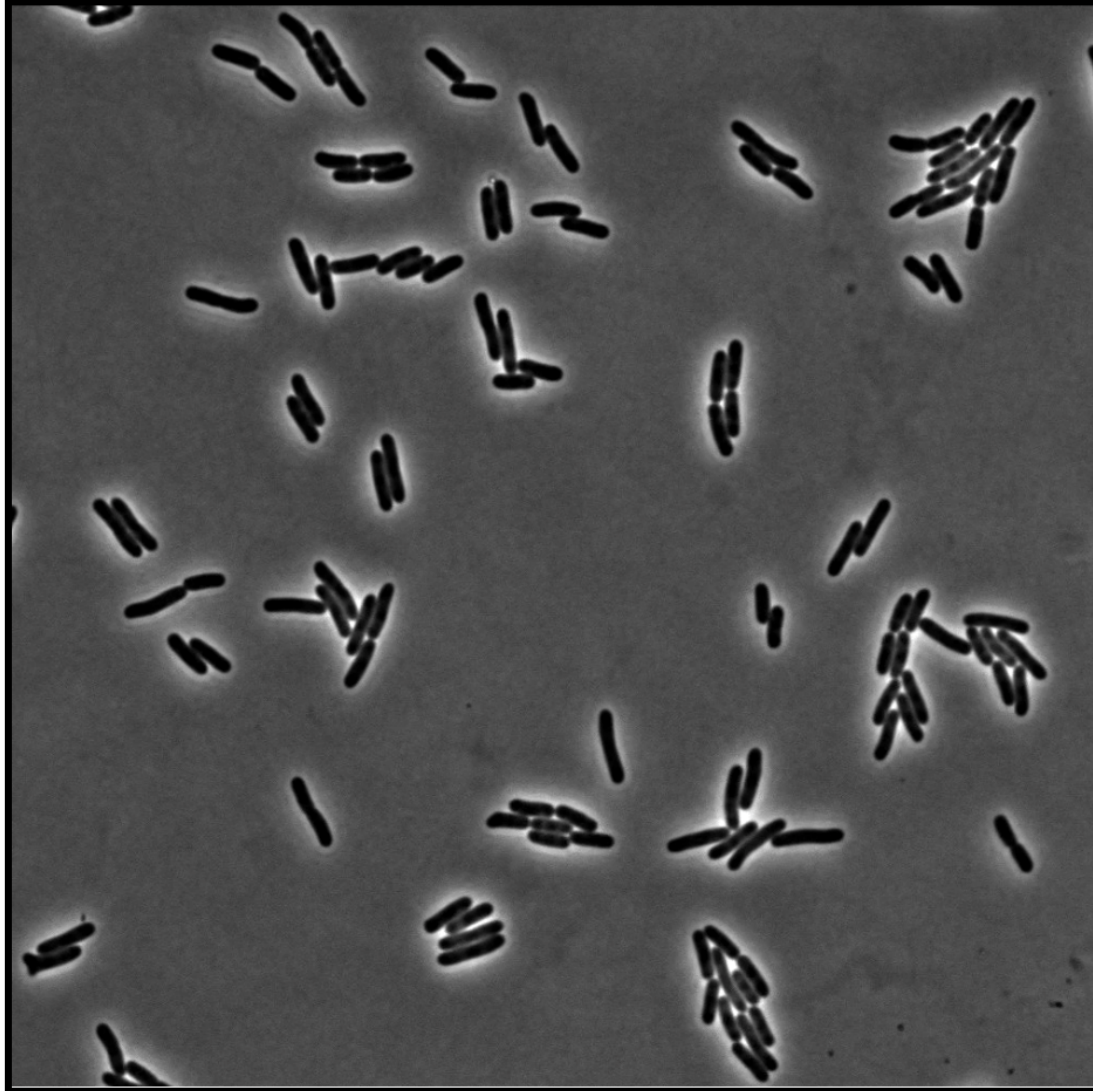


Towards a Whole-Cell Model of *Escherichia coli*

Derek Macklin
Covert Lab
Stanford University

How does a cell work?

How does a bacterial cell work?

