Collective phenomena in biology

Nigel Goldenfeld
Department of Physics
Institute for Genomic Biology
University of Illinois at Urbana-Champaign

Collective phenomena in biology
OR
Biology is the new condensed matter physics

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Who is involved?




- Nigel Goldenfeld (theory; physics, CPLC, IGB)
- Tom Kuhlman (experiment, physics, CPLC)
- Seppe Kuehn (experiment, physics, CPLC)
- James O'Dwyer (theory; plant biology, IGB)

“Ask not what physics can do for biology; ask what biology can do for physics”

Stanislaw Ulam

What is condensed matter physics?

- Unifying theme of condensed matter physics is arguably collective phenomena
  - Superfluidity in He II as well as neutron stars
  - BCS pairing in superconductors and QCD
  - Bose-Einstein condensation in atomic gases
  - Turbulence in water and in quark-gluon plasma

- Key difference between condensed matter and biological physics: importance of problem choice
  - Condensed matter: typically a few problems of over-riding importance at any one time
  - Biological matter: no clear consensus on a few hot topics
  - Implication: problem selection is a key “success factor” in biological physics

- My perspective: look for biology problems dominated by collective effects
  - Generally overlooked by the biophysics community (focus more on single-molecule biophysics)
  - Condensed matter physicists have something new to offer biologists

What is “biological physics”?

- **Traditional view of “biophysics” as the physics of molecular biology is too limited.**

- **Hallmark of condensed matter physics is the study of collective phenomena:**
  - **Should look beyond the single-molecular and single-cell level**
  - **Emergence, dynamics of spatially-extended systems and collective behaviour.**
  - **Examples: metabolic scaling laws, ecology (microbial ecology in particular) population biology, invasions and epidemics, genome dynamics, social organization, interaction of biological organisms with environment.**

What can physics do for biology?

Ask biologists …
Ask the NSF …

Biocomplexity

- What is "complexity"?
  - Complexity = structure + large fluctuations

- The big idea: research on the individual components of complex systems provides only limited information about the behavior of the systems themselves

- Biocomplexity arises from interplay of complex biological, physical and even social systems

What is biocomplexity?

NSF Solicitation 00-22

- "Biocomplexity arises from dynamics spanning several levels within a system, between systems, and/or across multiple spatial (microns to thousands of kilometers) and temporal (nanoseconds to eons) scales.
- This special competition will specifically support Research Projects which directly explore nonlinearities, chaotic behavior, emergent phenomena or feedbacks within and between systems and/or integrate across multiple components or scales of time and space in order to better understand and predict the dynamic behavior of systems."

Why do we care?

- **Steven Jay Gould, New York Times, Feb 19, 2001**
  - "Homo sapiens possesses between 30,000 and 40,000 genes... In other words, our bodies develop under the directing influence of only half again as many genes as the tiny roundworm ...."
  - "The collapse of the doctrine of one gene for one protein, and one direction of causal flow from basic codes to elaborate totality, marks the failure of reductionism for the complex system that we call biology."
  - "First, the key to complexity is not more genes, but more combinations and interactions generated by fewer units of code — and many of these interactions (as emergent properties, to use the technical jargon) must be explained at the level of their appearance, for they cannot be predicted from the separate underlying parts alone."

Seppe Kuehn

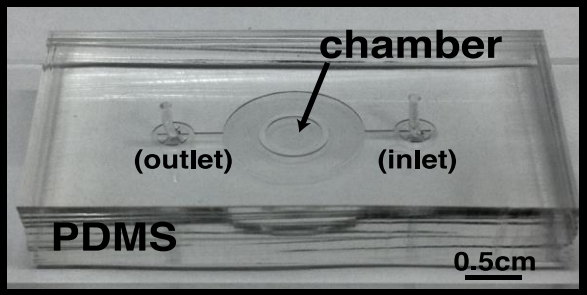
Testing the foundations of ecology – the spatial structure of communities

Kuehn lab for quantitative biology (#1)

Seppe Kuehn (seppe@illinois.edu)
Lab opening January, 2014

What is the structure of phenotypic variation?
How is phenotypic variation related to genetic variation?

Microbial swimming
as a model :

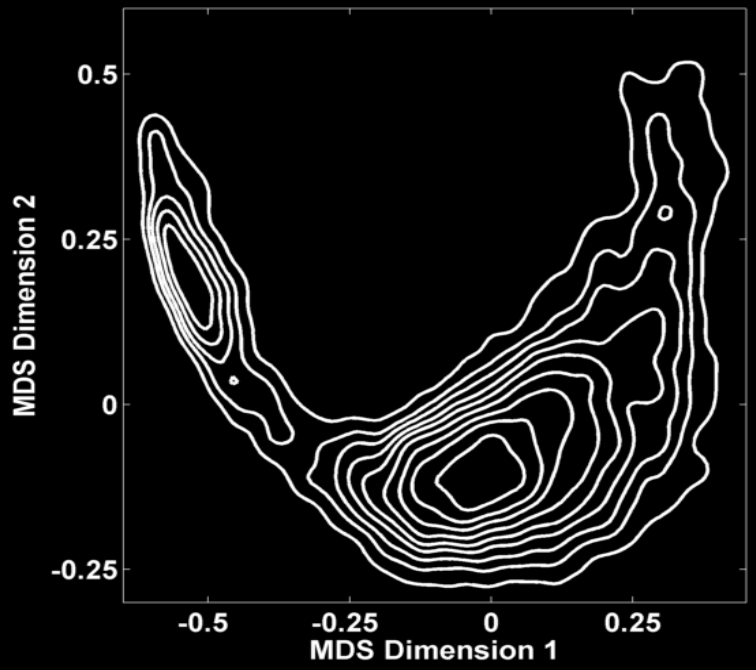


Microfluidics
+
Custom microscope

Full-lifetime tracking of
single cells (ciliates or bacteria)

New statistical method
To construct a phenotypic
"space" of behaviors

Behavioral variation is
low dimensional



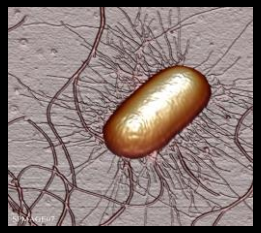
Details:
PNAS August 20, 2013
vol. 110 no. 34 14018-14023

Previous work

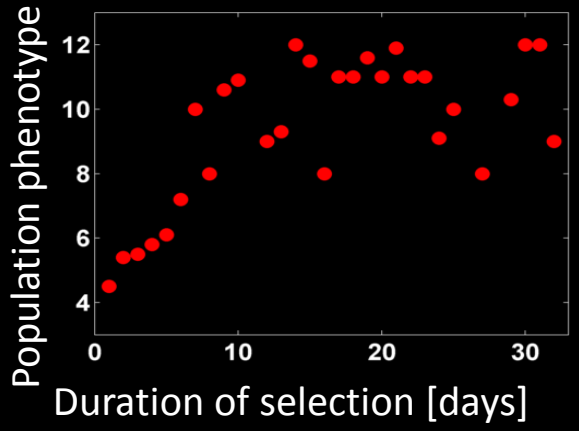
Kuehn lab for quantitative biology (#1 cont.)

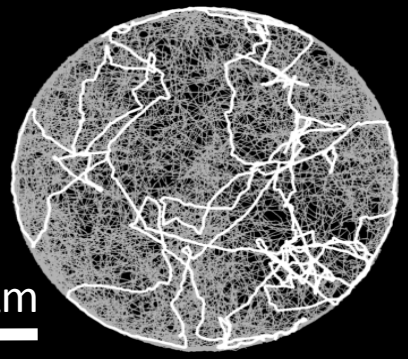
Seppe Kuehn (seppe@illinois.edu)
Lab opening January, 2014

Planned experiments: *E. coli*

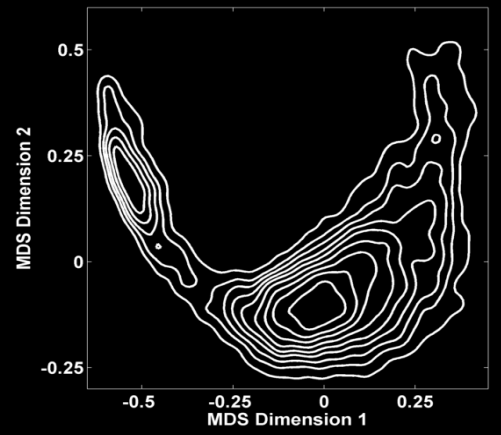


experimental evolution + single-cell tracking + DNA sequencing





E. coli. Full-lifetime (1.2 hrs).



Genetic basis of the structure of behavioral variation.

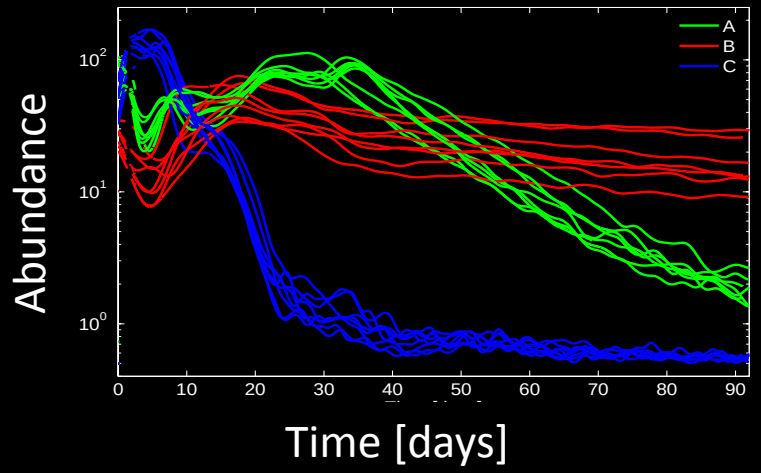
Contact: Seppe Kuehn (seppe@illinois.edu)
Lab opening January, 2014

Planned experiments

Kuehn lab for quantitative biology (#2)

Seppe Kuehn (seppe@illinois.edu)
Lab opening January, 2014

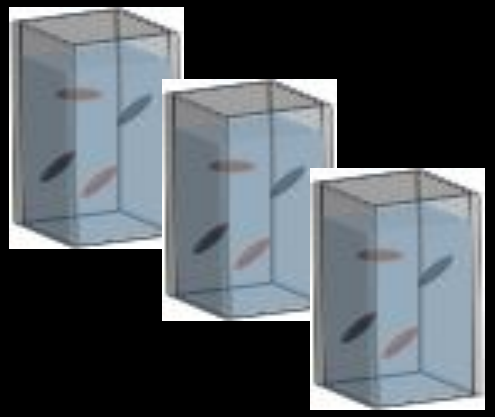
Are there statistical laws governing population dynamics in microbial ecosystems?



