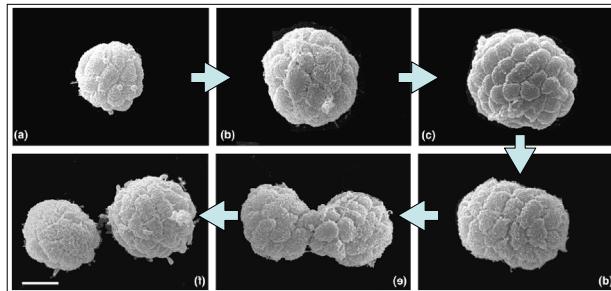
Cells appear to be equivalent

Keim et al. (2004). Multicellular life cycle of magnetotactic prokaryotes. *FEMS Microbiology Letters*, 240, 203-208.

Leão et al. (2018). Association of magnetotactic multicellular prokaryotes with *Pseudoalteromonas* species in a natural lagoon environment. *Antonie van Leeuwenhoek*, 111, 2213-2223.

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The presumed (colonial) life cycle: Initially, small and spherical, as it grows cell size (not cell number) increases. Later, cells synchronously divide without separating. Next, organisms become elliptical and then eight-shaped. The eight-shaped organism splits into two equal organisms. Scale bar: 4 um.

Keim et al (2004). Multicellular life cycle of magnetotactic prokaryotes. *FEMS Microbiology Letters*, 203-208.

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What drives multicellularity?

Phagotrophy by a flagellate selects for colonial prey:
A possible origin of multicellularity

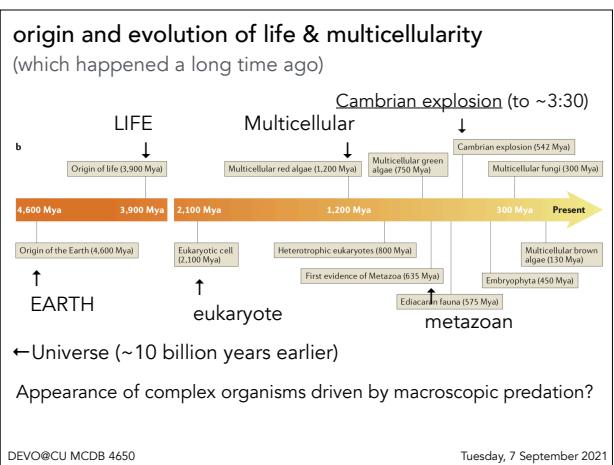
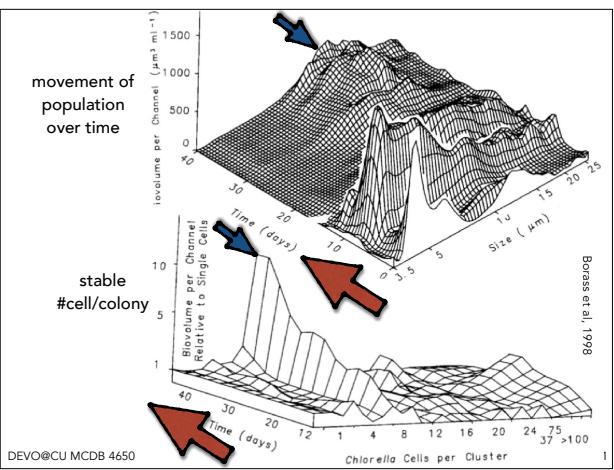
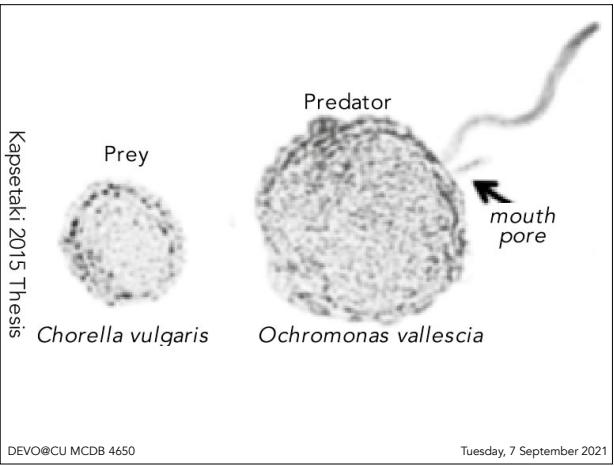
MARTIN E. BORAAS,* DIANNE B. SEALE and JOSEPH E. BOXHORN

