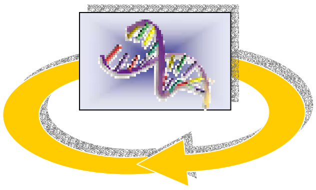
BCB 2004, Second Bertinoro Computational Biology Meeting
12-19 June 2004, University of Bologna Residential Center
Bertinoro (Forlì), Italy

Regulation of biochemical networks as interconnection: the *behavioral* approach



Lorenzo Farina
Department of Computer and System Science "A. Ruberti"
University of Rome "La Sapienza", Italy

Plant Computational Genomics Team

Experimental plant biology

Ida Ruberti, Nucleic Acids Research Center, Department of Genetic and Molecular Biology, University of Rome "La Sapienza"

Giorgio Morelli, Plant Biotechnology Unit, National Research Institute for Food and Nutrition (INRAN), Rome

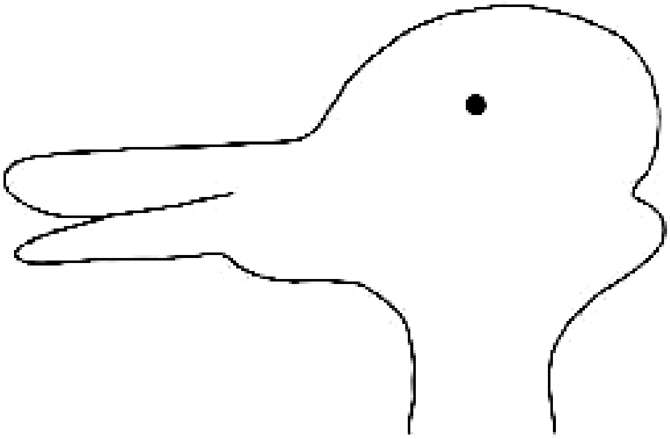
Dynamical systems & control engineering

Lorenzo Farina, Department of Computer and Systems Science, University of Rome "La Sapienza"

Additional researchers

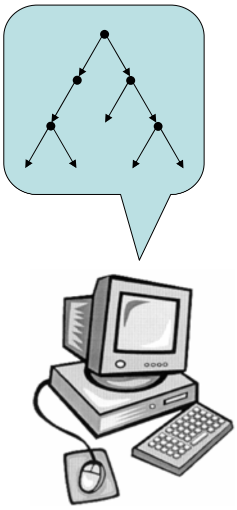
Paolo Marcatili (computer science) and **Paolo Uva** (PhD, biology)

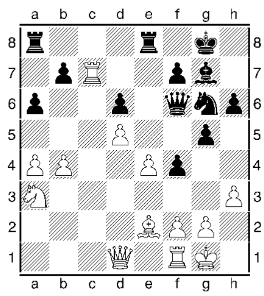
Observation vs theory

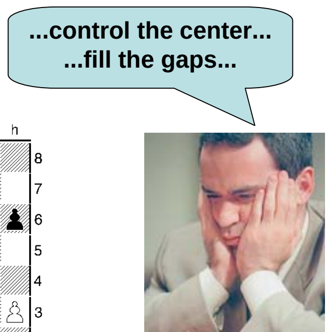


a duck or a rabbit?

