Cellular Information Processing

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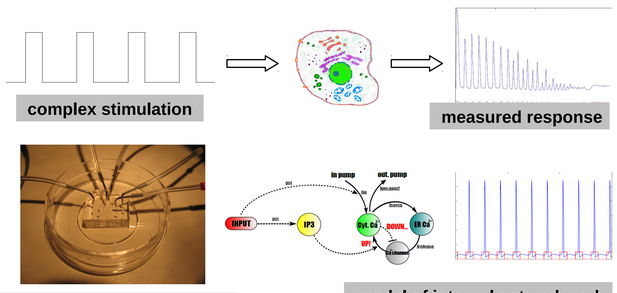
cellular interrogation

PLOS | COMPUTATIONAL BIOLOGY

Cellular Interrogation: Exploiting Cell-to-Cell Variability to Discriminate Regulatory Mechanisms in Oscillatory Signalling

Can we develop an "outside-in" strategy of interrogating cells to discover how they work, which complements the usual "inside-out" strategy of pulling cells apart by genetics and biochemistry? How can we design complex stimulations which can distinguish between different models of the internal molecular network?



polynomial invariants

Biophysical Journal Volume 95 December 2008 5533–5543

The Geometry of Multisite Phosphorylation

Journal of Theoretical Biology

Complex-linear invariants of biochemical networks

THE JOURNAL OF BIOLOGICAL CHEMISTRY

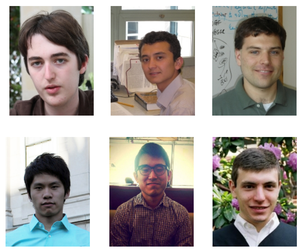
Dimerization and Bifunctionality Confer Robustness to the Isocitrate Dehydrogenase Regulatory System in *Escherichia coli*[*][S]

If a network of molecular reactions obeys mass-action kinetics, which is usually the case in biology, it yields a polynomial dynamical system, whose steady states form a real algebraic variety. By using methods of computational algebraic geometry, such as Gröbner bases, as well as the linear framework, we can often summarise the steady-state variety in a polynomial expression that we call an "invariant". We have found that invariants can tell us a great deal about network behaviour.

about us

We study how cells process information using a combination of experiments, mathematics and computation. We have a tradition of recruiting undergraduate students to our lab: over the last 10 years, 6 students have been first authors on published papers arising from their undergraduate work and 2 others have received Harvard's Thomas Hoopes Prize. This poster gives an overview of some of our research, with a focus on mathematical and computational problems, which are easier to accomplish within an internship or rotation. The photographs show some of the students who have worked in the lab over the years.

the linear framework



graph model for gene regulation

Bull Math Biol (2013) 75:2118–2149
DOI 10.1007/s11538-013-9884-8

Society for Mathematical Biology

ORIGINAL ARTICLE

Laplacian Dynamics on General Graphs

the FEBS Journal

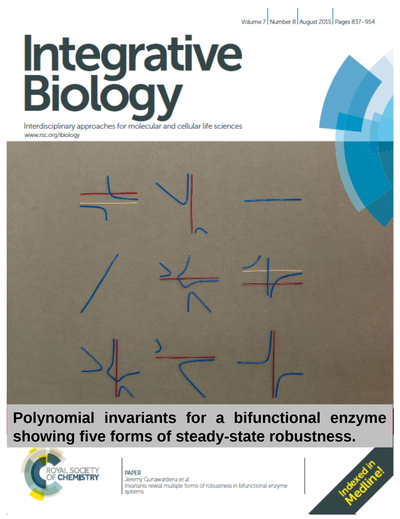
REVIEW ARTICLE

Time-scale separation – Michaelis and Menten's old idea, still bearing fruit

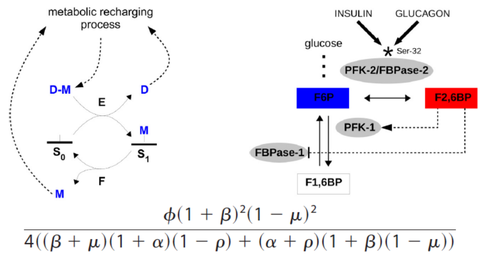
Cell

Information Integration and Energy Expenditure in Gene Regulation

We have developed a mathematical framework for doing time-scale separation in biochemical systems. It is based on graph theory and polynomial algebra. The framework allows us to eliminate the overwhelming molecular complexity found in cellular mechanisms like allostery, post-translational modification and gene regulation and construct mathematical representations of how these mechanisms process information. We are applying this framework to several biological problems and especially to gene regulation in eukaryotes, in collaboration with Angela DePace's lab.