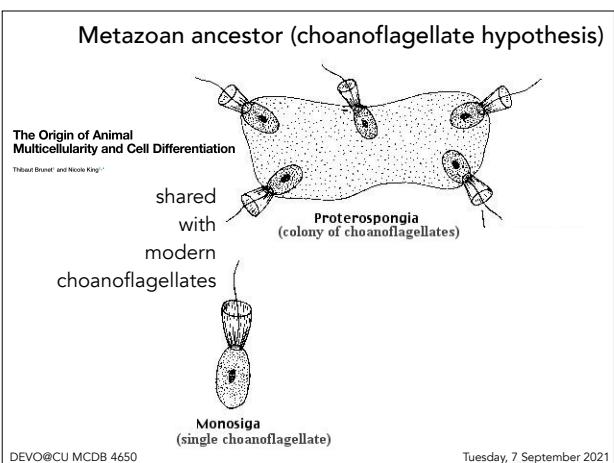
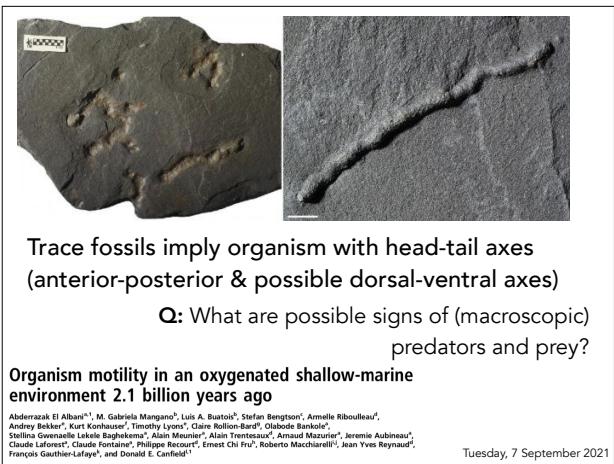
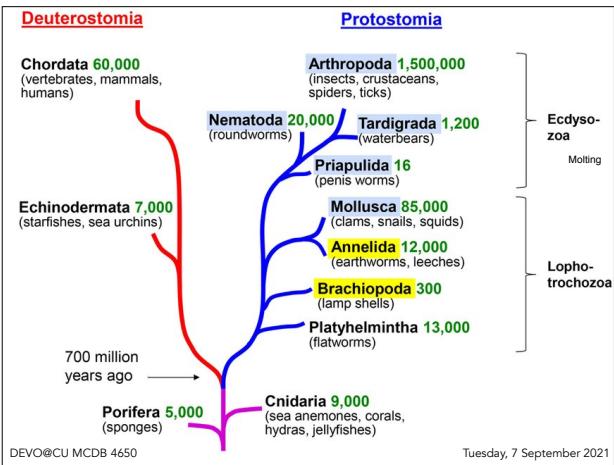
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origin of metazoans (choanoflagellate hypothesis)

Common structural details

Choanoflagellate Choanocyte

Q: Why does detailed structural similarity argues for homology (common ancestry) and against convergence

Improbability of building the same structure the same way twice (through evolutionary mechanisms)

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The Origin of Animal Multicellularity and Cell Differentiation

A Choanoflagellates
Rosette formation in *Sulpingoeca* rosetta

Thibaut Brunet¹ and Nicole King^{1,*}

[The transition to multicellular life video](#)

Cyaea Moraea Blastaea Gastraea

Mikhailov et al. (2018). The origin of metazoans: a transition from temporal to spatial cell differentiation. *Bioessays*, 31, 758-768.

origin of metazoans (choanoflagellate hypothesis)

- Supported by genome analyses: presence of similar genes in both choanocytes (holozoa) and metazoans (animals)
 - e.g. cadherin gene
 - BUT this gene is not involved in cell-cell adhesion - it is involved in binding bacteria

Exaptation: repurposing previously developed trait (gene) for a new purpose (which can then be adapted evolutionarily)

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Reconstruction of the ancestral metazoan genome reveals an increase in genomic novelty

Jordi Paps^{1,2} & Peter W.H. Holland²

groupQ: How would you go about it?

Understanding the emergence of the Animal Kingdom is one of the major challenges of modern evolutionary biology. Many genomic changes took place along the evolutionary lineage that gave rise to the Metazoa. Recent research has revealed the role that co-option of old genes played during this transition, but the contribution of genomic novelty has not been fully assessed. Here, using extensive genome comparisons between metazoans and multiple outgroups, we infer the minimal protein-coding genome of the first animal, in addition to other eukaryotic ancestors, and estimate the proportion of novelties in these ancient genomes. Contrary to the prevailing view, this uncovers an unprecedented increase in the extent of genomic novelty during the origin of metazoans, and identifies 25 groups of metazoan-specific genes that are essential across the Animal Kingdom. We argue that internal genomic changes were as important as external factors in the emergence of animals.