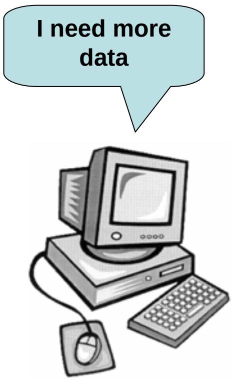
Kasparov vs Deep Blue - I

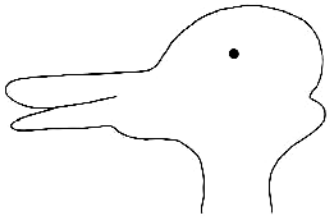


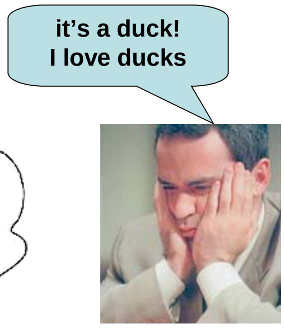




Kasparov vs Deep Blue - II

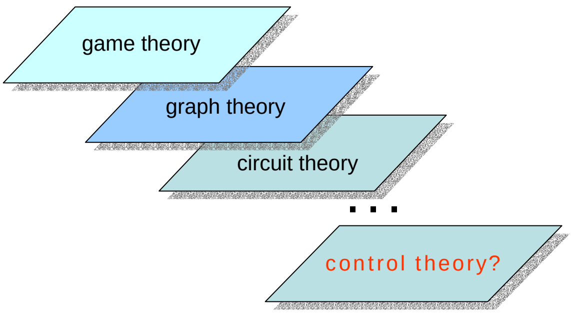






Metaphors and description spaces

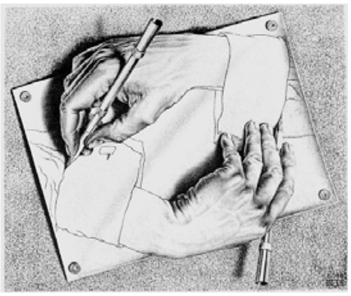
new metaphors *create* new description spaces or new contexts, that is they *provide meaning to observations*



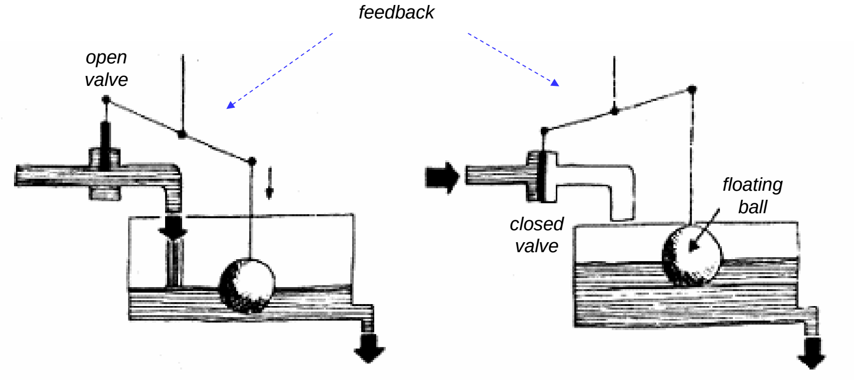
What is control theory?

- “Principles and methods used to design engineering systems that maintain desirable performance by automatically adapting to changes in the environment”
- More specifically, control theory is concerned with designing strategies that ensure the robust performance of a system
- Robustness is mainly provided by feedback
- Examples of control systems are everywhere

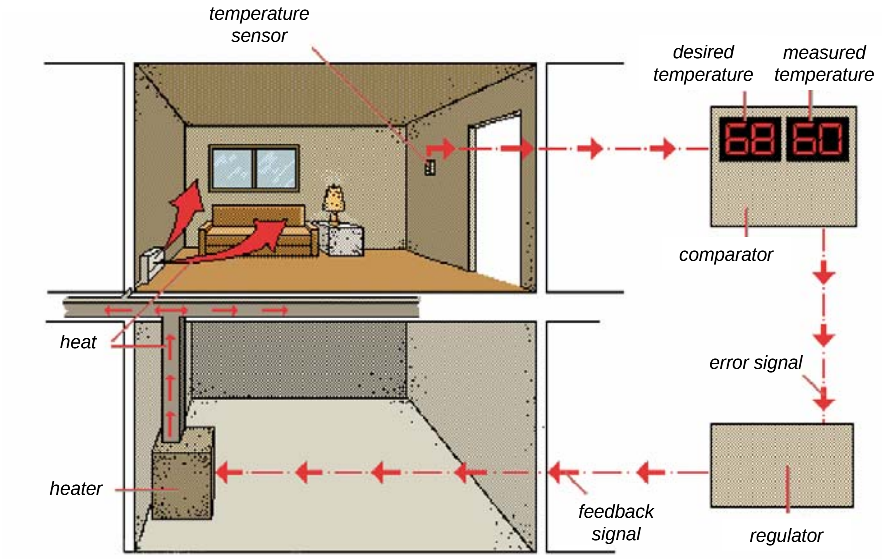
THE JOY OF FEEDBACK !