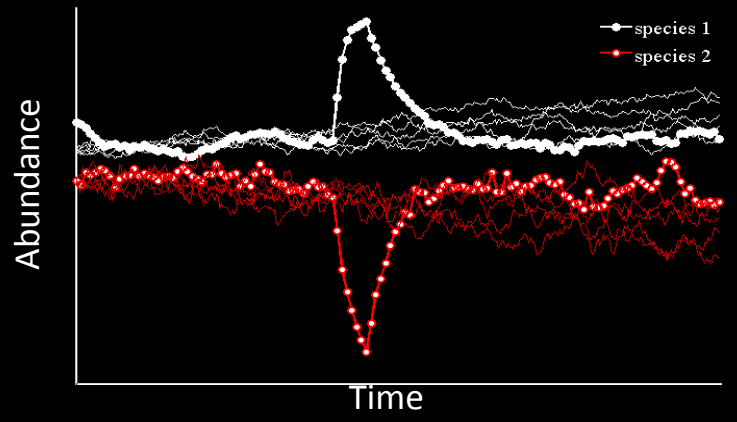
Long-term population dynamics in replicates 3-species model communities are highly repeatable. [Kuehn, Frentz, Leibler (2013)]

[Custom holographic microscopes measure abundences in time]
Rev. Sci. Instrum. 81, 084301 (2010)

Previous work



Perturbation response →



Planned experiments

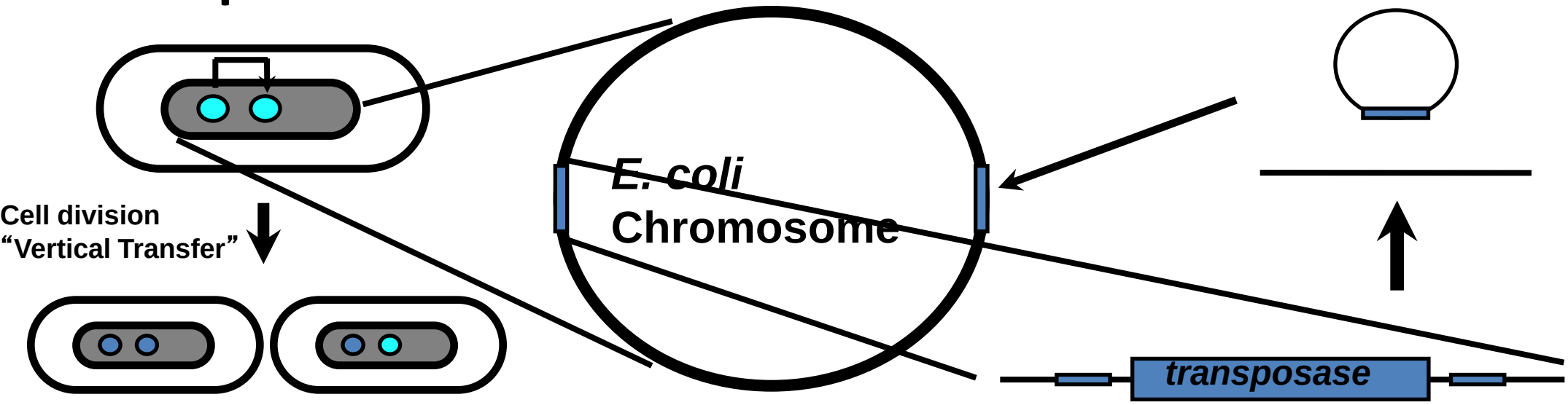
Plan to develop new method for sustaining/ measuring dynamics in replicate communities

Suspect simple *statistical* laws govern response to perturbations in complex microbial ecosystems.

Tom Kuhlman

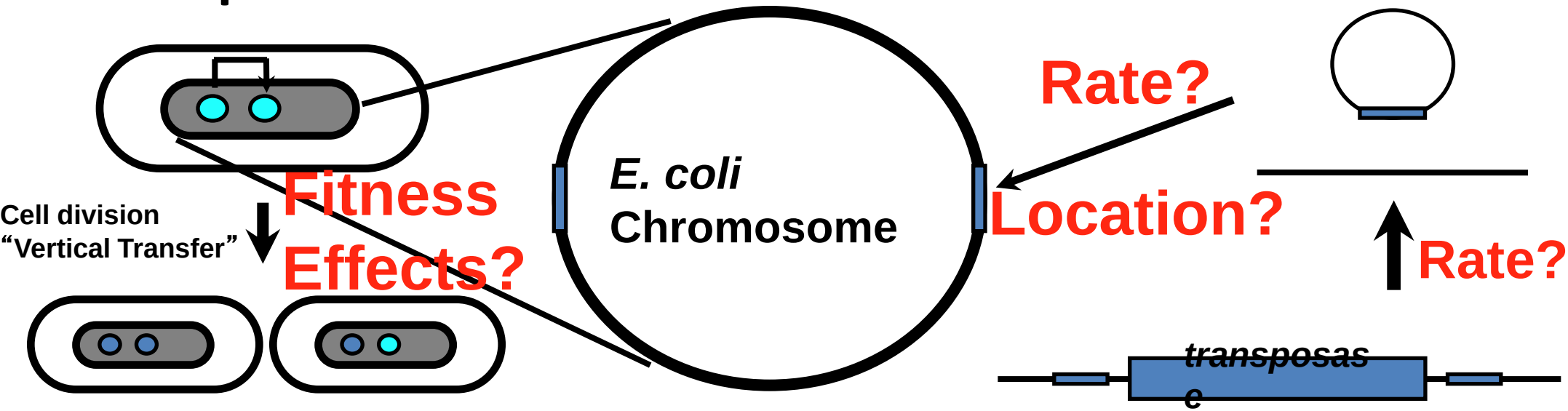
Watching evolution happen in the laboratory, at the molecular level

Transposons:



- Mobile genetic elements - "Jumping genes", present in all domains of life; make up ~45% of human genome, 85% of maize genome
- Can be "cut and paste" or "copy and paste"
- Thought to be a major source of mutations driving evolution

Transposons:

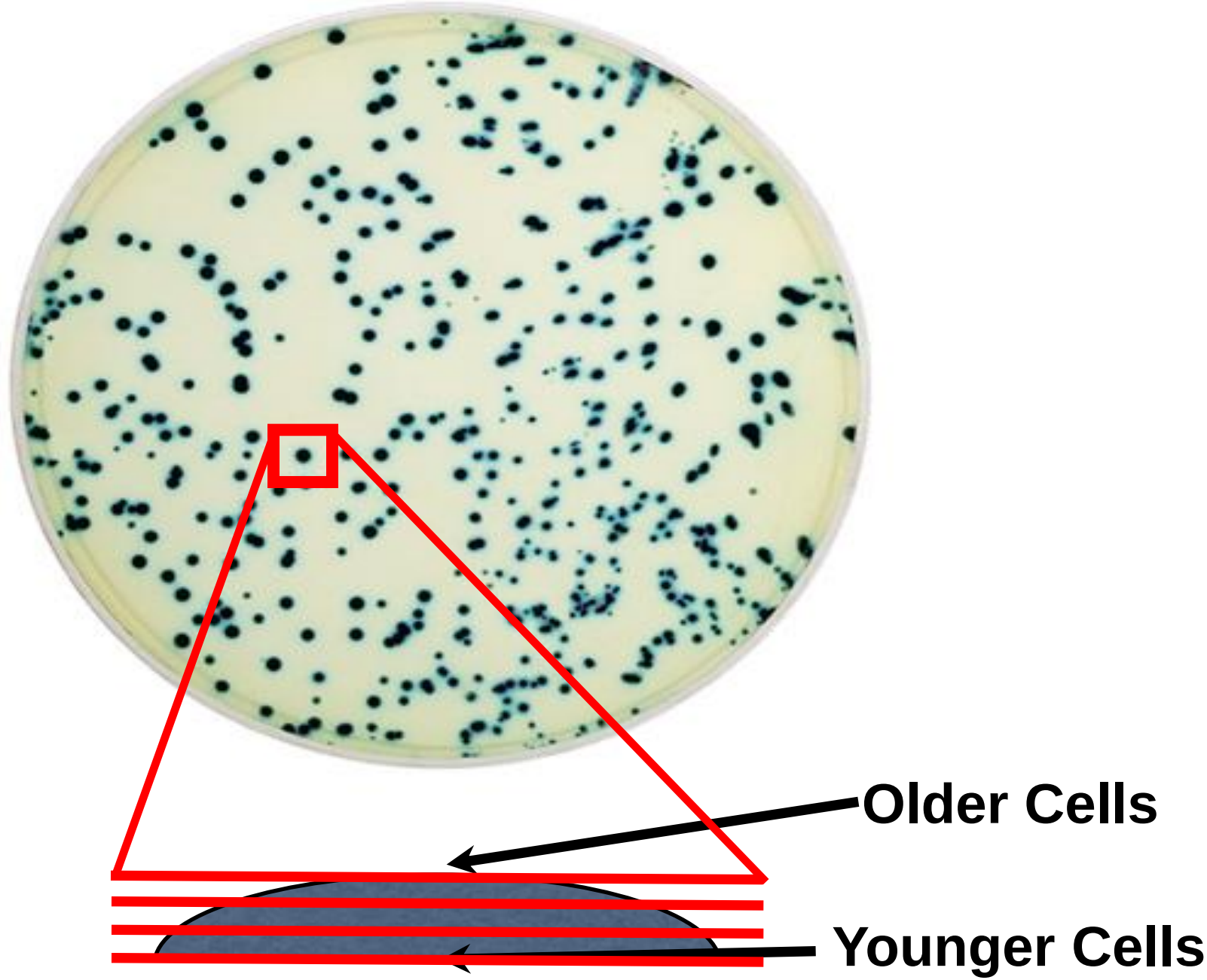


Problem:

- Everything that's known about dynamics of transposition is estimated by comparing the genomes of related species

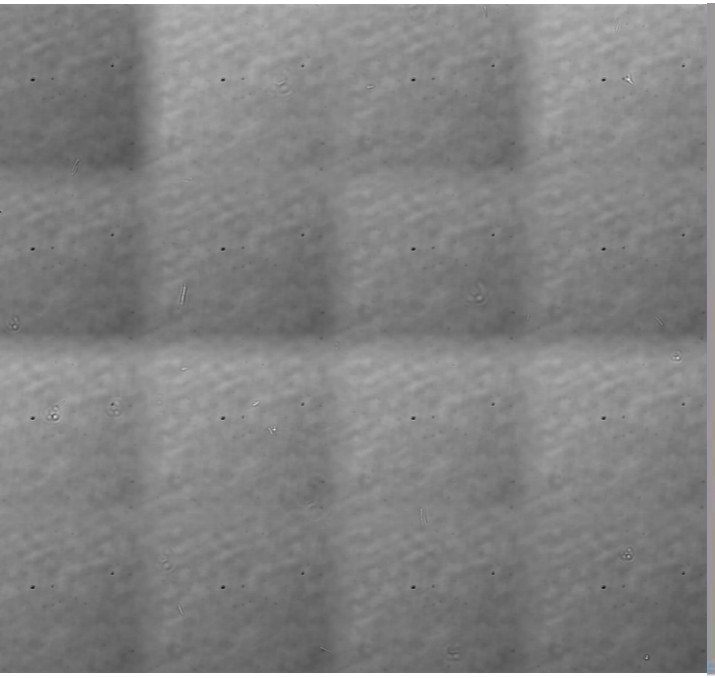
Goal:

- To develop an experimental system that allows use to observe and quantitatively measure transposition events in real time
- Use these measurements to model the intra-genome dynamics of transposons through populations


Older Cells
Younger Cells

Experiment

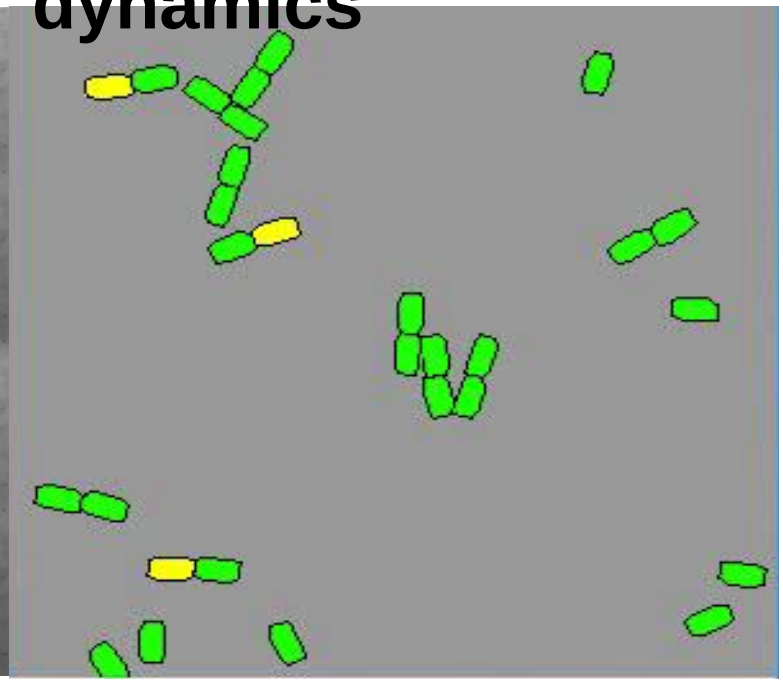
Measure single-cell transposition rates and effects



Real time single cell measurements in microfluidic device

Theory

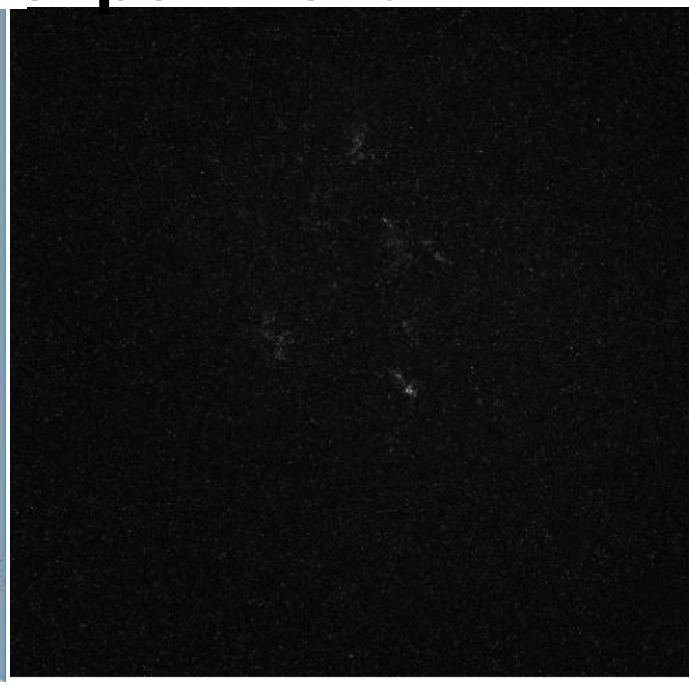
Model colony growth and population dynamics



Physical Model: Steric and elastic interactions, Transposition effects on growth rate

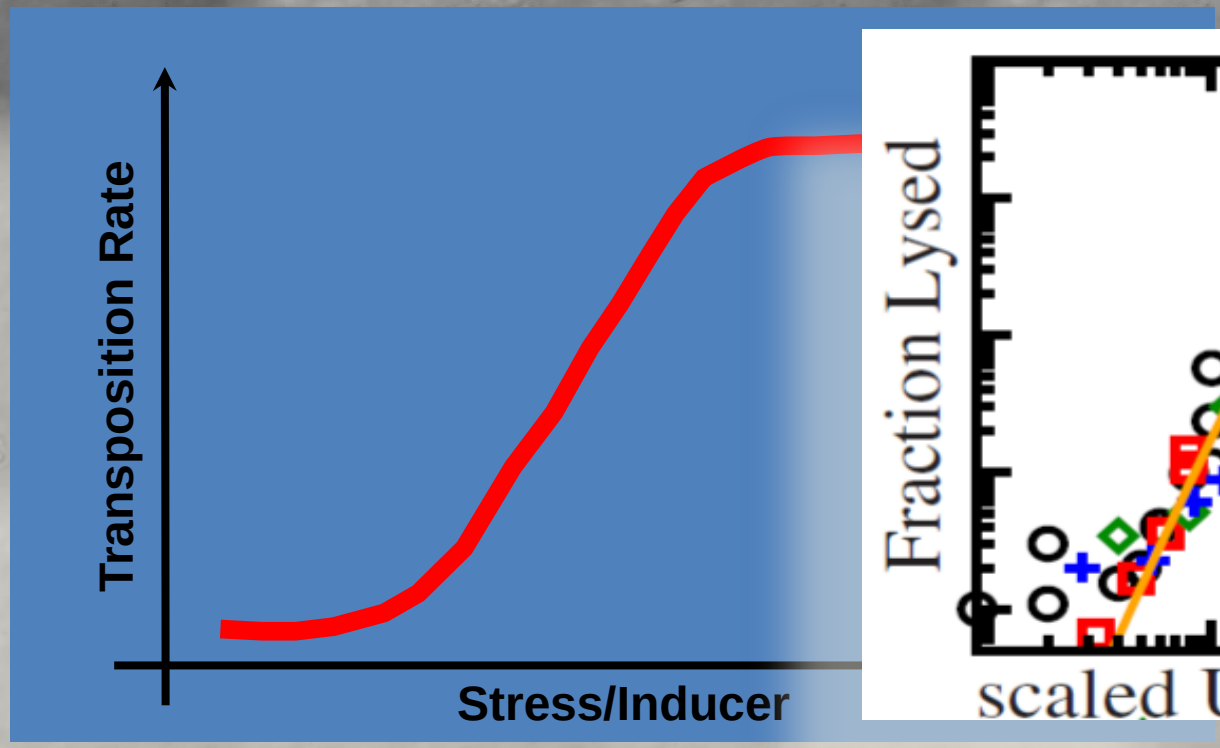
Compare

Does population model recapitulate experiment?



Real time population level dynamics

Is transposition rate a function of stress?



Can we explain transposon stress response based on known regulatory mechanisms?

[Goldenfeld and Golding, *PRE Rapid Communications*, 80, 030901 (R):1

James O'Dwyer

Applying statistical mechanics to ecology

James O'Dwyer

I am a theoretical ecologist, and my research focus is on the connections between macroecological patterns and the processes that underly these patterns. I work with data ranging from tropical forest communities, to plant and human host-associated microbial communities, and marine microbial data. These systems all have their own unique features and biology, and a common thread throughout my research is to understand both what is universal across these different systems, and also what are the signatures of their differences.

(1) Emergent phylogenetic patterns. I have identified highly consistent patterns across different bacterial communities, and related these patterns to a family of models known as coalescents much as with equilibrium phenomena in physics, many underlying processes coarse-grain to this same family of macroecological patterns.

(2) Dynamics of complexity across multiple scales of organization. Many biological systems seem driven to higher complexity over long timescales for example, the major transitions in organismal complexity. I am proposing to investigate whether such transitions occur across multiple levels of biological organization. When and why does complexity increase at the level of populations, ecological communities or whole ecosystems, in contrast to the organismal level? And what are the appropriate range of metrics to quantify this complexity? I plan to address these questions both in terms of theoretical models, and in the longer term with empirical and experimental data.