Some novel core (animal) genes (homology groups)

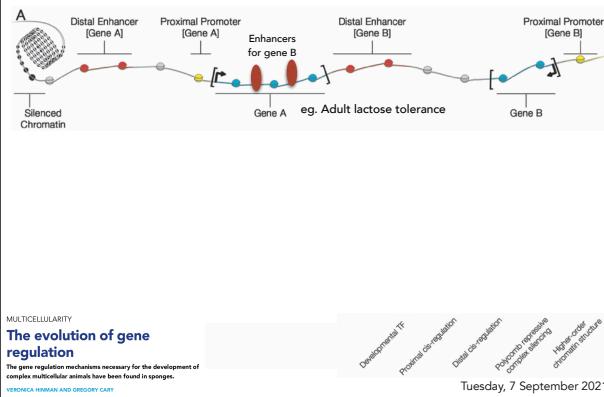
Table 1 Novel Core genes in the Animal Kingdom

	Transcription factors	Fruit fly genes examples	Human gene examples
Homeobox	NKL subclass,	trimman, distalless, ems	NKX2-5, DLX1, EMX1, VAX1, HLX, DBX1, BARO, NKX2-6
	ANTP class	sine oculis, opbx	SIX1, SIX4, ANHX
	SIX class	pou proteins, nubbi, ventral veins	POU1FL, POU2FL, POU4F1
	POU class	lacking	
bHLH	hex/hairy	hex, hairy, wingless, deadpan, clickwork, orange	HEX1, HEZ2, HEY1, HEYL
	bHLH-PAS	single minded, spindles, tracheoblasts	EPAS1, HIF1A, SIM1, AHR, NPAS1
ETS	twist/hand	twist, hand, target of Paen, taxii, atonal	TWIST1, HAND1, SCLX, TCF15, PTIF1A, NEUROD1, NEUROG1
		ets5A, anterior open, pointed	ETV4, ETS1, ELK1, ERG, FEV
Signalling pathways	Wnt	wingless	WNT1, WNT2, WNT3, WNT4, WNT10A
	Frizzled, pargolin/TCF-LEF, armadillo/beta-catenin	frizzled, smoothened, pargolin, armadillo	SMO, FZD1, CORIN, SFRP2, FRZB, TCF7, LEF1, TCF7L1, JUP, CTNNB1
TGF-Beta	TGF-beta/BMP	decapentaplegic, screw, activin beta	BMP2, BMP10, GDF1, INHBA, NODAL, TGFBB1
	SMAD, TGF-beta receptor, INK pathway interaction	mothers against decapentaplegic, punt, saxophone, wif1b thinking, sunday driver	SMAD1, SMAD2, SMAD3, SMAD9, TGFBR1, ACVR1B, AMHR2, BMPR1B, MAPK8IP3, SPAG9

Reconstruction of the ancestral metazoan genome reveals an increase in genomic novelty

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Bilateria and other metazoans have several regulatory features that are absent in related unicellular species.



Evolution of individuality during the transition from unicellular to multicellular life

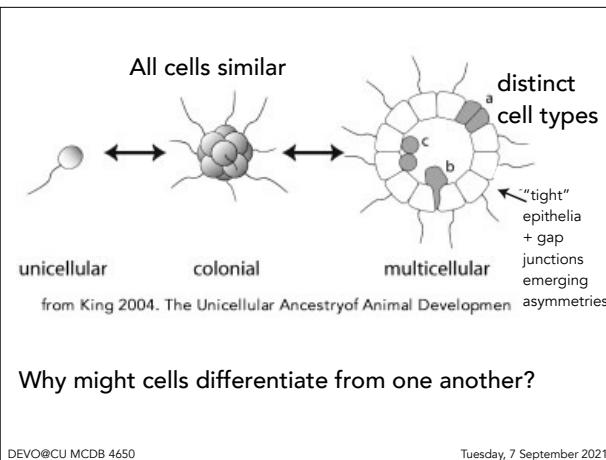
Richard E. Michod^{*}

Department of Ecology and Evolutionary Biology, University of Arizona, Tucson, AZ 85721

- Advantages of group formation
 - avoid predation / cell specialization
 - new life styles (niche)
 - avoid competition / exploit new resources
- Depends upon "reproductive altruism"
 - restrictions associated with differentiation
- How do groups become individuals
 - close kinship (clonal)
 - transfer of fitness from individual cell to group

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