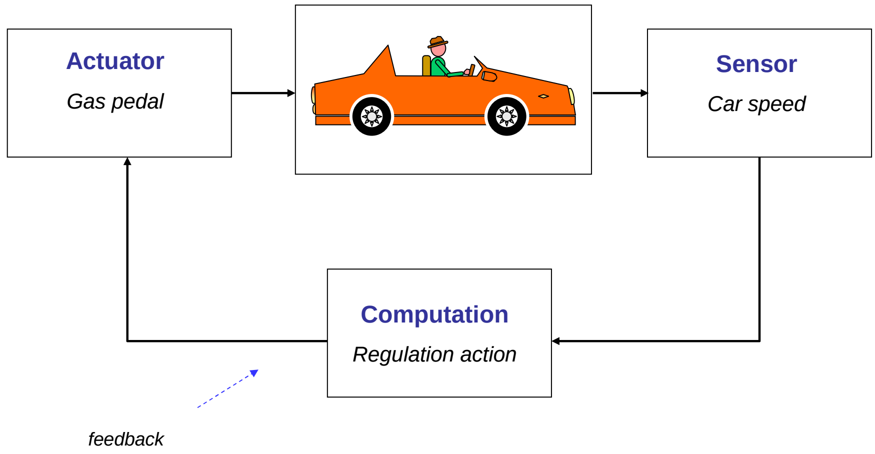
Water level control



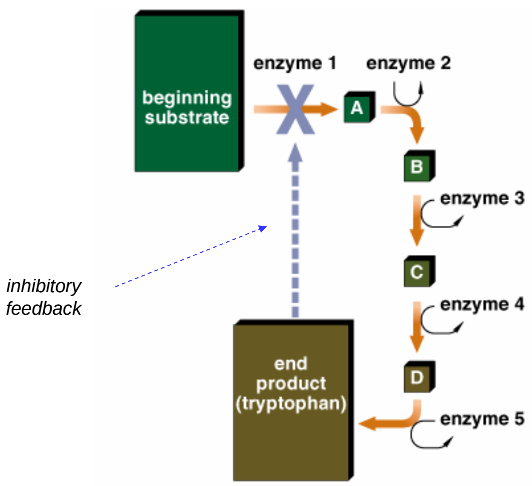
Thermostat



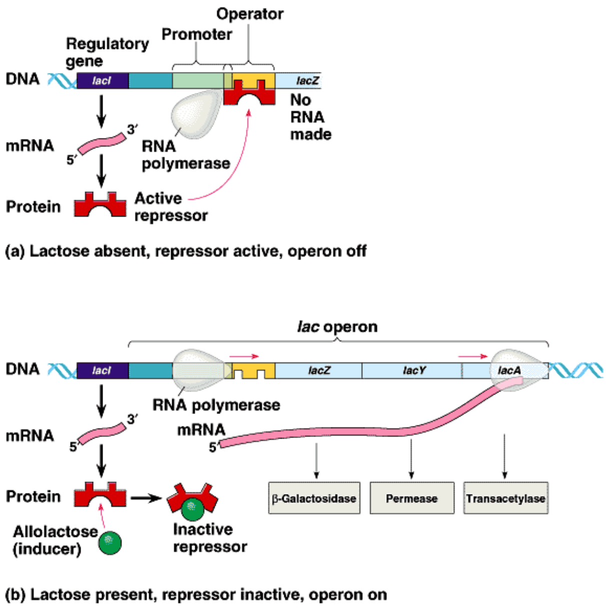
Autopilot



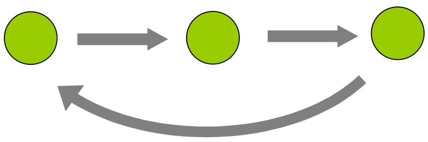
Enzyme regulation



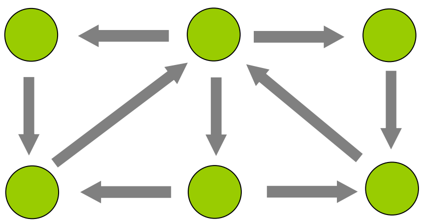
Gene regulation



Where is feedback?