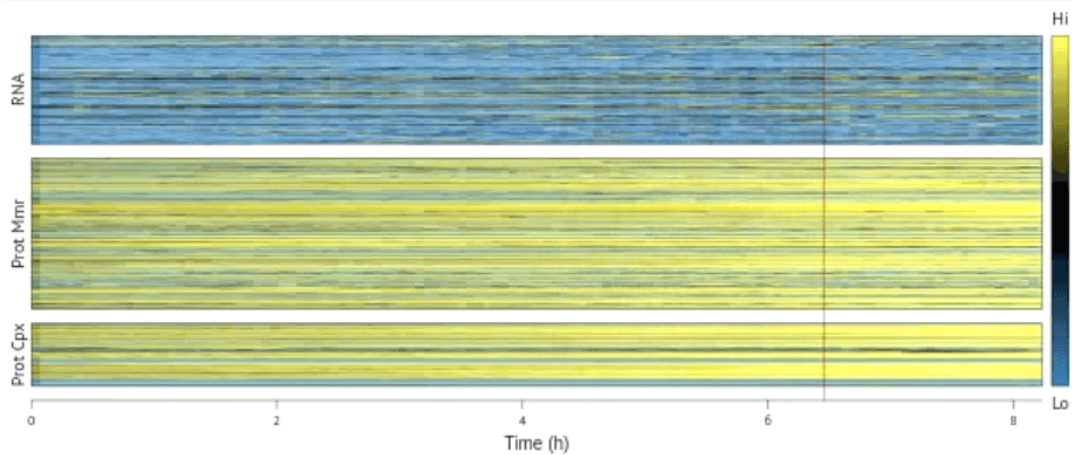


Credit: David Van Valen

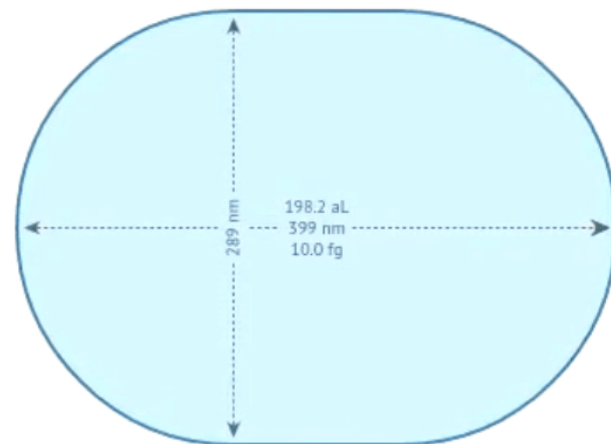
"The ultimate test of understanding a simple cell, more than being able to build one, would be to build a computer model of the cell, because that really requires understanding at a deeper level."

