Control Theory: Design and Analysis of Feedback Systems

Richard M. Murray

21 April 2008

Goals:

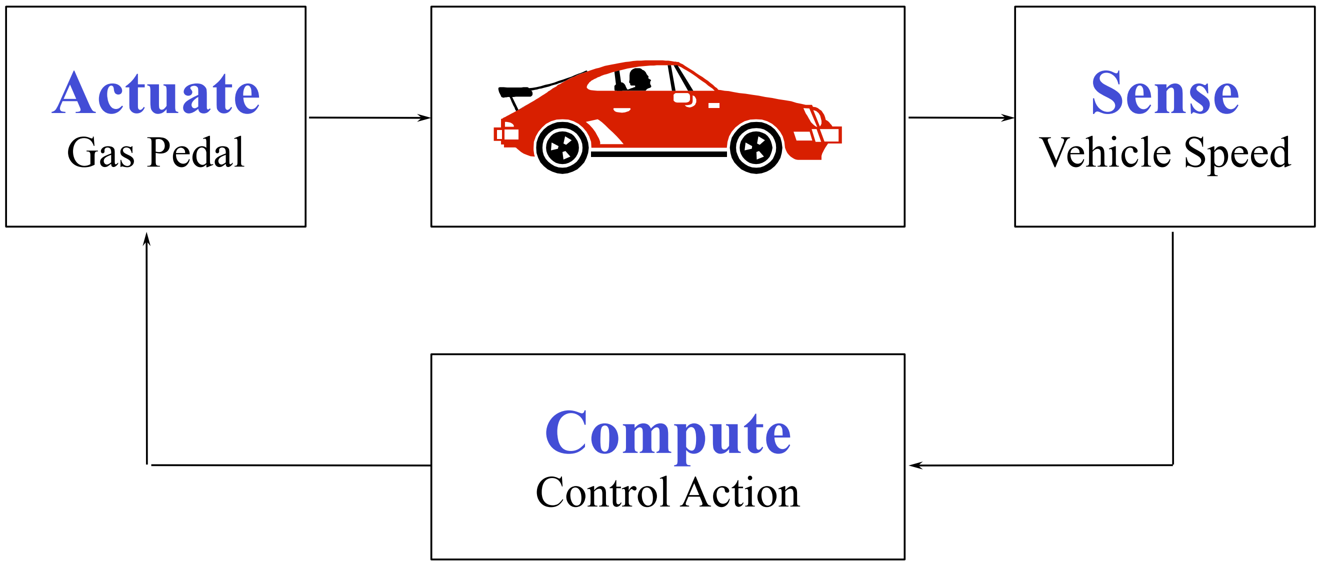
- Provide an introduction to key concepts and tools from control theory
- Illustrate the use of feedback for design of dynamics and robustness in the presence of uncertainty (using biological and engineering examples)
- Describe some open problems in control theory for biological systems

Reading:

- Åström and Murray, *Feedback Systems: An Introduction for Scientists and Engineers.* Princeton University Press, 2008. Available online (for free): http://www.cds.caltech.edu/~murray/amwiki

- Uri Alon, *An Introduction to Systems Biology.* Chapman & Hall/CRC, 2007

Control = Sensing + Computation + Actuation (in feedback loop)

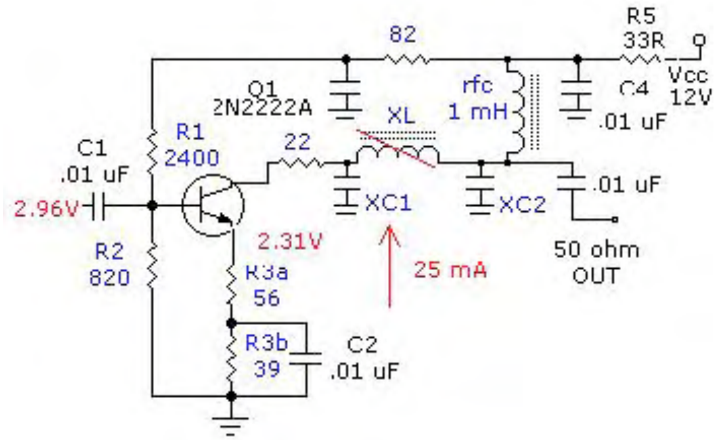


Goals: Stability, Performance, Robustness

Two Main Principles of Control

Robustness to Uncertainty thru Feedback

- Feedback allows high performance in the presence of uncertainty
- Example: repeatable performance of amplifiers with 5X component variation
- Key idea: accurate *sensing* to compare actual to desired, correction through *computation* and *actuation*