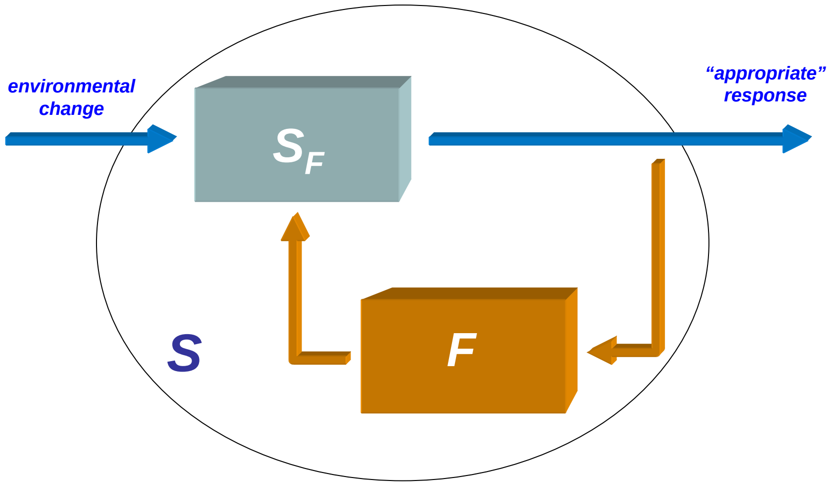


easy!

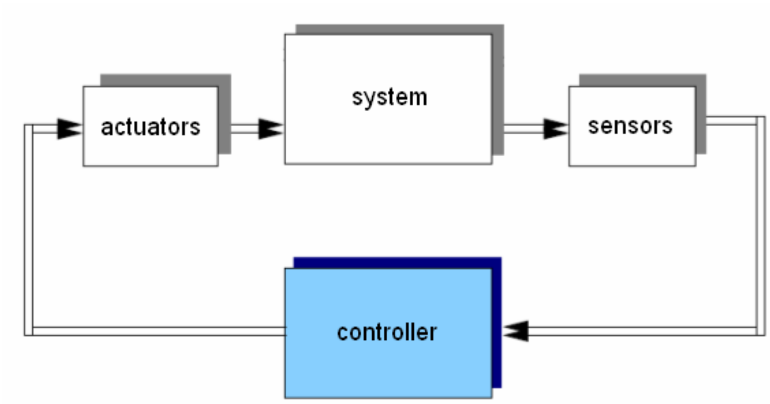


here, there and everywhere...