—Clyde Hutchison

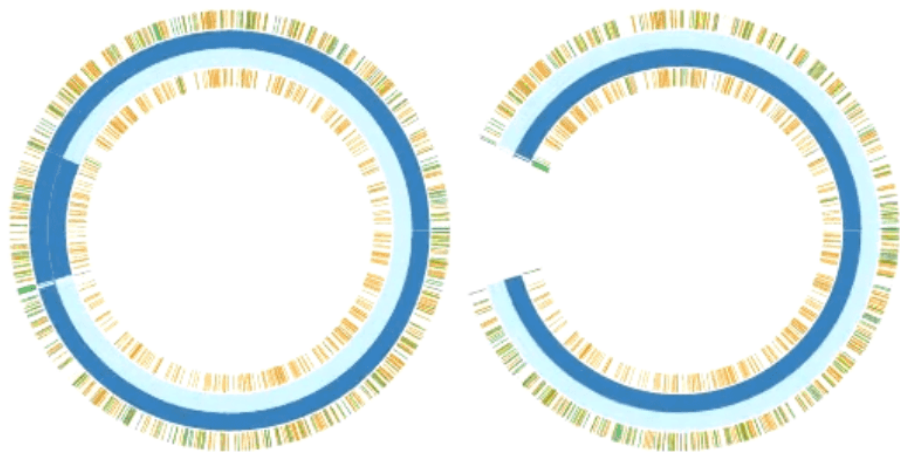
Gene expression



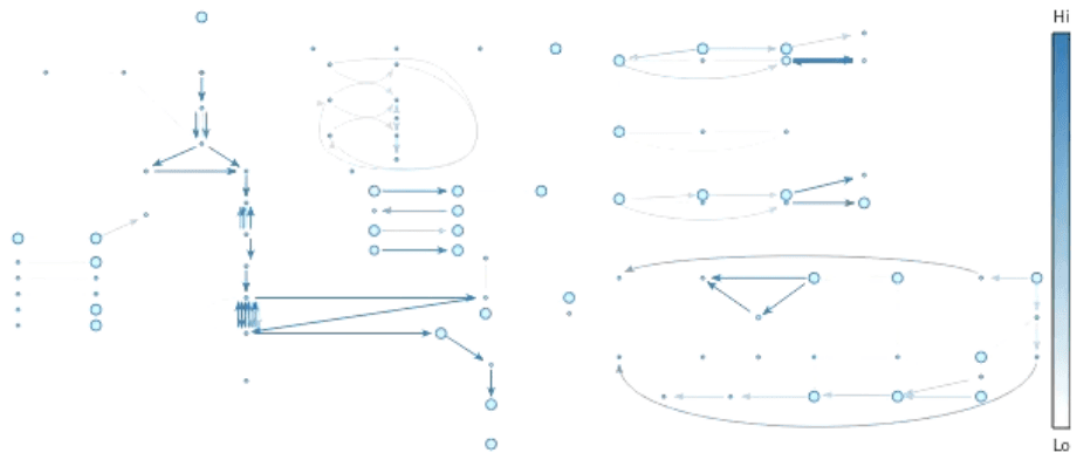
Cell shape



DNA replication, protein occupancy, methylation, & damage



Metabolism



Mycoplasma genitalium

Smallest culturable self-replicating organism

525 genes

300-500 nm diameter