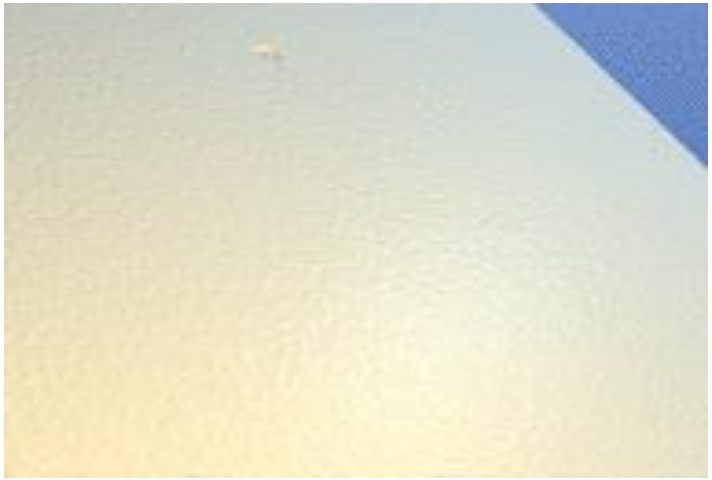
Nigel Goldenfeld

Statistical mechanics of ecology and evolution, metagenomics, the origin of life

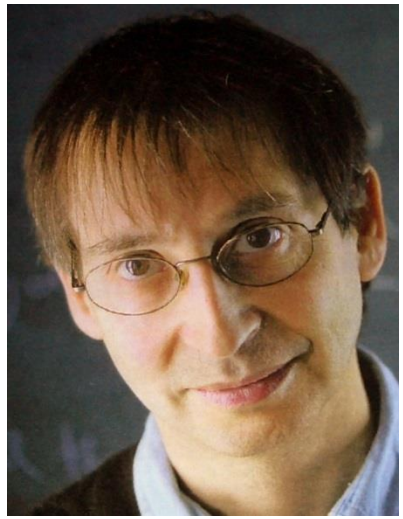
Microbial ecology

How does the metabolism of microbes influence the dynamics of the environment?

We study this at Yellowstone's geothermal hot springs, by observation and computer simulation.



Collective phenomena in biology



Nigel Goldenfeld's group studies collective dynamics in biological systems. The three main areas are evolution, ecology and systems biology.

We especially work on statistical mechanics applied to genes, microbes and viruses in marine environments, biofilms and the evolution of complex biological structures, such as the genetic code.

Microbes engage in a global marketplace for genes. Viruses and plasmids are the "brokers".

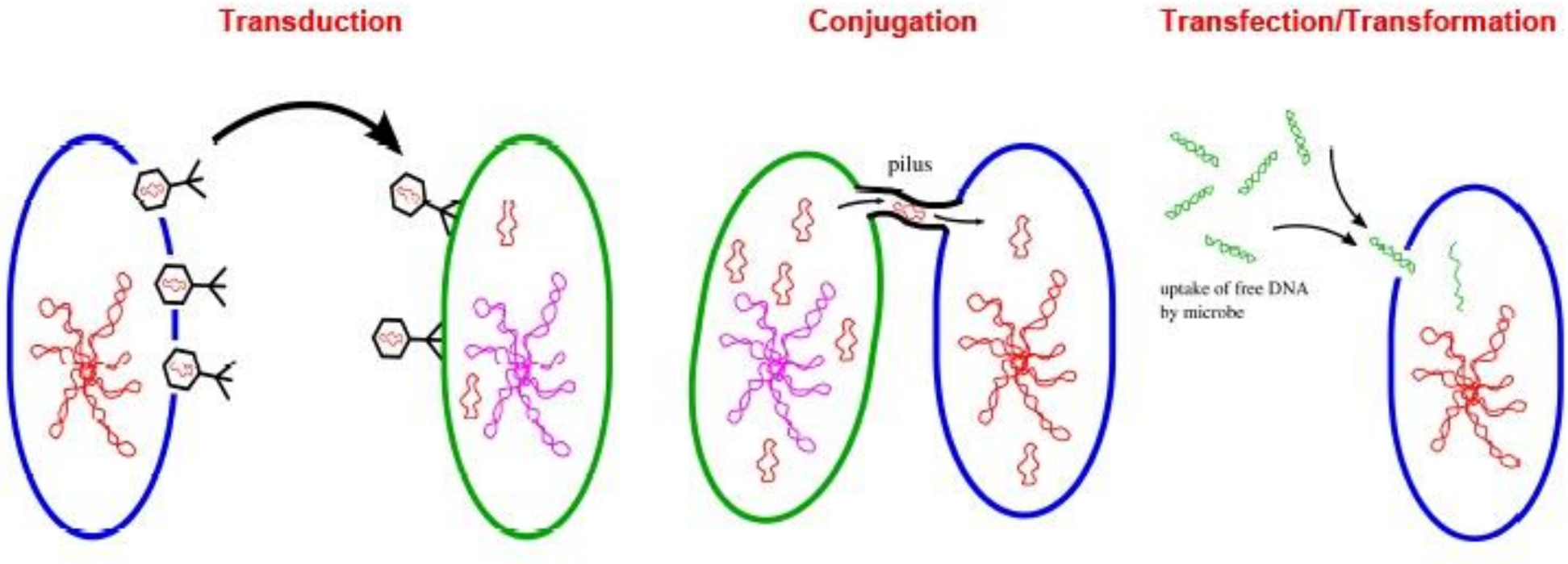
Microbes swap genes readily and acquire new characteristics without having to inherit them. This is how bacteria have become immune to antibiotics after only 60 years.

Gene-swapping collective phenomena profoundly influence evolution, speciation and the global biosphere.

Cooperative effects in biology

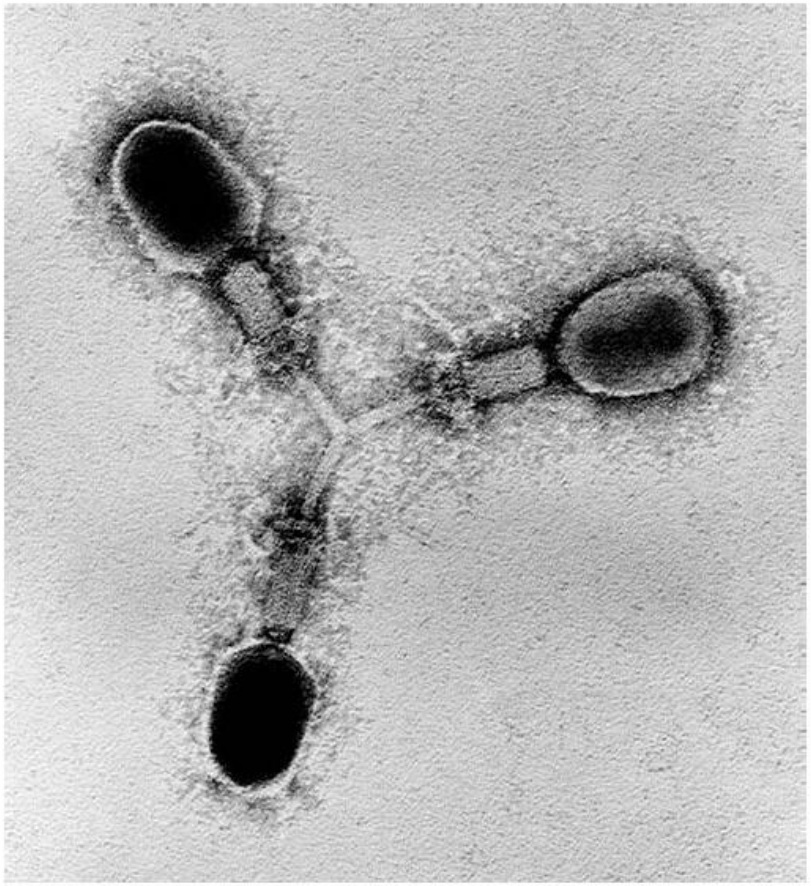
Example: horizontal gene transfer

Horizontal gene transfer



Microbes can do this … but what happens when they all do it?

Gene transfer between host and virus

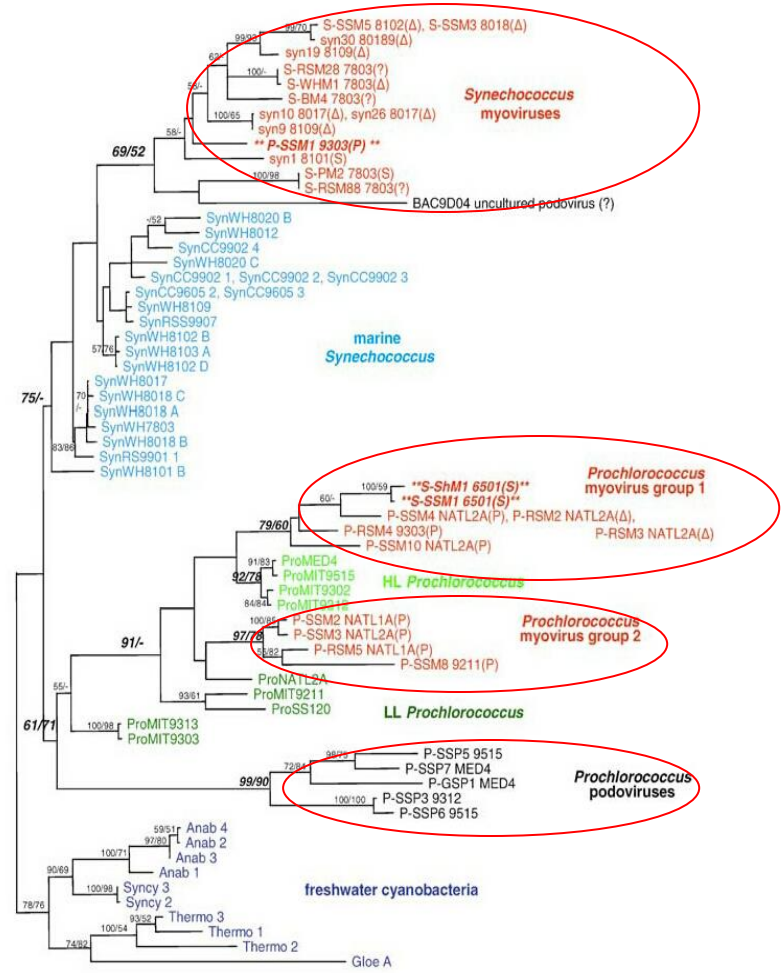


DOI: 10.1371/journal.pbio.0040264.g001

Cyanophages—viruses that infect photosynthetic marine bacteria—not only possess genes for photosynthesis but also exchange genetic material with their cyanobacterial hosts.