Feedback and self-regulation systems

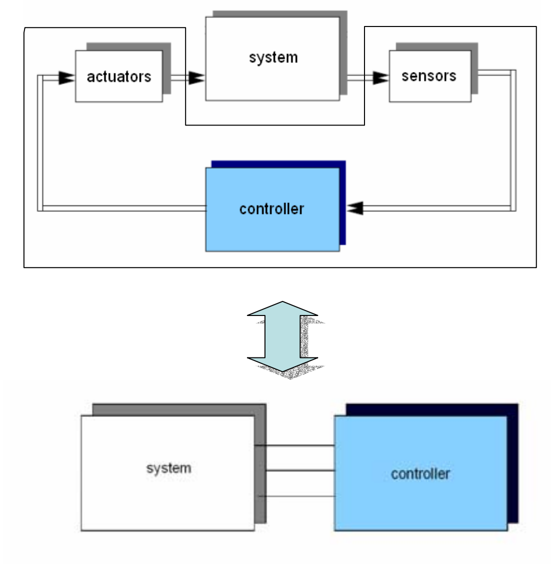


The "*intelligent control*" paradigm



functional separation among sensors / actuators / decision system

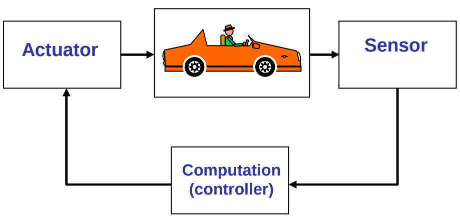
Control as *interconnection*

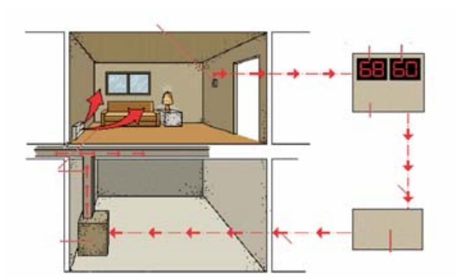


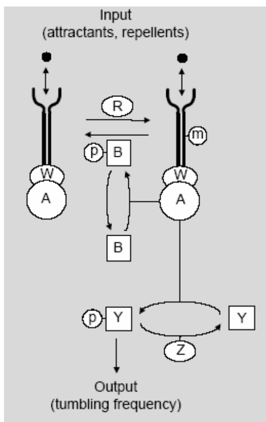
interconnection changes the overall system properties i.e. its "behavior"

no clear functional separation

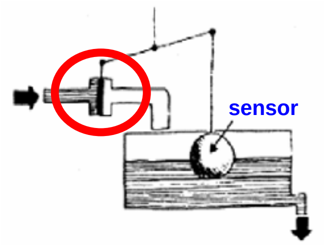
Examples of "intelligent" control systems