Requires biosafety level 2 space

Can't see under the light microscope

Difficult to genetically manipulate

Escherichia coli

60+ years of published data

Experimentally tractable

10X more genes than *M. genitalium*

50X more molecules than *M. genitalium*

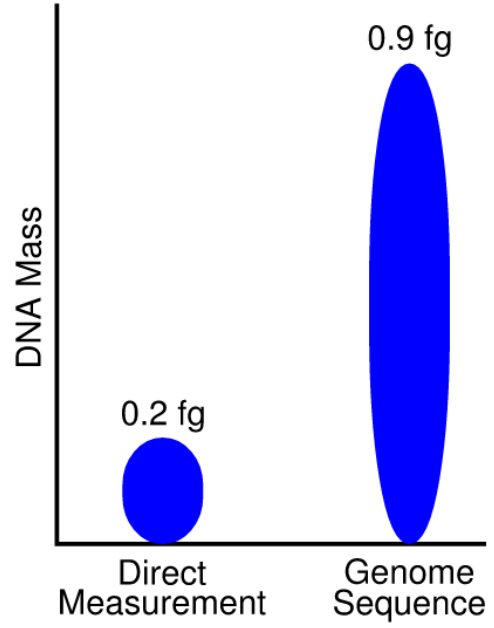
Challenges in whole-cell modeling

Don't have governing equations of a cell

Data

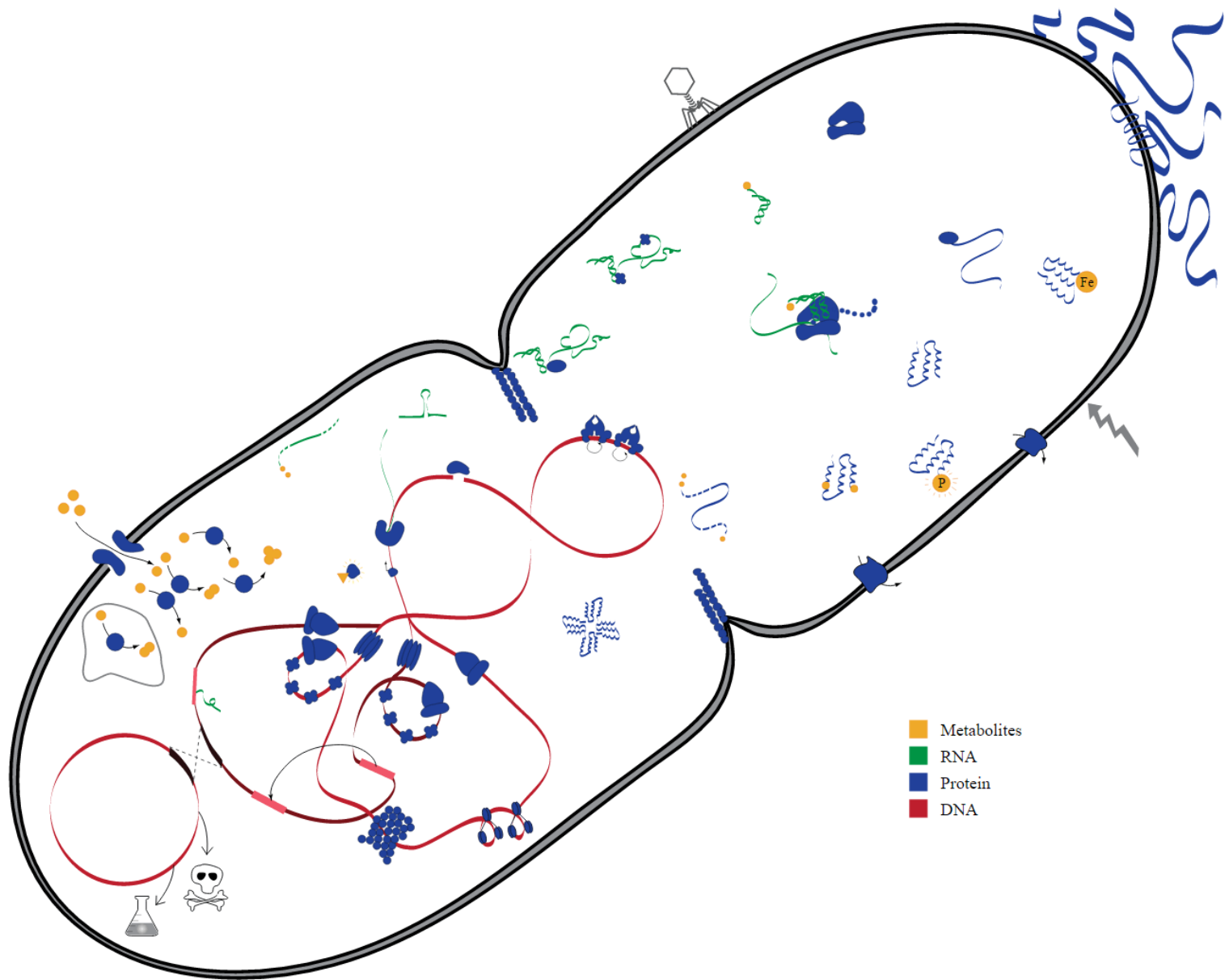
Sparsity

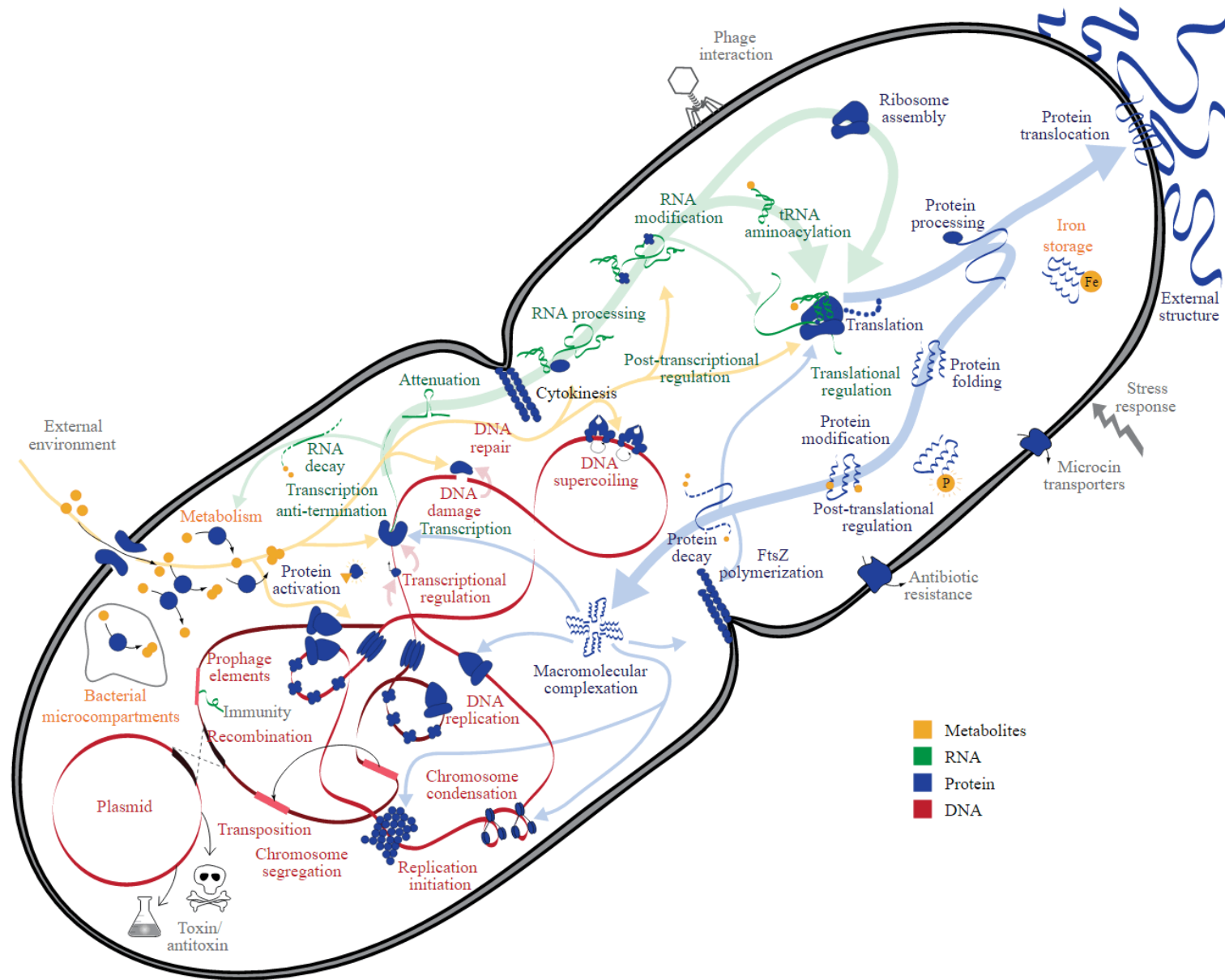
Variability

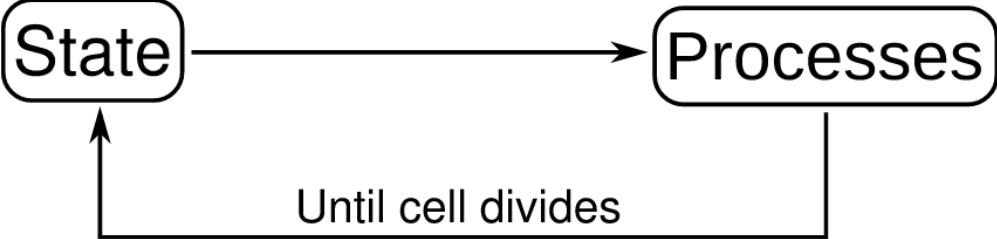


Morowitz et al. 1962
Glass et al. 2006

How do you build a whole-cell model?