Hill, PlosBiol (2006)

Sullivan et al. , PlosBiol (2006)



PsbA gene acquired by phage

Phylogeny of psbA gene in cultured cyanobacteria and cyanophages

Is there a benefit to microbes of viruses?

"Therefore, mounting evidence indicates that host-like genes acquired by phages undergo a period of diversification in phage genomes and serve as a genetic reservoir for their hosts. Thus, a complex picture of overlapping phage and host gene pools emerges, where genetic exchange across these pools leads to evolutionary change for host and phage. Fully understanding the mechanisms of microbial and phage coevolution clearly requires an improvement in our ability to quantify horizontal gene transfer at the whole and partial gene level and in our ability to accurately estimate the relative fluxes into and out of these pools." (Sullivan et al. 2006)

Yes: microbe-phage interactions create a global reservoir of photosynthetic genes, benefiting both microbes and phages. **(E. Anderson (1966), N. Anderson (1970), S. Sonea (1988, 2001), M. Syvanen (1984) & many others, including L. Villareal, Weinbauer, Ochman, Lawrence, Groisman, Hatfull, Hendrix, Brussow …)**

Spread of antibiotic resistance genes

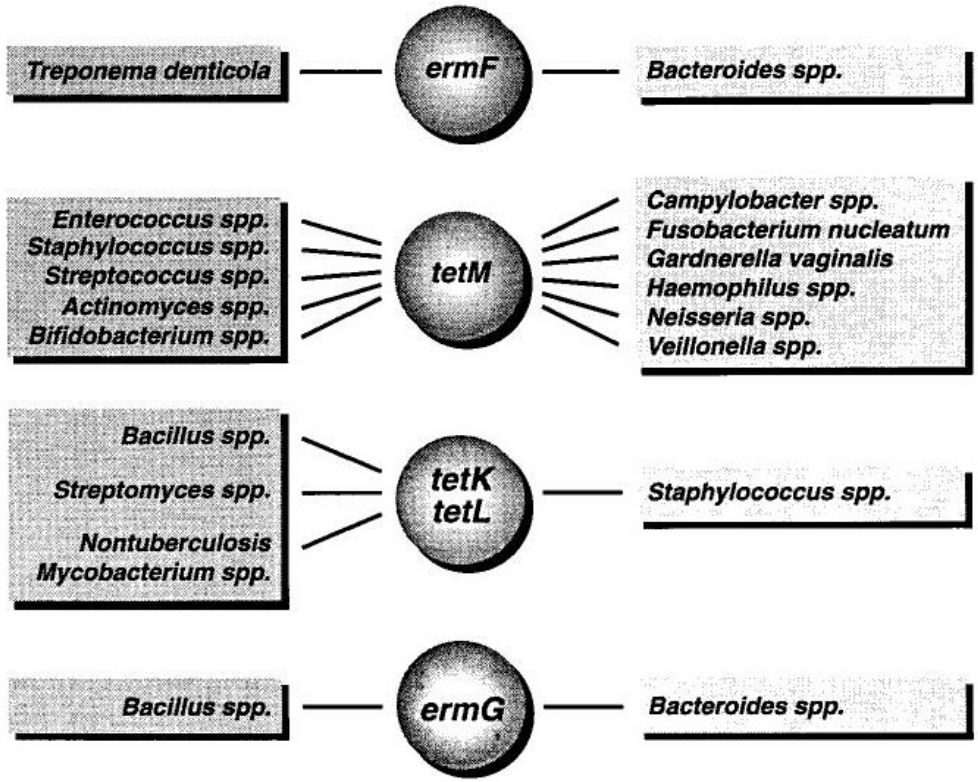


FIG. 1. Evidence that broad-host-range transfer of resistance genes occurs readily in nature (18–20). In each of the cases depicted here, virtually identical copies of the gene in the circle have been found in the species listed in the boxes connected to the circle. Such examples do not prove direct transfer between the species listed but indicate that there is some way for genes to move, whether directly or indirectly, between these genera.

Salyers & Amabile-Cuevas (1997)

- **Virtually identical copies of resistance genes found in distantly related bacteria**
  - Genes are being expressed
- **Genes cross species and phylum boundaries**
  - Gram-positive/enteric
  - Bacteroides/enteric
- **Genes cross physical locations**
  - Bacteroides spp. (colon)/Bacillus spp. (soil)

Life is Physics: Evolution as a Collective Phenomenon Far From Equilibrium

Nigel Goldenfeld[1] and Carl Woese[1,2]

Abstract

Evolution is the fundamental physical process that gives rise to biological phenomena. Yet it is widely treated as a subset of population genetics, and thus its scope is artificially limited. As a result, the key issues of how rapidly evolution occurs and its coupling to ecology have not been satisfactorily addressed and formulated. The lack of widespread appreciation for, and understanding of, the evolutionary process has arguably retarded the development of biology as a science, with disastrous consequences for its applications to medicine, ecology, and the global environment. This review focuses on evolution as a problem in nonequilibrium statistical mechanics, where the key dynamical modes are collective, as evidenced by the plethora of mobile genetic elements whose role in shaping evolution has been revealed by modern genomic surveys. We discuss how condensed matter physics concepts might provide a useful perspective in evolutionary biology, the conceptual failings of the modern evolutionary synthesis, the open-ended growth of complexity, and the quintessentially self-referential nature of evolutionary dynamics.

Annu. Rev. Condens. Matter Phys. 2011. 2:375–99

ESSAY

Putting the pieces together

Biology's next revolution

The emerging picture of microbes as gene-swapping collectives demands a revision of such concepts as organism, species and evolution itself.

Nigel Goldenfeld and Carl Woese

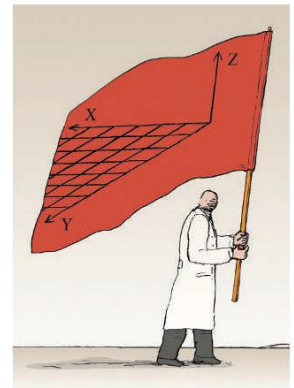
One of the most fundamental patterns of scientific discovery is the revolution in thought that accompanies a new body of data. Satellite-based astronomy has, during the past decade, overthrown our most cherished ideas of cosmology, especially those relating to the size, dynamics and composition of the Universe.

Similarly, the convergence of fresh theoretical ideas in evolution and the coming avalanche of genomic data will profoundly alter our understanding of the biosphere — and is likely to lead to revision of concepts such as species, organism and evolution. Here we explain why we foresee such a dramatic transformation, and why we believe the molecular reductionism that dominated twentieth-century biology will be superseded by an interdisciplinary approach that embraces collective phenomena.

The place to start is horizontal gene transfer (HGT), the non-genealogical transfer of genetic material from one organism to another — such as from one bacterium to another or from viruses to bacteria. Among microbes, HGT is pervasive and powerful — for example, in accelerating the spread of antibiotic resistance. Owing to HGT, it is not a good approximation to regard microbes as organisms dominated by individual characteristics. In fact, their communications by genetic or quorum-sensing channels indicate that microbial behaviour must be understood as predominantly cooperative.

In the wild, microbes form communities, invade biochemical niches and partake in biogeochemical cycles. The available studies strongly indicate that microbes absorb and discard genes as needed, in response to their environment. Rather than discrete genomes, we see a continuum of genomic possibilities, which casts doubt on the validity of the concept of a 'species' when extended into the microbial realm. The uselessness of the species concept is inherent in the recent forays into metagenomics — the study of genomes recovered from natural samples as opposed to clonal cultures. For example, studies of the spatial distribution of rhodopsin genes in marine microbes suggest such genes are 'cosmopolitan', wandering among bacteria (or archaea) as environmental pressures dictate.

Equally exciting is the realization that viruses have a fundamental role in the biosphere, in both immediate and long-term evolutionary senses. Recent work suggests that viruses are an important repository and



KAPLISTA

memory of a community's genetic information, contributing to the system's evolutionary dynamics and stability. This is hinted at, for example, by prophage induction, in which viruses latent in cells can become activated by environmental influences. The ensuing destruction of the cell and viral replication is a potent mechanism for the dispersal of host and viral genes.

It is becoming clear that microorganisms have a remarkable ability to reconstruct their genomes in the face of dire environmental stresses, and that in some cases their collective interactions with viruses may be crucial to this. In such a situation, how valid is the very concept of an organism in isolation? It seems that there is a continuity of energy flux and informational transfer from the genome up through cells, community, virosphere and environment. We would go so far as to suggest that a defining characteristic of life is the strong dependency on flux from the environment — be it of energy, chemicals, metabolites or genes.

Nowhere are the implications of collective phenomena, mediated by HGT, so pervasive and important as in evolution. A computer scientist might term the cell's translational apparatus (used to convert genetic information to proteins) an 'operating system', by which all innovation is communicated and realized. The fundamental role of translation, represented in particular by the genetic code, is shown by the clearly documented optimization of the code. Its special role in any form of life leads to the striking prediction that early life evolved in a lamarckian way, with vertical descent marginalized by the more powerful early forms of HGT.