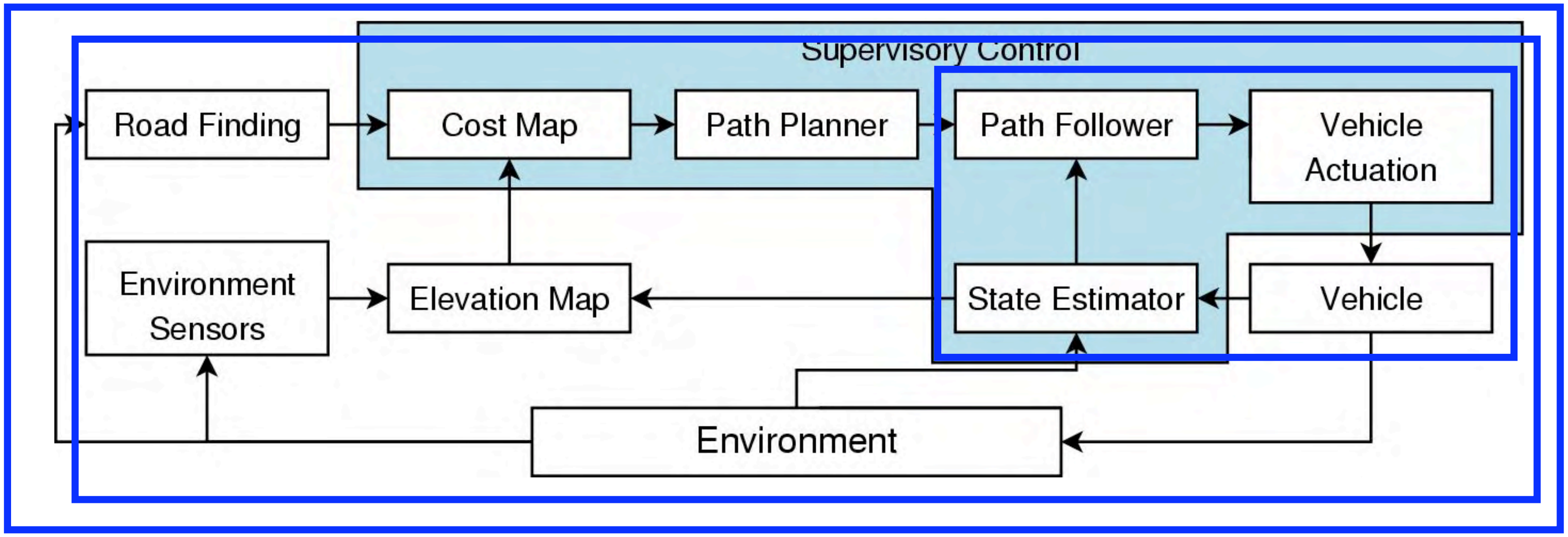
Design of Dynamics through Feedback

- Feedback allows the dynamics of a system to be modified
- Example: stability augmentation for highly agile, unstable aircraft
- Key idea: interconnection gives *closed loop* that modifies natural behavior

Control involves (computable) *tradeoffs* between robustness and performance

Cremean et al, 2006
J. Field Robotics

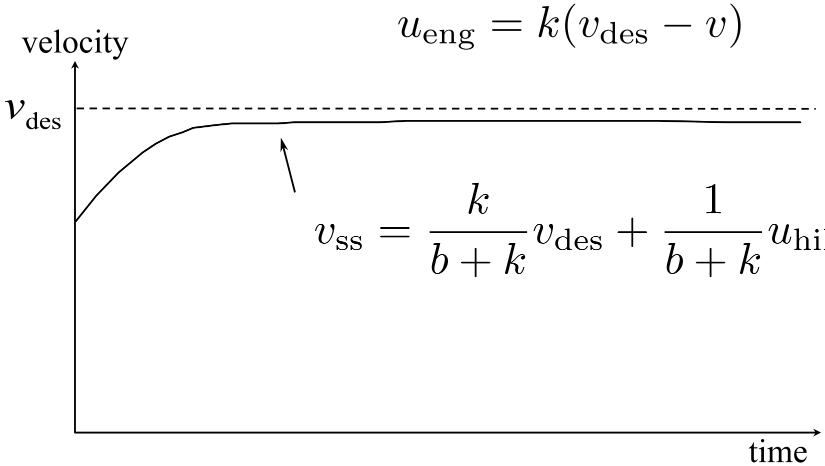
Example 1: Autonomous Driving



Speed control:

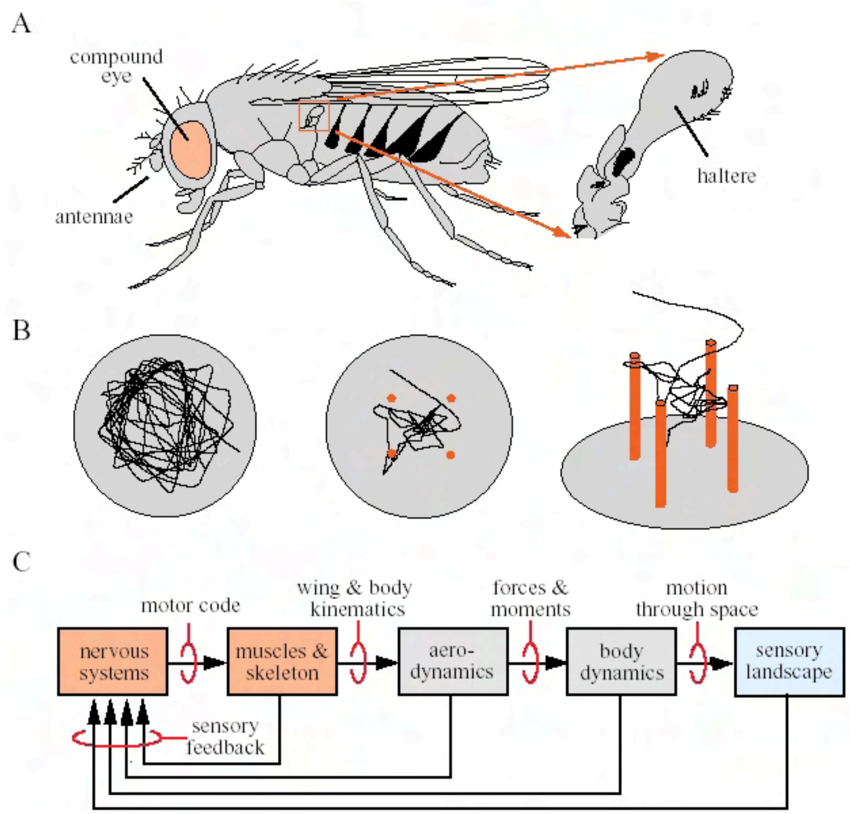
$$m\dot{v} = -bv + u_{\text{eng}} + u_{\text{hill}}$$

$$u_{\text{eng}} = k(v_{\text{des}} - v)$$



$$v_{\text{ss}} = \frac{k}{b+k} v_{\text{des}} + \frac{1}{b+k} u_{\text{hill}}$$

Example #2: Insect Flight



Flight behavior in Drosophila

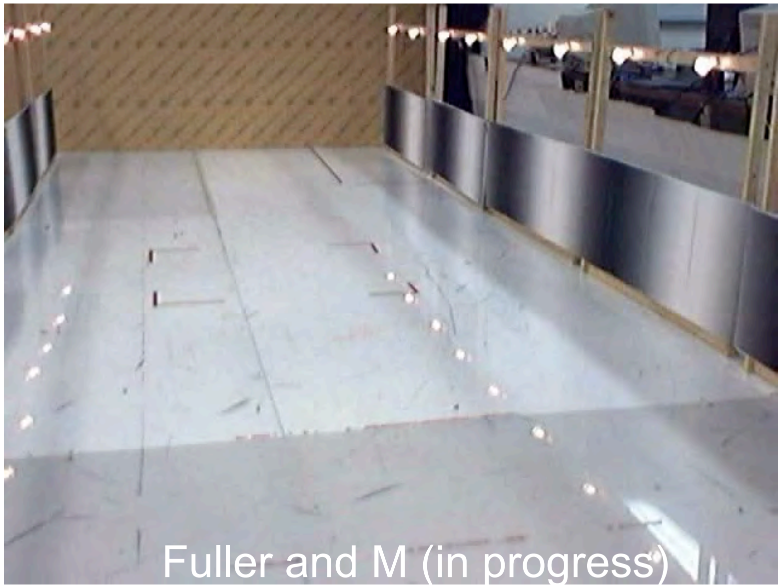
(a) Cartoon of the adult fruit fly showing the three major sensor strictures used in flight: eyes, antennae, and halteres (detect angular rotations)

(b) Example flight trajectories over a 1 meter circular arena, with and without internal targets.