Polynomial invariants for a bifunctional enzyme showing five forms of steady-state robustness.



$$\frac{\phi(1+\beta)^2(1-\mu)^2}{4((\beta+\mu)(1+\alpha)(1-\rho)+(\alpha+\rho)(1+\beta)(1-\mu))}$$

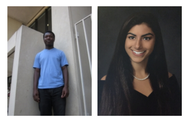
The formula above gives the sharpness with which a modification-demodification cycle (top left) switches in response to changes in enzyme concentration. It was calculated from an invariant derived using the linear framework. It explains why the bifunctional enzyme *6-phosphofructo-2-kinase/fructose-2,6-bisphosphatse* (PFK-2/FBPase-2) (top right), which regulates glucose homeostasis in the liver, is able to switch sharply between production and consumption of glucose, without exhibiting noisy, incoherent behaviour across different cells.

THE JOURNAL OF BIOLOGICAL CHEMISTRY

A Fundamental Trade-off in Covalent Switching and Its Circumvention by Enzyme Bifunctionality in Glucose Homeostasis*

ASBMB

computational pathology

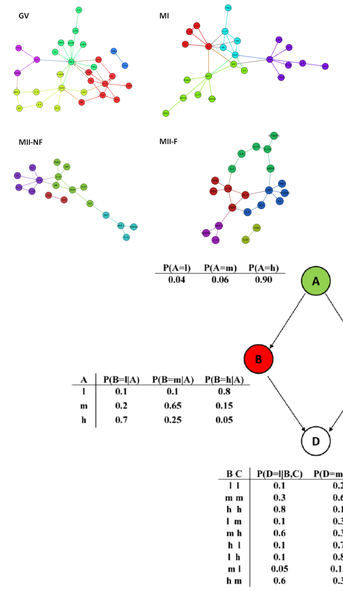


RESEARCH ARTICLE Open Access

Bayesian modeling suggests that IL-12 (p40), IL-13 and MCP-1 drive murine cytokine networks *in vivo*

BMC Systems Biology

Clinicians can acquire extensive molecular data from biopsy samples. But what do they tell us? Our lab is interested in cytokines, which provide aggregated information about the sample micro-environment and we are using high-dimensional computational techniques (Bayesian inference, topological data analysis, deep learning, etc) to develop predictive measures that can guide diagnosis and treatment, in collaboration with Nicolas Orsi at the Leeds Institute of Cancer and Pathology in England.



P(A=l)	P(A=m)	P(A=h)
0.04	0.06	0.90

P(E=l)	P(E=m)	P(E=h)
0.8	0.15	0.05

A	P(B=l|A)	P(B=m|A)	P(B=h|A)
l	0.1	0.1	0.8
m	0.2	0.65	0.15
h	0.7	0.25	0.05

A	P(C=l|A)	P(C=m|A)	P(C=h|A)
l	0.75	0.15	0.1
m	0.15	0.65	0.2
h	0.1	0.2	0.7

B C	P(D=l|B,C)	P(D=m|B,C)	P(D=h|B,C)
l l	0.1	0.2	0.7
m m	0.3	0.6	0.1
h h	0.8	0.1	0.1
l m	0.1	0.3	0.6
m h	0.6	0.3	0.1
h l	0.1	0.7	0.2
l h	0.1	0.8	0.1
m l	0.05	0.15	0.8
h m	0.6	0.3	0.1

Bayesian networks inferred for 41 follicular fluid cytokines during maturation of human oocytes.
GV: germinal vesicle; MI: metaphase I; MII-NF: metaphase II non-fertilised; MII-F, metaphase II fertilised.

Hypothetical Baysiean network, shown as a directed graph with a table associated to each vertex. Vertices are variables discretised into "low", "medium" and "high" values and the table gives the probability that the corresponding vertex has the specified discrete value, conditional on the parent vertices having specified discrete values.

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