BOOLEAN
MODELS

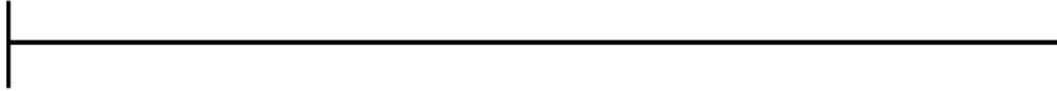
CONSTRAINT-BASED
MODELS

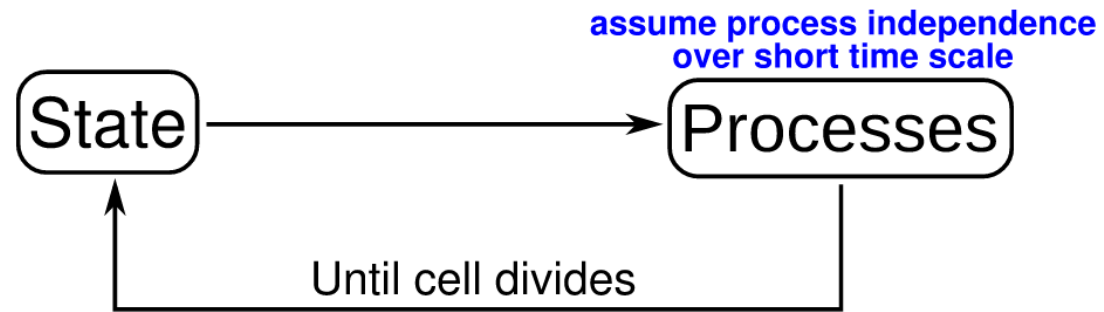
ODE
MODELS

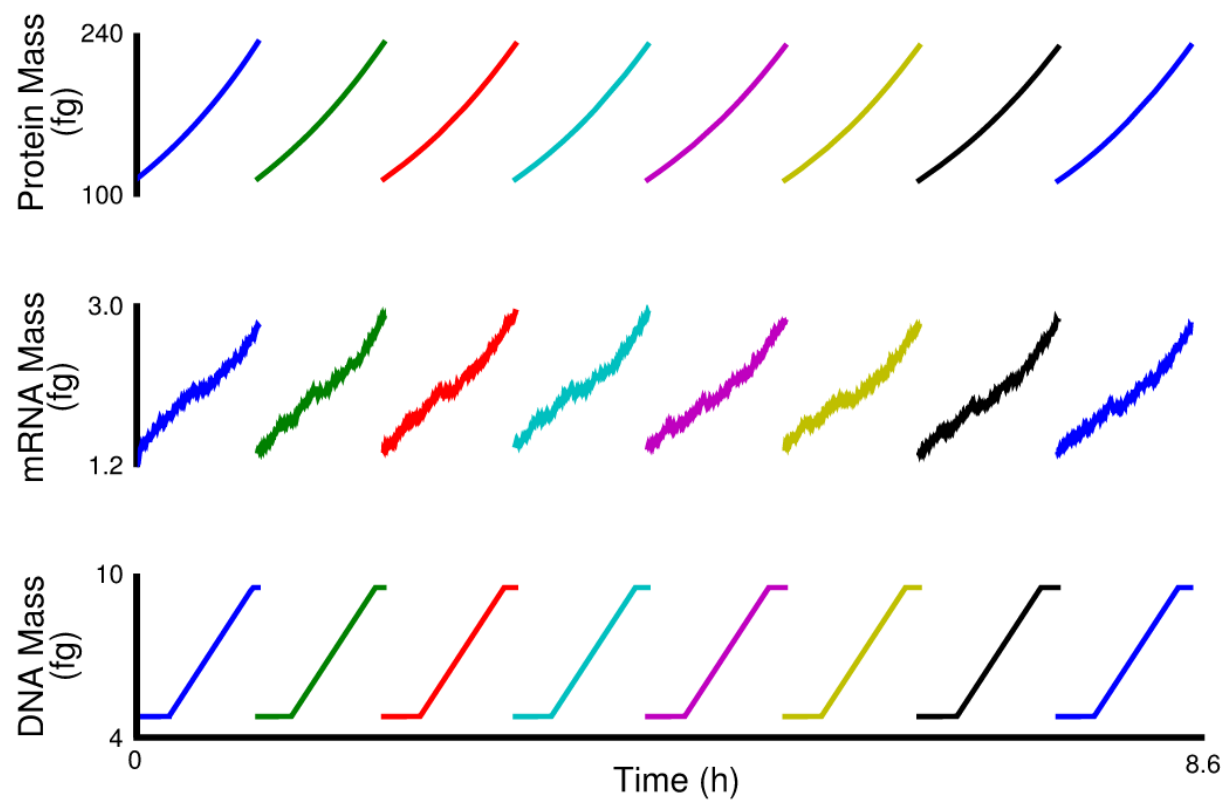
STOCHASTIC
MODELS

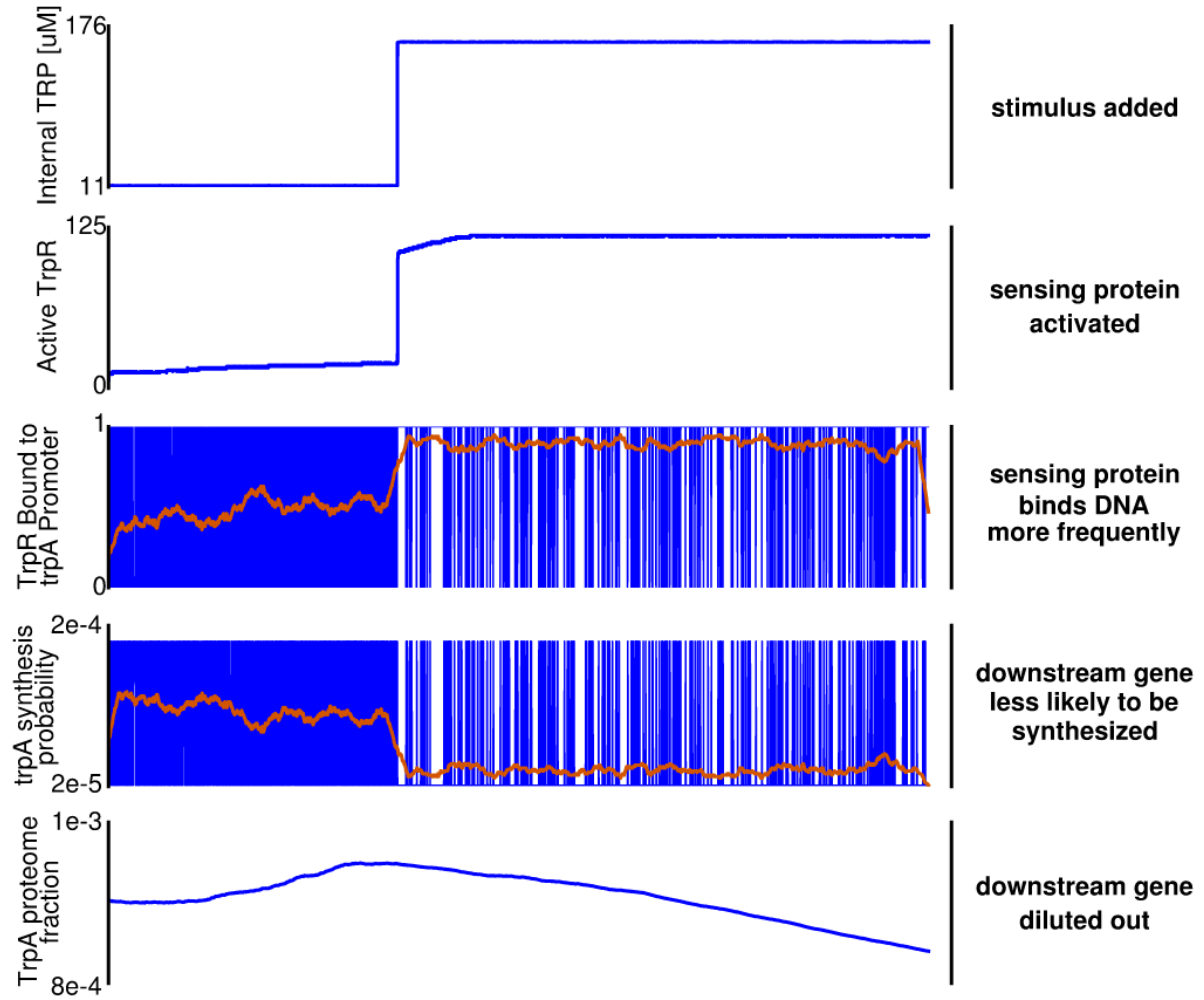
Processes we know
little about

Processes we know
a lot about







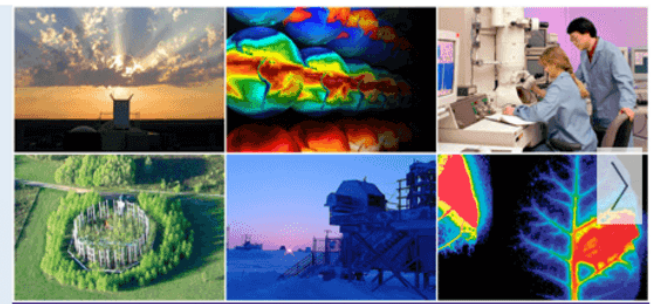


Going forward

- BER Home**
- About
- Research
- Facilities
- Science Highlights
- Benefits of BER
- Funding Opportunities
- Biological & Environmental Research Advisory Committee (BERAC)
- Community Resources

Understanding Complex Biological and Environmental Systems

across many spatial and temporal scales by coupling theory, observations, experiments, models, and simulations.