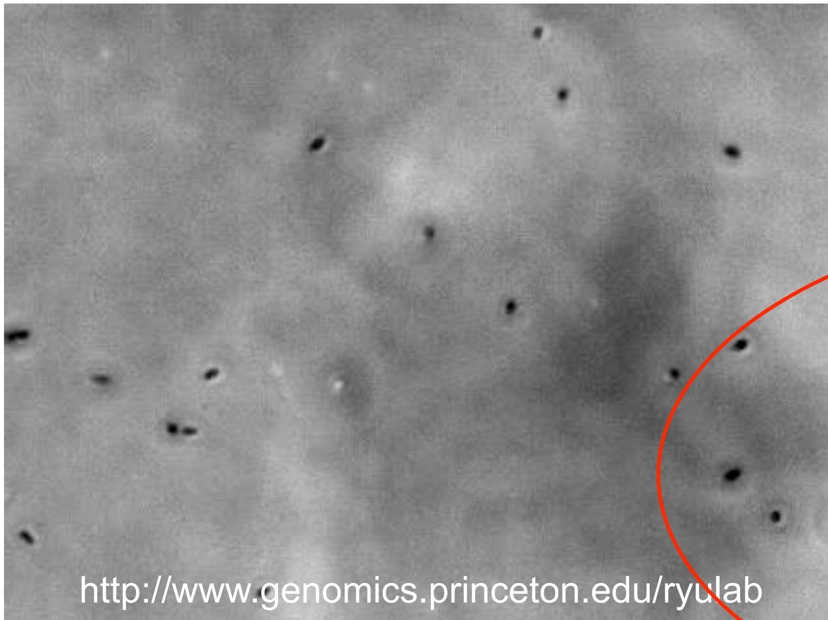
(c) Schematic control model of the flight system

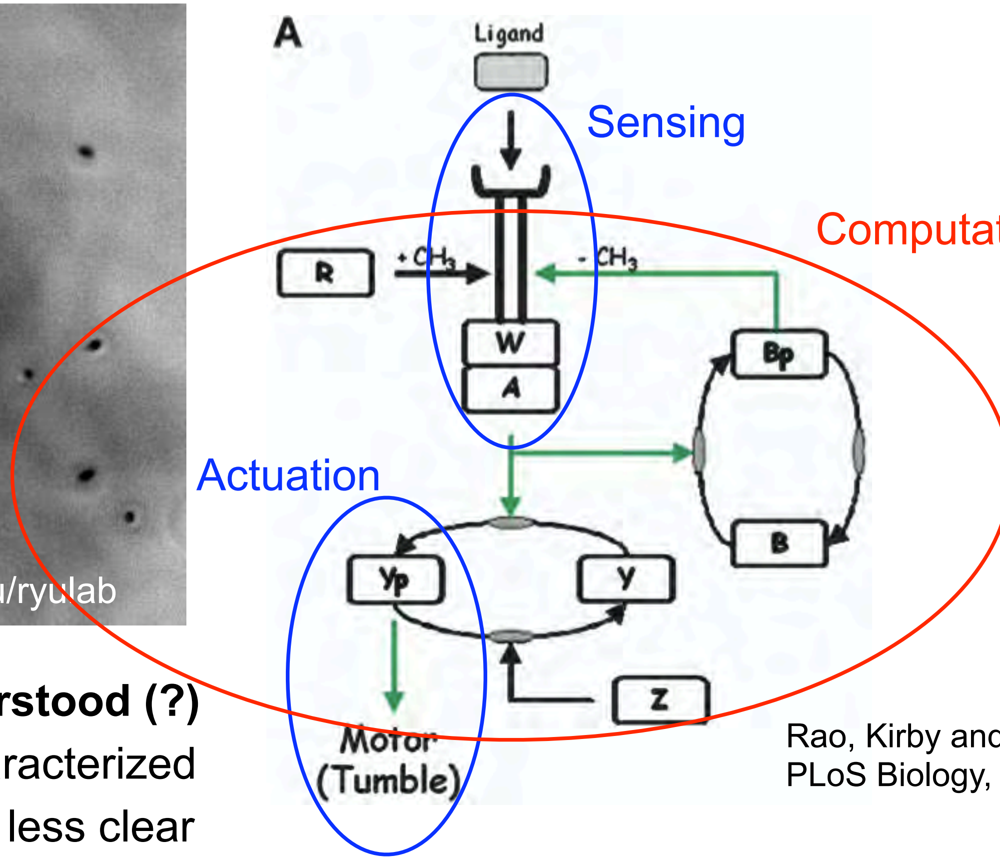
Different architecture than engineering

- Large collection of diverse sensors (many more than required)
- Very slow computation with lots of parallel pathways



Example #3: Chemotaxis





Rao, Kirby and Arkin
PLoS Biology, 2004

Major mechanisms well understood (?)

- Stochiometry matrix well characterized
- Dynamics of the interactions less clear
- Effects of perturbations (noise, unknown interconnection, etc) muddy

Can we do better?

- Make use of modular sensors and actuators (ala Smolke) to redesign (?)
- Synthetic pathway might exploit different elements (eg, RNA-based regulation)

Control Tools: 1940-2000

Modeling

- Input/output representations for subsystems + interconnection rules
- System identification theory and algorithms
- Theory and algorithms for reduced order modeling + model reduction

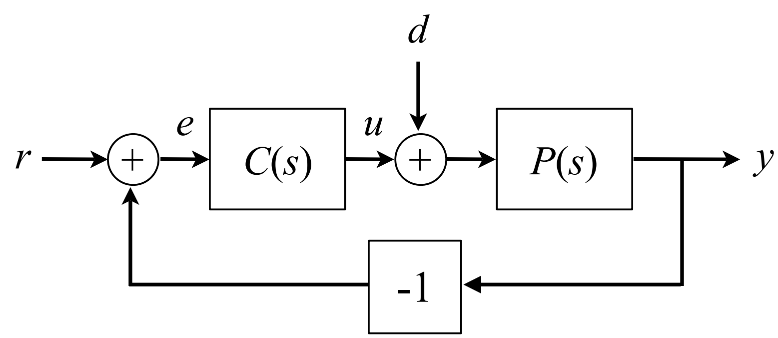
Analysis

- Stability of feedback systems, including robustness "margins"
- Performance of input/output systems (disturbance rejection, robustness)