Refinement through the horizontal sharing of genetic innovations would have triggered an explosion of genetic novelty, until the level of complexity required a transition to the current era of vertical evolution. Thus, we regard as regrettable the conventional concatenation of Darwin's name with evolution, because other modalities must also be considered.

This is an extraordinary time for biology, because the perspective we have indicated places biology within a context that must necessarily engage other disciplines more strongly aware of the importance of collective phenomena. Questions suggested by the generic energy, information and gene flows to which we have alluded will probably require resolution in the spirit of statistical mechanics and dynamical systems theory. In time, the current approach of post-hoc modelling will be replaced by interplay between quantitative prediction and experimental test, nowadays more characteristic of the physical sciences.

Sometimes, language expresses ignorance rather than knowledge, as in the case of the word 'prokaryote', now superseded by the terms archaea and bacteria. We foresee that in biology, new concepts will require a new language, grounded in mathematics and the discoveries emerging from the data we have highlighted. During an earlier revolution, Antoine Lavoisier observed that scientific progress, like evolution, must overcome a challenge of communication: "We cannot improve the language of any science without at the same time improving the science itself; neither can we, on the other hand, improve a science without improving the language or nomenclature which belongs to it." Biology is about to meet this challenge. ■

Nigel Goldenfeld is in the Department of Physics and Institute for Genomic Biology, University of Illinois at Urbana-Champaign, 1110 West Green Street, Urbana, Illinois 61801, USA. Carl Woese is in the Department of Microbiology and Institute for Genomic Biology, 601 South Goodwin Avenue, Urbana, Illinois 61801, USA.

FURTHER READING

Frigaard, N., Martinez, A., Mincer, T. & DeLong, E. *Nature* **439,** 847–850 (2006).

Sullivan, M. *et al. PLoS Biol.* **4,** e234 (2006).

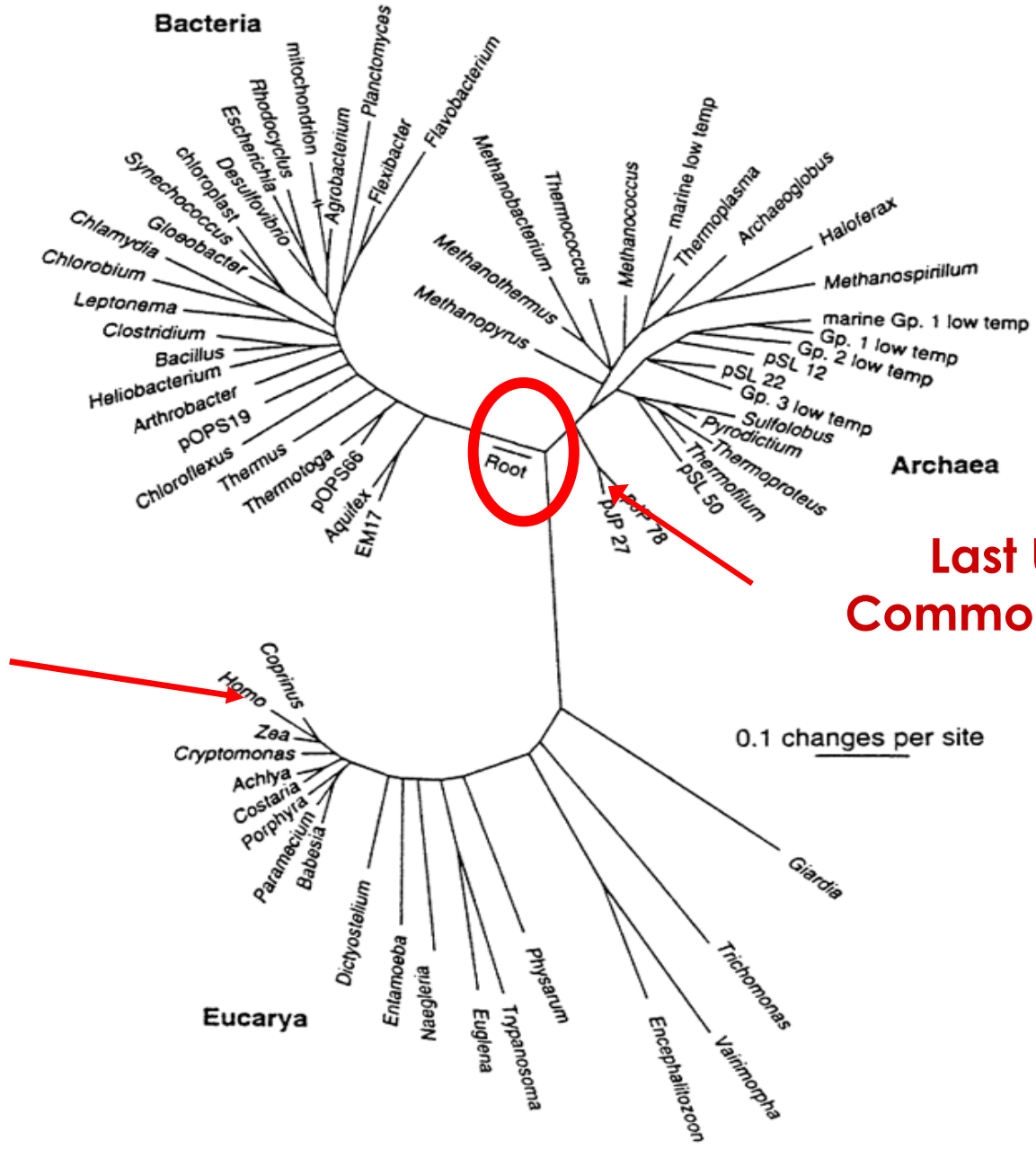
Pedulla, M. *et al. Cell* **113,** 171–182 (2003).

Vetsigian, K., Woese, C. & Goldenfeld, N. *Proc. Natl Acad. Sci. USA* **103,** 10696–10701 (2006).

For other essays in this series, see http://nature.com/nature/focus/arts/connections/index.html

CONNECTIONS

The Tree of Life



You are here

Last Universal Common Ancestor ?

- NR Pace, Science 1997

If we rebooted life on Earth, would we have the same genetic code?

Yes! **(or very similar)**

The canonical genetic code is universal and nearly optimal in minimising errors

	U	C	A	G	
U	Phe	Ser	Tyr	Cys	U
					C
	Leu		STOP	STOP	A
				Trp	G
C	Leu	Pro	His	Arg	U
					C
			Gln		A
					G
A	Ile	Thr	Asn	Ser	U
					C
			Lys	Arg	A
	Met				G
G	Val	Ala	Asp	Gly	U
					C
			Glu		A
					G

Mechanism for genetic code evolution

PNAS

Collective evolution and the genetic code

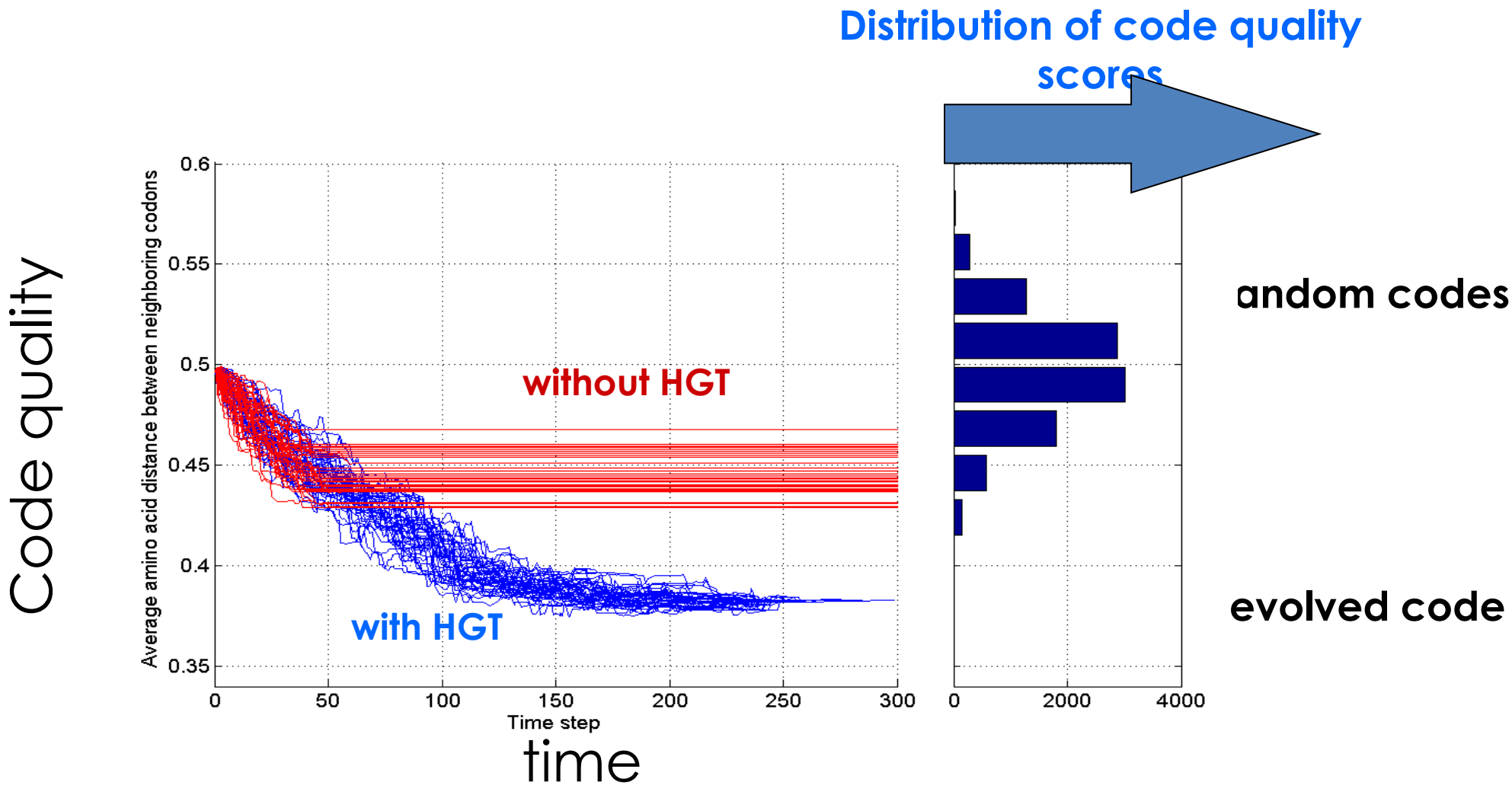
Kalin Vetsigian*, Carl Woese†‡§, and Nigel Goldenfeld*‡¶

Departments of *Physics and †Microbiology and ‡Institute for Genomic Biology, University of Illinois at Urbana–Champaign, Urbana, IL 61801

A dynamical theory for the evolution of the genetic code is presented, which accounts for its universality and optimality. The central concept is that a variety of collective, but non-Darwinian, mechanisms likely to be present in early communal life generically lead to refinement and selection of innovation-sharing protocols, such as the genetic code. Our proposal is illustrated by using a simplified computer model and placed within the context of a sequence of transitions that early life may have made, before the emergence of vertical descent.