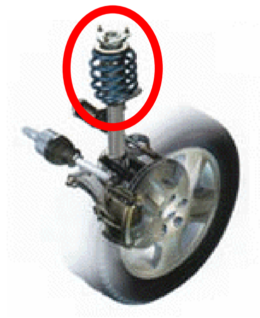


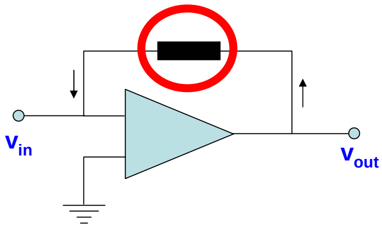




Examples of "interconnected" control systems



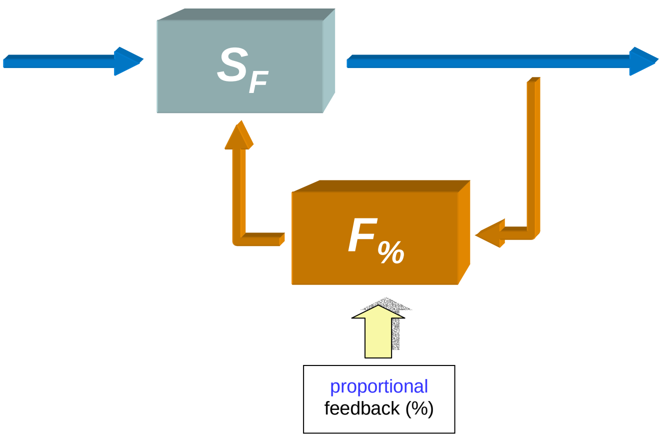




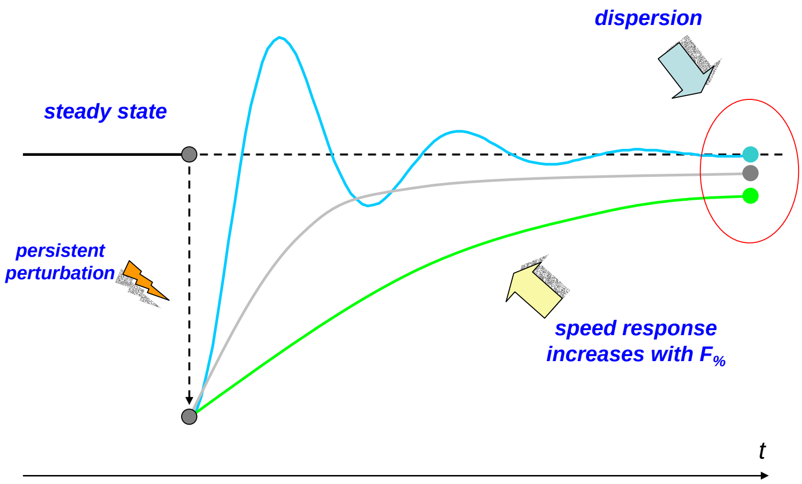
A biological example?

SELF REGULATION SYSTEMS *BEHAVIORS*

Proportional control system



The behavior of proportional control

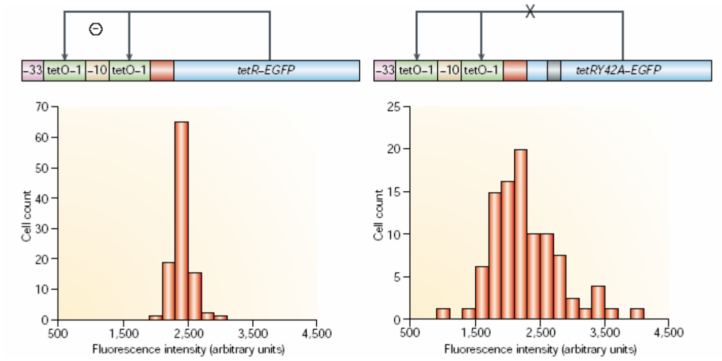


Engineering stability in gene networks by autoregulation

Attila Becskei & Luis Serrano

NATURE | VOL 405 | 1 JUNE 2000

Dispersion



strong feedback

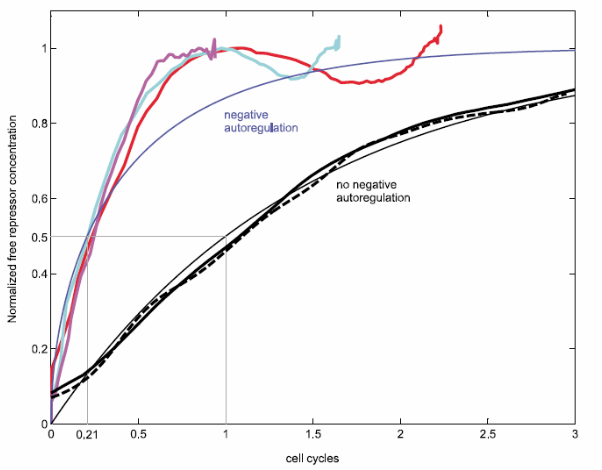
weak feedback

Negative Autoregulation Speeds the Response Times of Transcription Networks

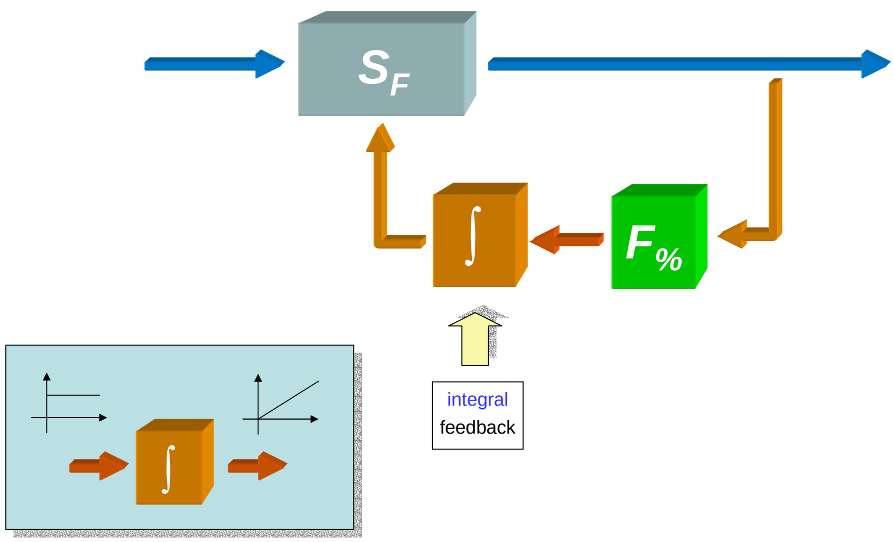
Nitzan Rosenfeld[1], Michael B. Elowitz[2] and Uri Alon[1*]