Synthesis

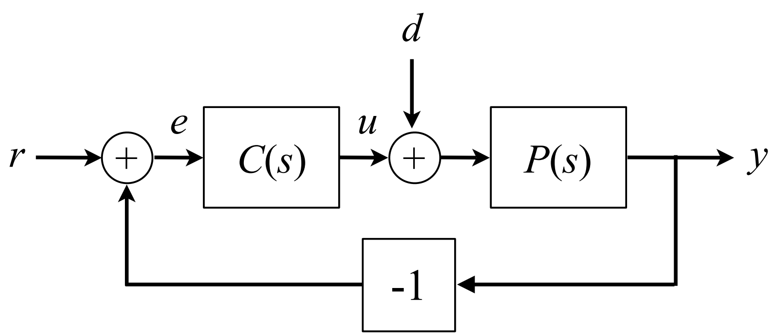
- Constructive tools for design of feedback systems
- Constructive tools for signal processing and estimation

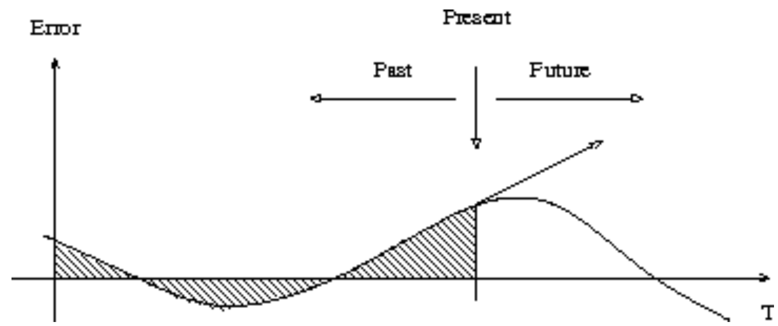
Basic feedback loop



- Plant, *P* = process being regulated
- Reference, *r* = external input (often encodes the desired setpoint)
- Disturbances, *d* = external environment
- Error, *e* = reference - actual
- Input, *u* = actuation command
- Feedback, *C* = closed loop correction
- Uncertainty: plant dynamics, sensor noise, environmental disturbances

Canonical Feedback Example: PID Control





$$\dot{x} = Ax + Bu$$
$$y = Cx + Du$$

$$u(t) = ke(t) + k_i \int_0^t e(\tau)\, d\tau + k_d \frac{de(t)}{dt}$$

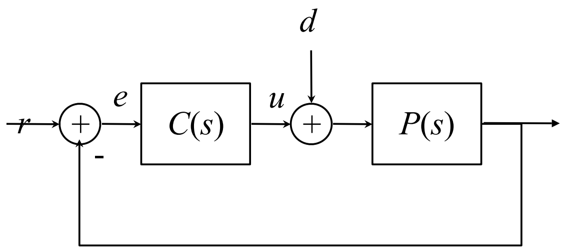
Three term controller

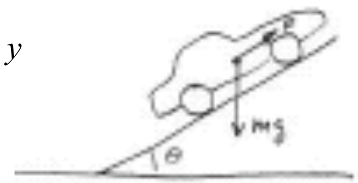
- Present: feedback proportional to current error
- Past: feedback proportional to *integral* of past error
  - Insures that error eventual goes to 0
  - Automatically adjusts setpoint of input
- Future: derivative of the error
  - *Anticipate* where we are going

PID design

- Choose *gains* k, k_i, k_d to obtain the desired behavior
- *Stability*: solutions of the closed loop dynamics should converge to eq pt
- *Performance*: output of system, y, should track reference
- *Robustness*: stability & performance properties should hold in face of disturbances and plant uncertainty

PID Example: Cruise (or Motion) Control





Dynamics around v_0, u_0:

$$\dot{\tilde{v}} = a\tilde{v} - g\theta + b\tilde{u}$$

$$y = v = \tilde{v} + v_0$$

where $\tilde{v} = v - v_0, \ \tilde{u} = u - u_0$

PI controller: $u(t) = ke(t) + k_i \int_0^t e(\tau)\, d\tau$

$$\dot{z} = r - y$$

$$u = -k_p \tilde{v} - k_i z + k_r r$$

Closed loop dynamics

$$\frac{d}{dt}\begin{bmatrix}\tilde{v} \\ z\end{bmatrix} = \begin{bmatrix} a - bK & -bK_i \\ -1 & 0 \end{bmatrix}\begin{bmatrix}\tilde{v} \\ z\end{bmatrix} + \begin{bmatrix} bK_r & -g \\ 1 & 0 \end{bmatrix}\begin{bmatrix} r \\ \theta \end{bmatrix}$$

$$\det\big(sI - (A - BK)\big) = s^2 + (bK - a/m)s - bK_i$$

Stability

- Can use feedback to place eigenvalues arbitrarily (design of dynamics)

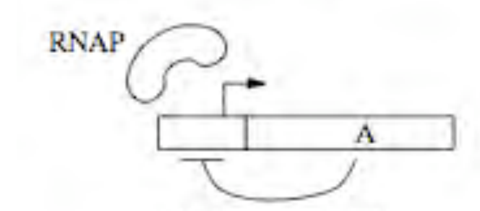
Performance

- v_{ss} = v_r (due to integral feedback)
- Response time and disturbance rejection determined by K, K_i

Robustness

- Steady state response (v_{ss}) is independent of gains (assuming stability)
- High gain provides insensitivity to parameters (assuming good sensor)

Example: Self-Repression (Proportional Feedback)



Common motif in transcriptional regulation

- A binds to its own promotor region
- If A is bound, represses binding of RNA polymerase

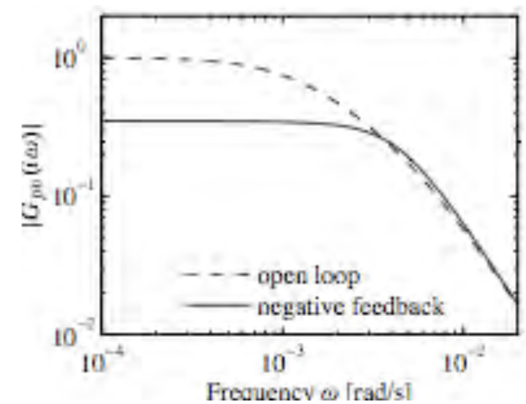
Use #1: decrease sensitivity to input disturbances