DISCOVERING the physical, chemical, and biological drivers of climate change



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CONTACT INFORMATION
Biological and Environmental Research
 U.S. Department of Energy
 SC-23/Germantown Building
 1000 Independence Ave., SW
 Washington, DC 20585
 P: (301) 903-3251
 F: (301) 903-5051
 E: [Email Us](#)


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Mission

BER advances world-class biological and environmental research programs and scientific user facilities to support DOE's energy, environment, and basic research missions.

The Biological and Environmental Research (BER) program supports fundamental research and scientific user facilities to address diverse and critical global challenges. The program seeks to understand how genomic information is translated to functional capabilities, enabling more confident redesign of microbes and plants for sustainable [biofuel production, improved carbon storage, or contaminant bioremediation](#). BER research advances understanding of the roles of Earth's biogeochemical systems (the atmosphere, land, oceans, sea ice, and subsurface) in determining climate so we can predict climate decades or centuries into the future, information needed to plan for future energy and resource needs. Solutions to these challenges are driven by a foundation of scientific knowledge and inquiry in atmospheric chemistry and physics, ecology, biology, and biogeochemistry.

ANNOUNCEMENTS

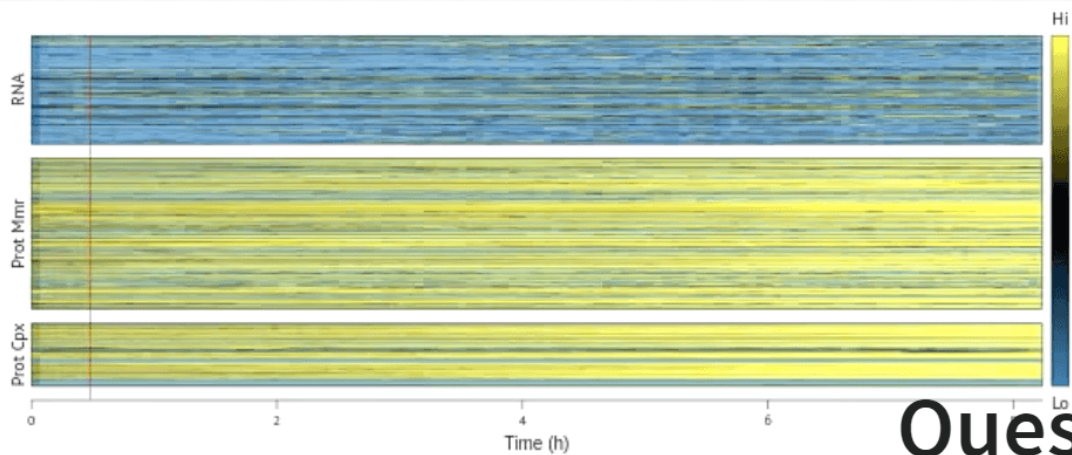
New FOA  (442KB) on Bioenergy Research Centers. This Funding Opportunity Announcement (FOA) requests applications from the scientific community for Bioenergy Research Centers (BRCs) that develop novel biological solutions for the production of specialty biofuels and other bioproducts from plants

Acknowledgments

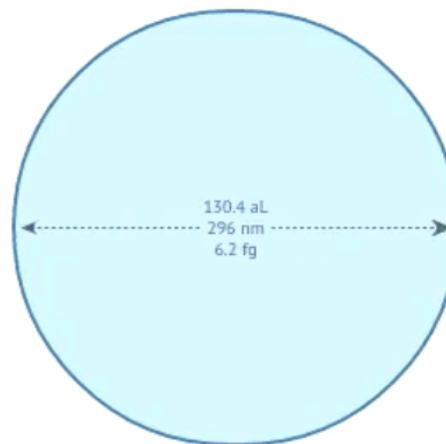


DOE CSGF Fellowship
Benchmark Stanford Graduate Fellowship
Siebel Scholarship

Gene expression



Cell shape



Questions?

DNA replication, protein occupancy, methylation, & damage



Metabolism