J. Mol. Biol. (2002) **323**, 785–793

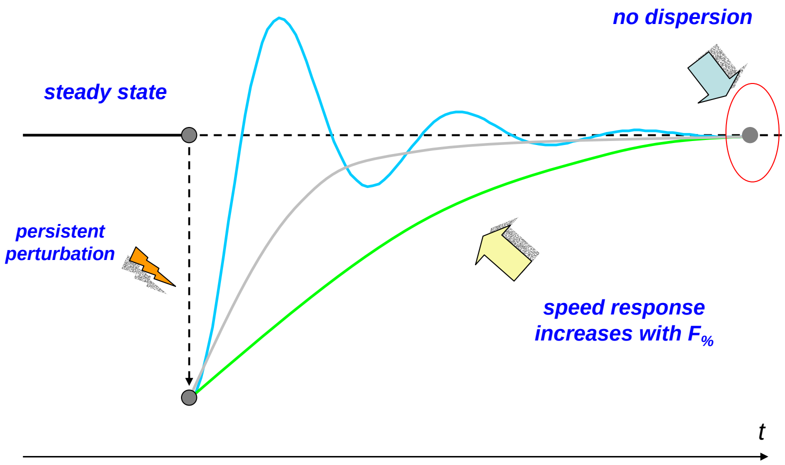
Response speed



Integral control system



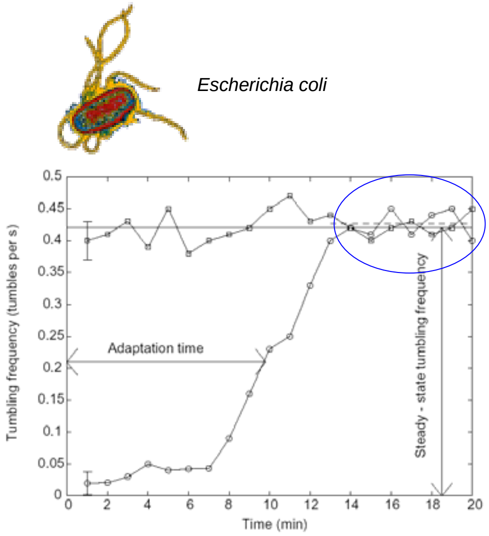
The behavior of integral control



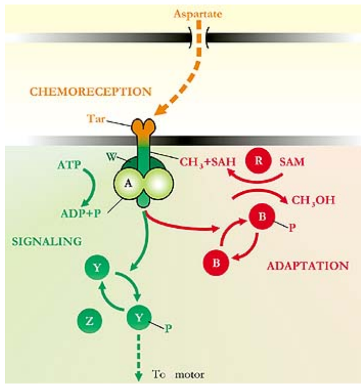
Robustness in bacterial chemotaxis

U. Alon*†, M. G. Surette‡, N. Barkai† & S. Leibler*†

NATURE | VOL 397 | 14 JANUARY 1999



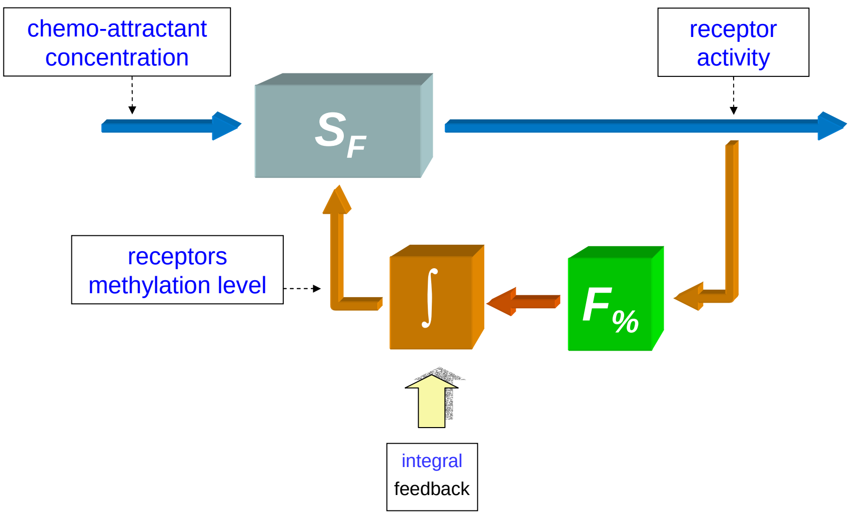
Perfect adaptation



Robust perfect adaptation in bacterial chemotaxis through integral feedback control

Tau-Mu Yi*†, Yun Huang†‡, Melvin I. Simon*§, and John Doyle‡

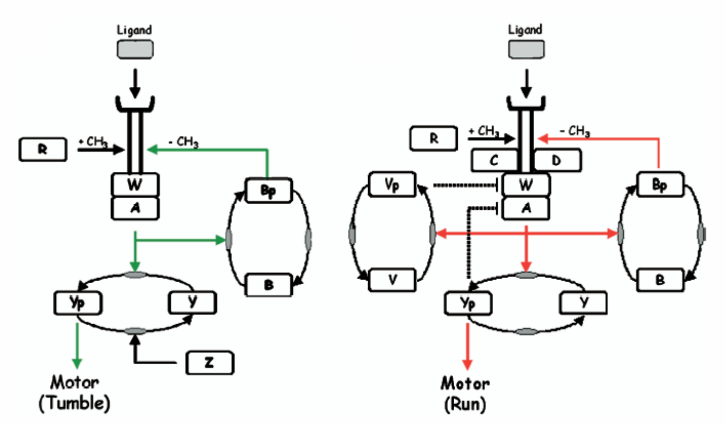
PNAS | April 25, 2000 | vol. 97 | no. 9 | 4649–4653



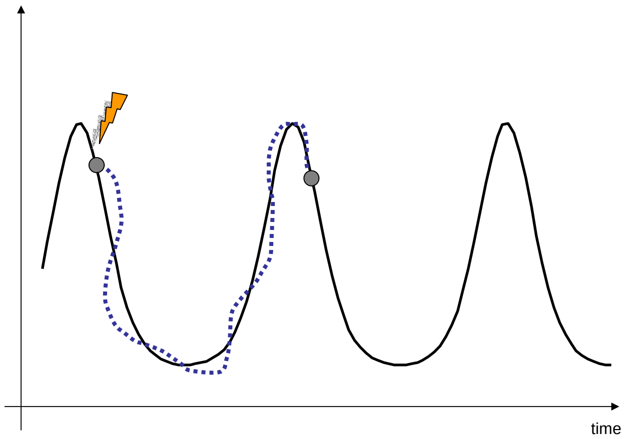
Design and Diversity in Bacterial Chemotaxis: A Comparative Study in *Escherichia coli* and *Bacillus subtilis*

Christopher V. Rao[1], John R. Kirby[2], Adam P. Arkin[1,3*]

PLoS BIOLOGY February 2004 | Volume 2 | Issue 2



Trajectory tracking



Conclusions

- Control theory provides strategies aiming to obtain “appropriate” responses to environmental changes
- Control theory may be able to give meaningful intepretation to data and indications on possible underlying biochemical mechanisms
- Feedback control is the major source of robustness
- A control system may be composed of separate units acting as sensors / controllers / actuators or may be **not**
- The presence of a control system may be argued by looking at “behaviors”
- A control system may be implemented in many equivalent ways, but some “behaviors” remain the same