- Frequency responses demonstrates effect

$$\frac{dm}{dt} = \alpha(p) - \gamma m - u, \qquad \frac{dp}{dt} = \beta m - \delta p,$$

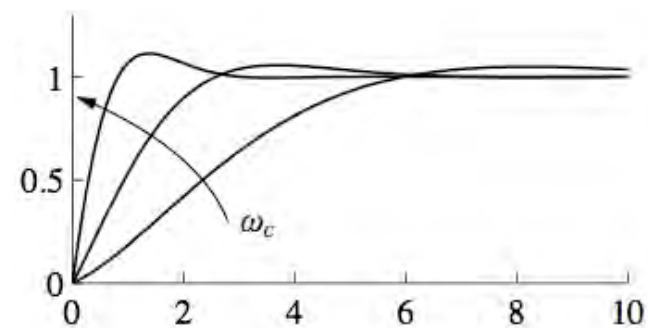
$$G^{\mathrm{ol}}_{pv}(s) = \frac{-\beta}{(s+\gamma)(s+\delta)}.$$

$$G^{\mathrm{cl}}_{pv}(s) = \frac{\beta}{(s+\gamma)(s+\delta)+\beta\sigma}, \qquad \sigma = \frac{2\beta\alpha k p_e}{(1+kp_e^n)^2}.$$



Use #2: use to decrease response time

- Use a stronger promotor to increase low freq gain
- Increases bandwidth ⇒ faster response



Example: Integral Action in Chemotaxis (from Alon '07)

Chemotactic response has "perfect adaptation"

- When exposed to a high attractant level, receptors are methylated to provider higher ligand binding
- Result: activity level returns to nominal level in presence of a constant input

Mathematical model shows integral action

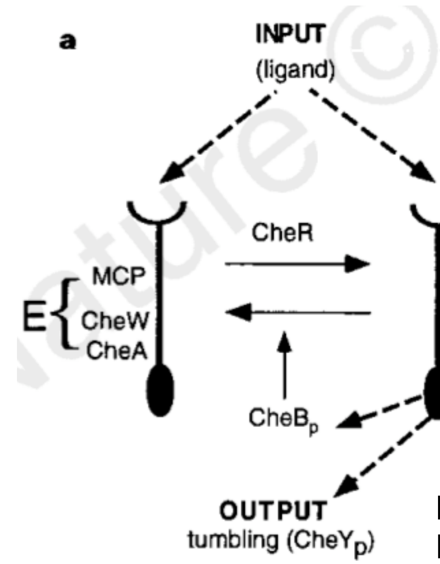
- Can use simplified two-state model (Barkai & Leibler, 1997).

$$\frac{d(X_m + X_m^*)}{dt} = V_R R - \frac{V_B B X_m^*}{K + X_m^*} \approx -V_B B (X_m^* - \frac{V_R R}{V_B B})$$

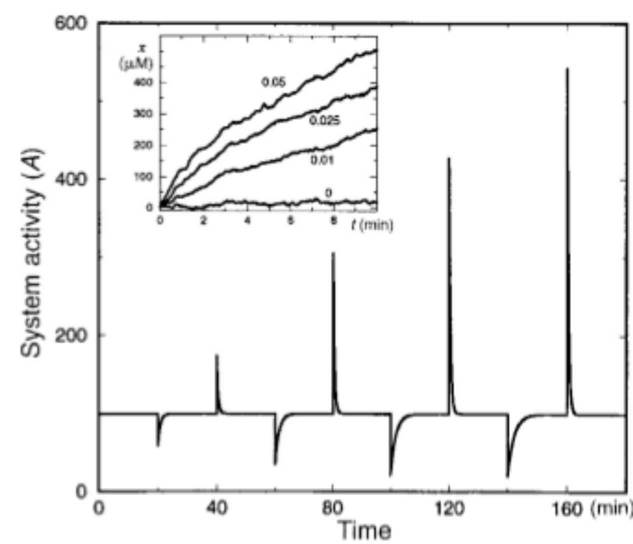
$$\frac{dX_m^*}{dt} = k(l) X_m - k'(l) X_m^* - V_B B X_m$$

- Steady state activity level independent of input concentration

$$X_{m,e}^* = \frac{K V_R R}{V_B B - V_R R}$$



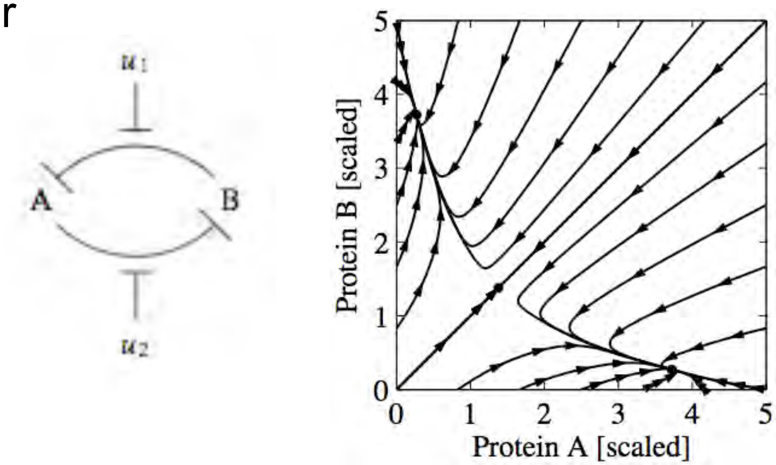
Barkai & Leibler, Nature 1997



Design of (Nonlinear) Dynamics Using Feedback

Beyond regulation: designing dynamic behavior

- Feedback can also be used to design behavior
- Engineering examples: switches (flip-flops), oscillators, fluid mixing