10696–10701 | PNAS | July 11, 2006 | vol. 103 | no. 28

Evolution of code quality

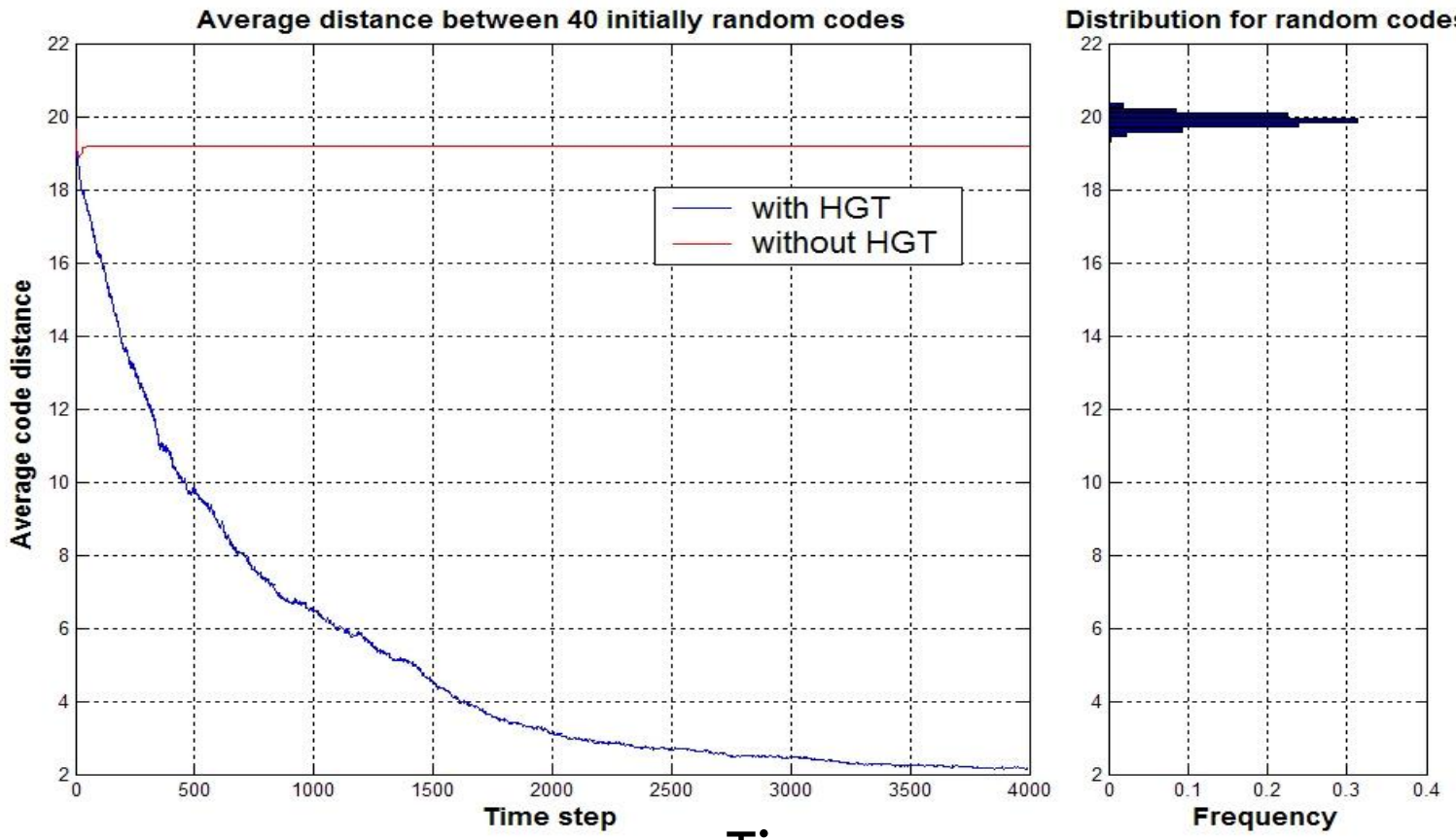


HGT leads to optimality

Evolution of code distances

Distribution of code distances

Average code distance



random codes

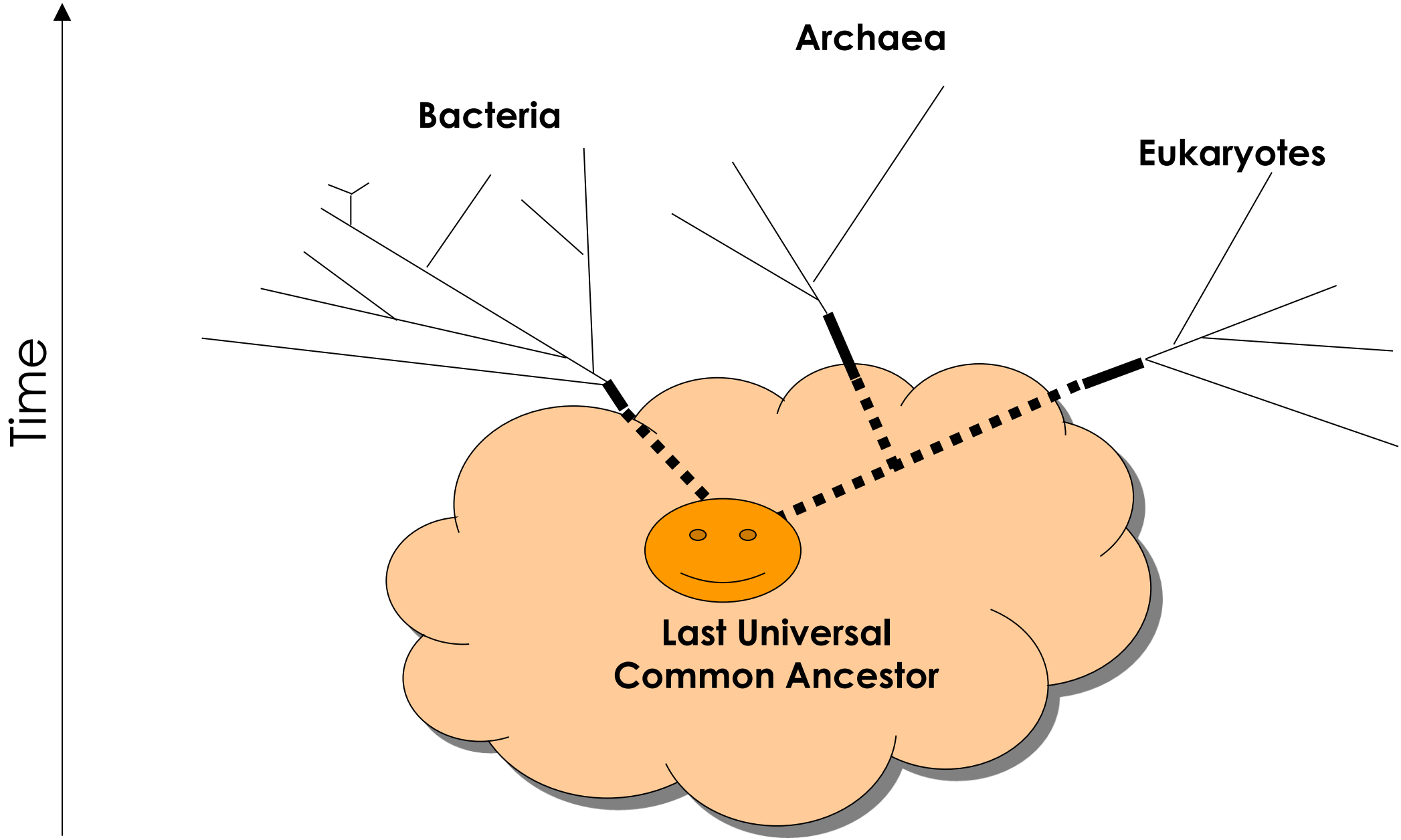
evolved code

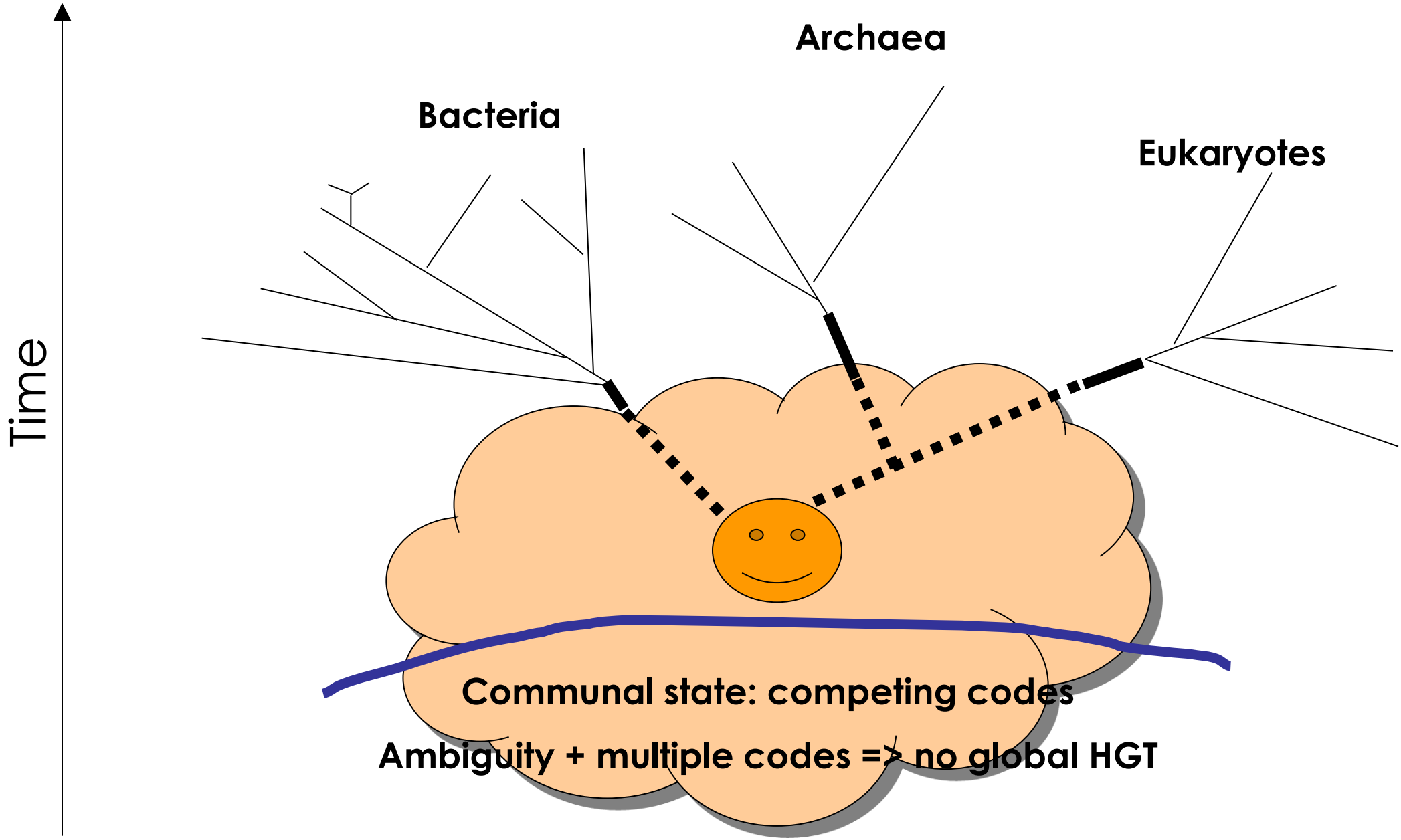
Time

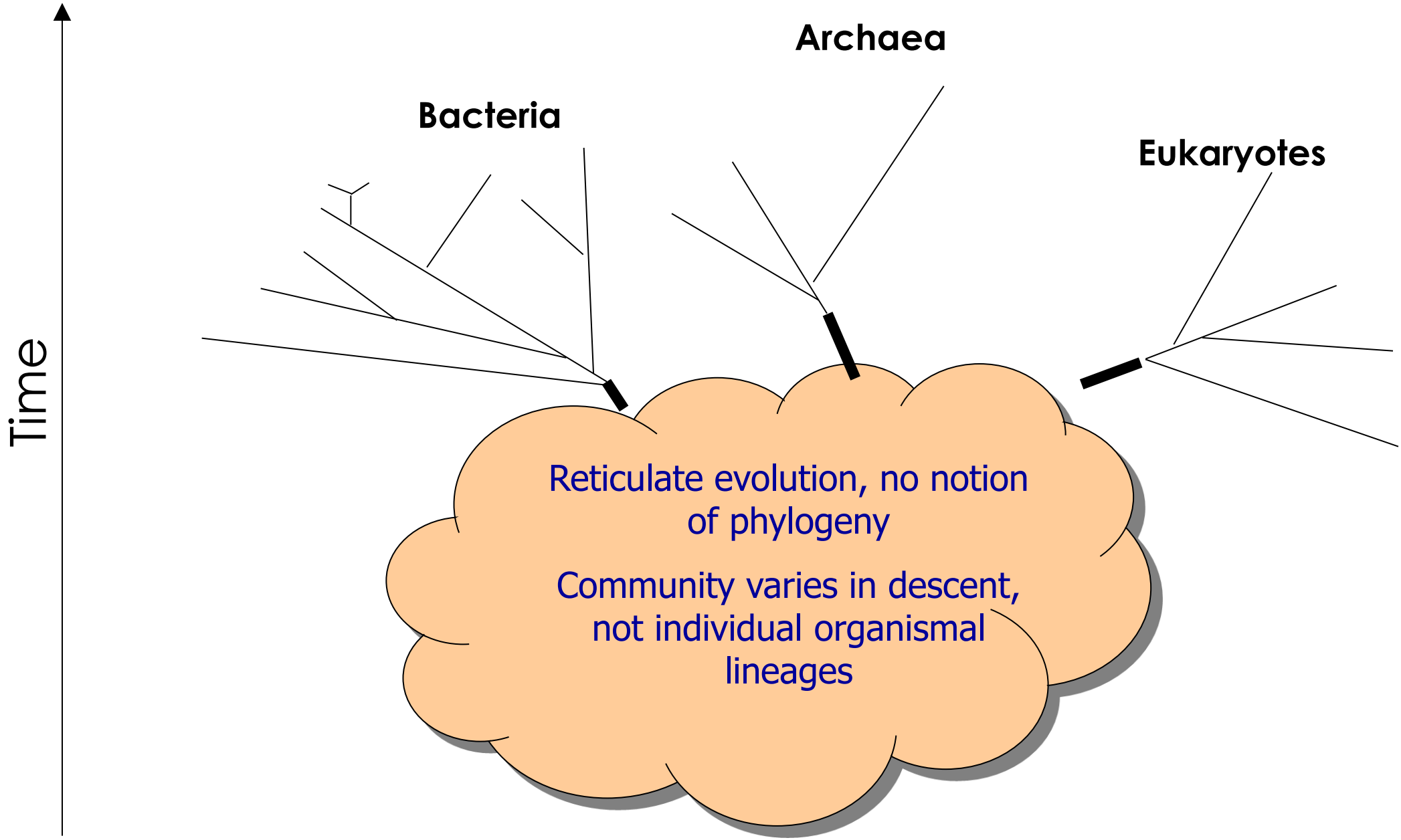
HGT leads to universality

The phase diagram of life …

… as inferred from the collective dynamics
of innovation-sharing protocols


Archaea
Bacteria
Eukaryotes
Time
Last Universal
Common Ancestor

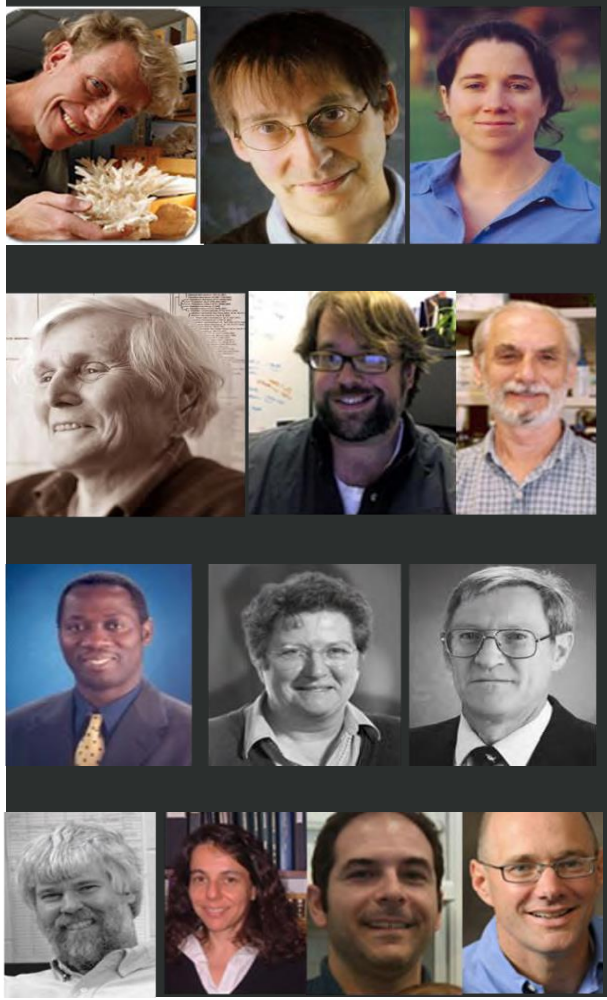

Archaea
Bacteria
Eukaryotes
Time
Communal state: competing codes
Ambiguity + multiple codes => no global HGT


Archaea
Bacteria
Eukaryotes
Time
Reticulate evolution, no notion of phylogeny
Community varies in descent, not individual organismal lineages

INSTITUTE FOR UNIVERSAL BIOLOGY

NASA ASTROBIOLOGY INSTITUTE

Institute for Universal Biology



- One of two new research groups joining NASA Astrobiology Institute (NAI)

BIG QUESTIONS:

- Why does life exist?
- How does it arise in different environments and planets?
- How did life evolve before there were genes, species, individual organisms and cells? Clearly not Darwinian!
- What was the nature of evolution at this early time?

BIG ANSWERS

- Build a “Hubble telescope for genes”, exploring deep evolutionary time
- Seek signatures of early collective states of life occurring before individual organisms on earth

- Highly diverse research team includes fields of microbiology, geobiology, computational chemistry, genomics, physics and engineering. This research could only be done at UIUC.
- Significant outreach component - new middle school teacher partnership, web-based video series, massive online open astrobiology course (pending Coursera inclusion).

Positions available




- Nigel Goldenfeld (theory; physics, CPLC, IGB)
- Tom Kuhlman (experiment, physics, CPLC)
- Seppe Kuehn (experiment, physics, CPLC)
- James O’Dwyer (theory; plant biology, IGB)