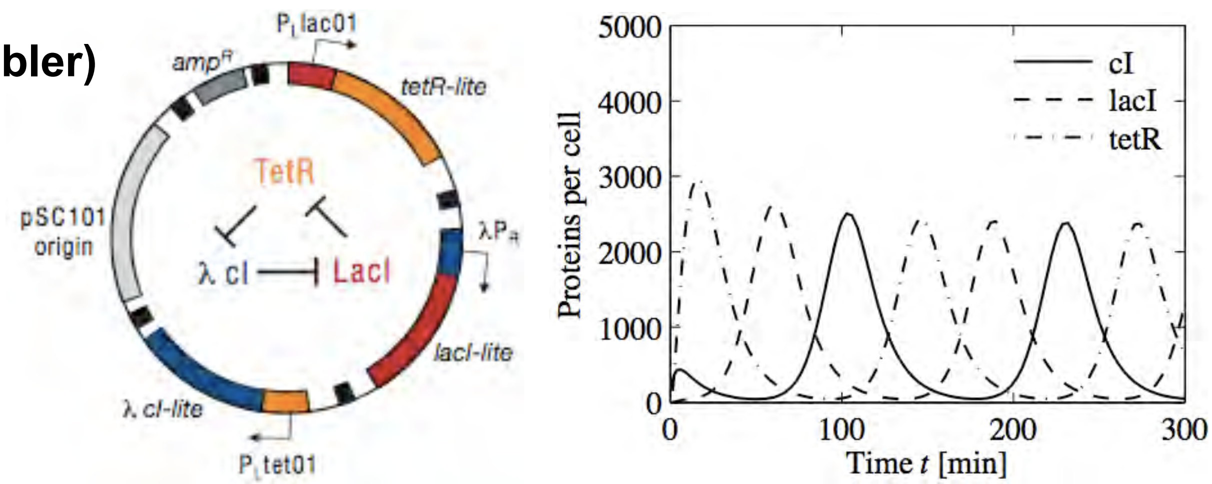


Genetic Switch (Collins and others)

- Interconnect two genes via cross-repression
- Resulting circuit has two states: “(1,0)”, “(0,1)”
- Can analyze robustness, speed of response

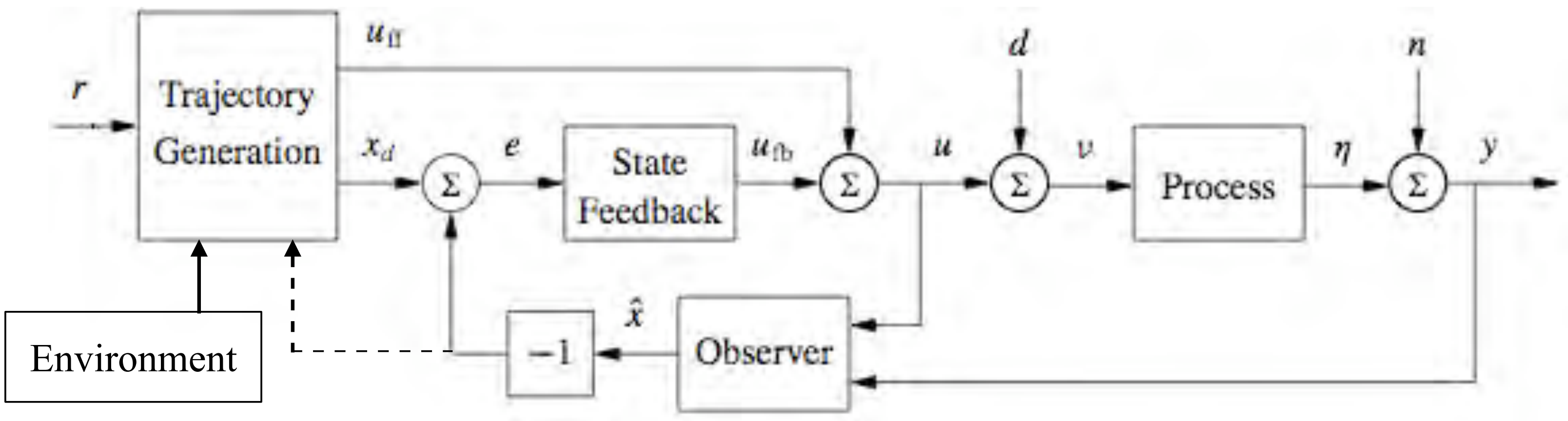
Represilator (Elowitz & Leibler)

- Ring oscillator with three repressors in a cycle
- Provides oscillations at frequency comparable to cell cycle



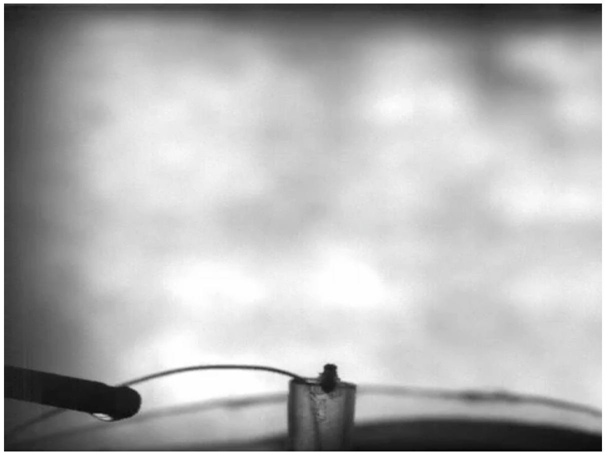
NB: control design tools not as well developed for this type of problem

Feedforward and Feedback



Benefits of feedforward compensation

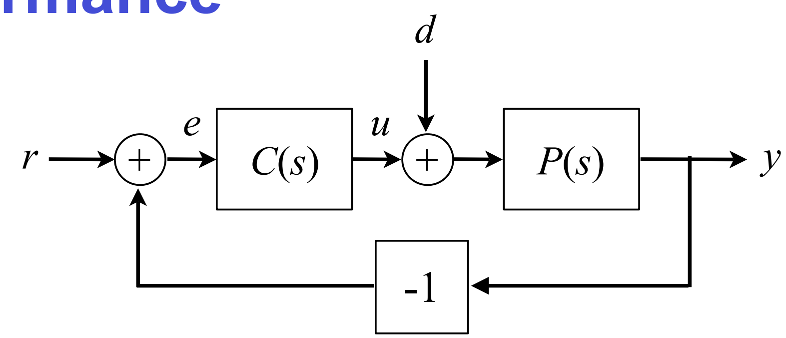
- Allows online generation of trajectories based on current situation/environment
- Optimization-based approaches can handle constraints, tradeoffs, uncertainty
- Trajectories can be pre-stored and used when certain conditions are met



Replanning using receding horizon

- Idea: regenerate trajectory based on new states, environment, constraints, etc
- Provides "outer loop" feedback at slower timescale
- Stability results available

Limits of Performance



Q: How well can you reject a disturbance?

- Would like *v* to be as small as possible
- Assume that we have signals *v*(*t*), *d*(*t*) that satisfy the loop dynamics
- Take Fourier transforms *V*(*ω*), *D*(*ω*)
- *Sensitivity function*: *S*(*ω*) = *V*(*ω*)/*D*(*ω*); want *S*(*ω*) « 1 for good performance

Thm (Bode) Under appropriate conditions (causality, non-passivity)

$$\int_0^\infty \log |S(\omega)| d\omega \geq 0$$

Consequences: achievable performance is bounded

- Better tracking in some frequency band ⇒ other bands get worse
- For linear systems, formula is known as the *Bode integral formula* (get equality)
- “Passive” (positive real) systems can beat this bound

Extensions

- Discrete time nonlinear systems: similar formula holds (Doyle)
- Incorporate Shannon limits for communication of disturbances (Martins et al)

Example: Magnetic Levitation System

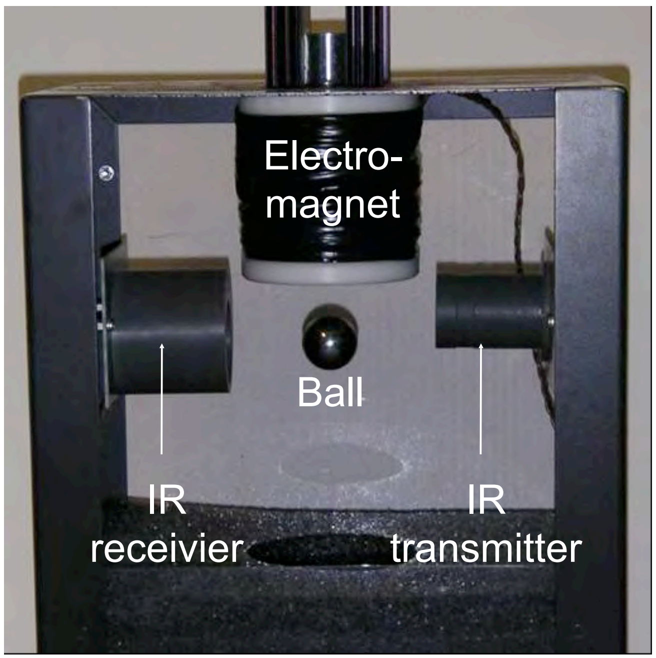
Nominal design gives low perf

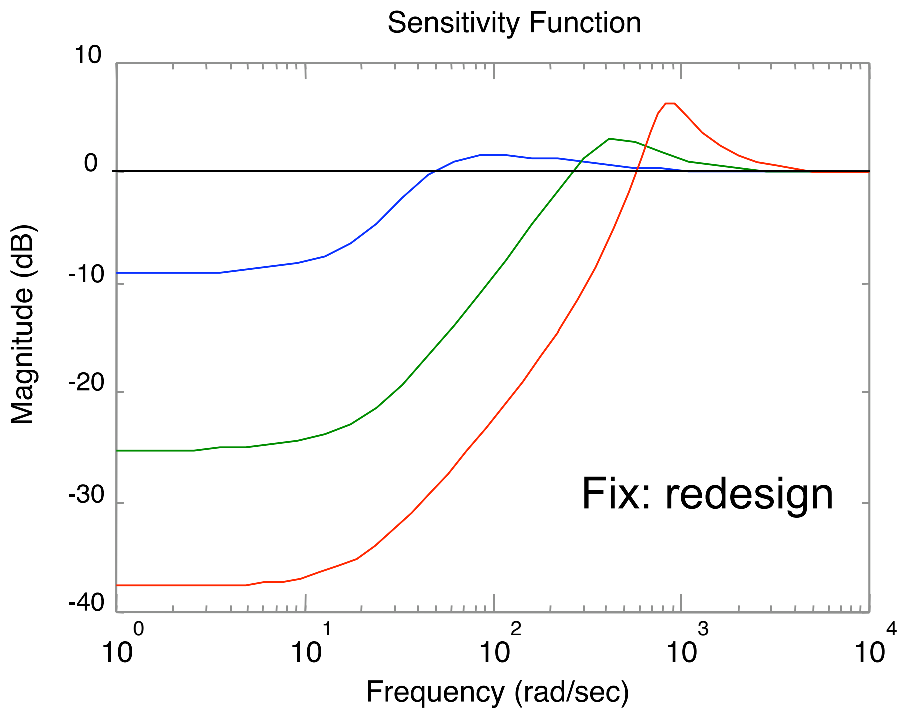
- Not enough gain at low frequency
- Try to adjust overall gain to improve low frequency response
- Works well at moderate gain, but notice waterbed effect

Bode integral limits improvement

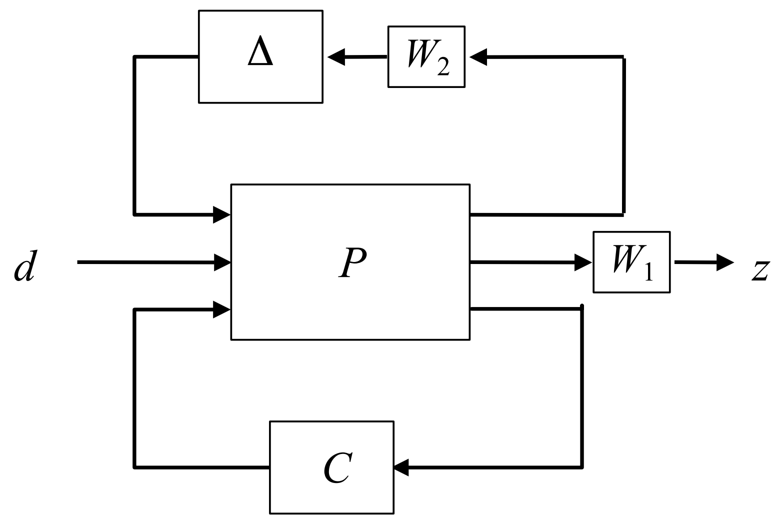
$$\int_0^\infty \log|S(j\omega)|d\omega = \pi r$$

- Must increase sensitivity at some point





Robust Control Theory



Model components as I/O operators

$$y(\cdot) = P(u(\cdot), d(\cdot), w(\cdot))$$

d disturbance signal
z output signal

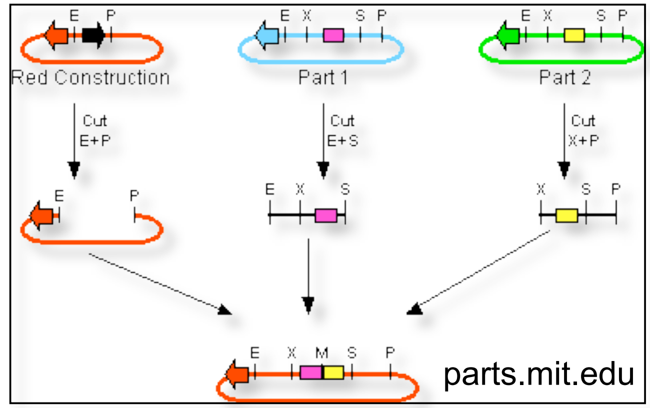
Δ uncertainty block
W_1 performance weight
W_2 uncertainty weight

Goal: guaranteed performance in presence of uncertainty

$$\|z\|_2 \leq \gamma \|d\|_2 \quad \text{for all} \quad \|\Delta\| \leq 1$$

- Compare energy in disturbances to energy in outputs
- Use frequency weights to change performance/uncertainty descriptions
- "Can I get X level of performance even with Y level of uncertainty?"

Toward a Control Theory for Synthetic Biology



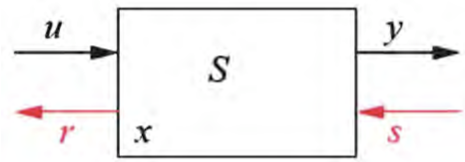
parts.mit.edu

Differences from traditional systems

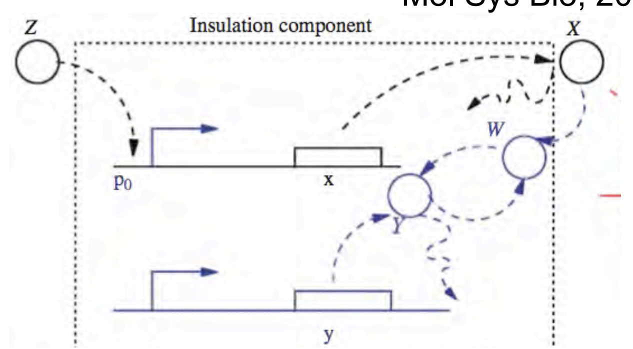
- *Complexity* - biological systems are *much* more complicated than engineered systems
- *Communications* - signal representations are very different (spikes, proteins, etc)
- *Uncertainty* - very large uncertainty in components; don't match current tools
- *Evolvability* - mutation, selection, etc

(Engineered) Modularity would be very useful

- To build complex systems, we need to be able to isolate subsystems (probably)
- Biobricks: modularity at DNA + device level
- Retroactivity (Del Vecchio, Nimfa, Sontag): candidate methods for minimizing effects of loading by downstream devices



Del Vecchio et al, Mol Sys Bio, 2008



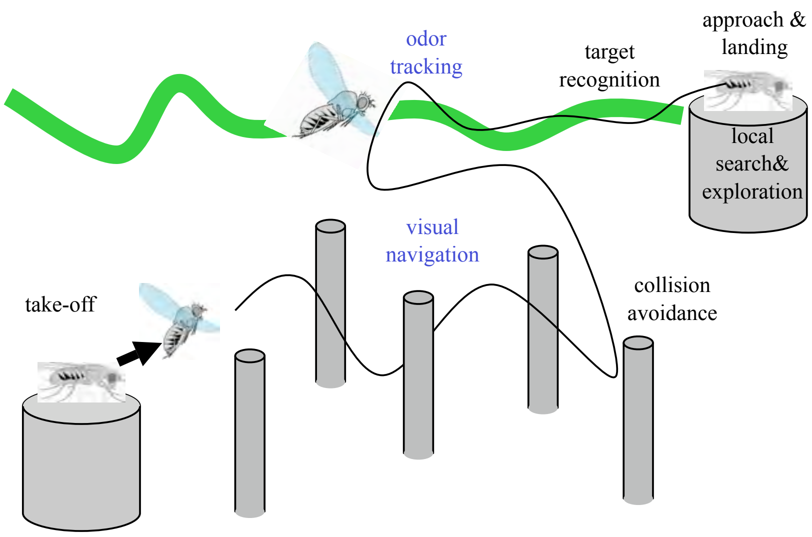
Probabalistic computation is likely

- Program distributions to achieve desired function

Control Using Slow Computing

Task: find food

- Take off, avoid obstacles, find plume, track plume to source

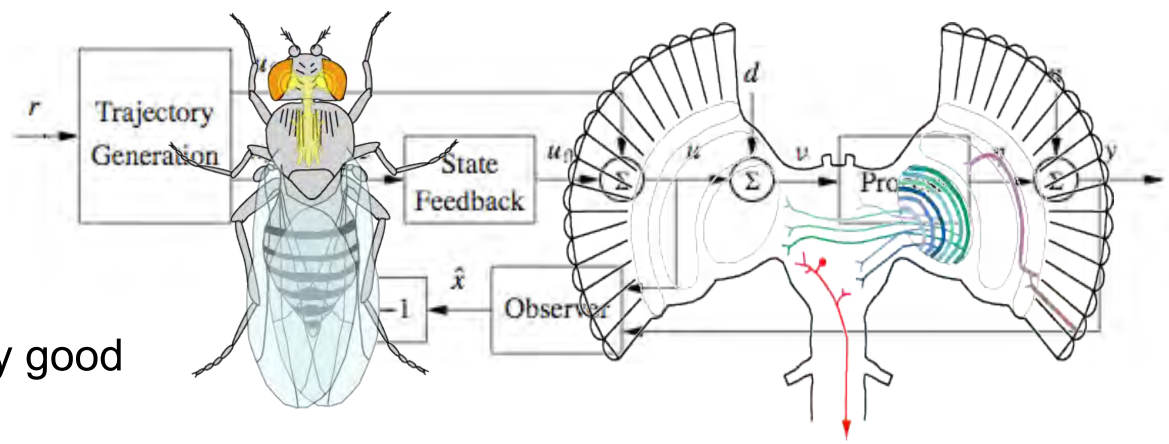


Approach #1: traditional control

- Trajectory generation + feedback
- Requires substantial sensing and computing (ala Alice)

Approach #2: sensory-motor cascade

- 300-500k neurons with millisecond response times
- Large number of redundant sensors
- Excellent robustness, very good performance (over time)



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  - Electronic: http://www.cds.caltech.edu/~murray/amwiki
  - Printed: http://press.princeton.edu or http://amazon.com
- U. Alon, *An Introduction to Systems Biology.* Chapman & Hall/CRC, 2007
- M. D. Dickinson, Solving the mystery of insect flight, *Scientific American*, June 2001