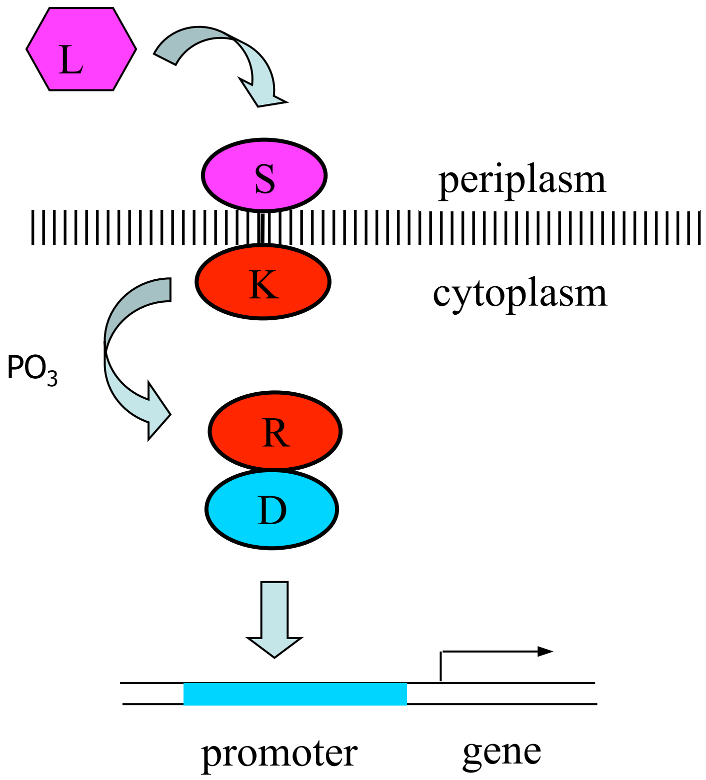
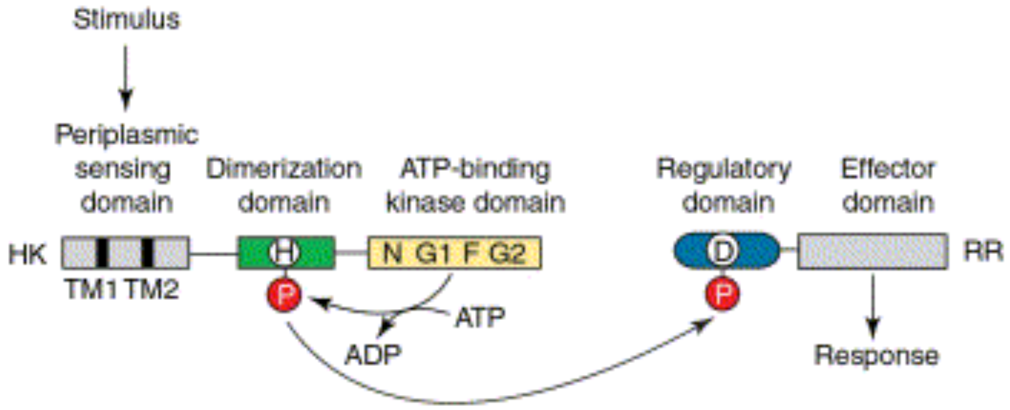
Physics 176/276
Quantitative Molecular Biology

Lecture IX: Two transduction pathways

The EnvZ-OmpR two-component system and the Goldebeter-Koshland push-and-pull module

❖ two-component signaling systems

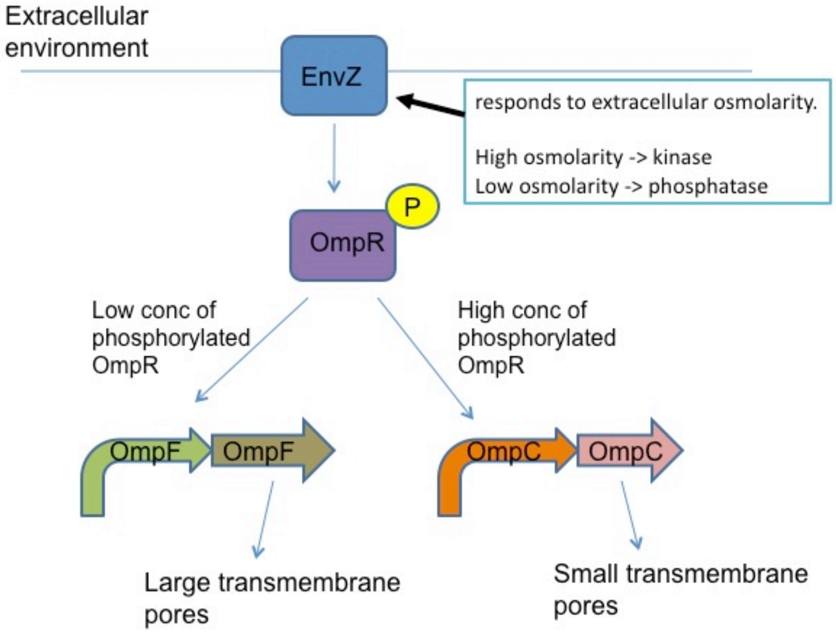




Notable examples in E. coli control osmoregulation (EnvZ/OmpR system) and the response to chemicals (CheA/CheY system)

Phenomenology of the EnvZ-OmpR system

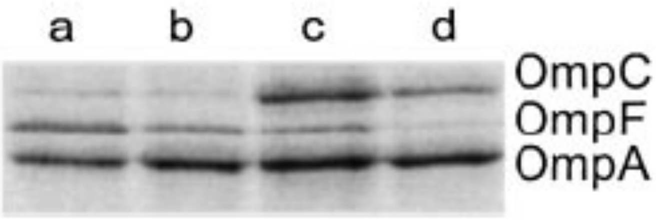
OmpC and OmpF in nature

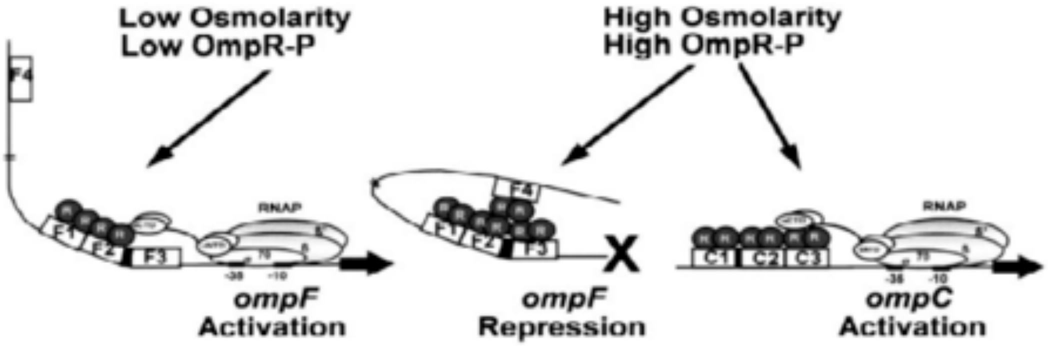


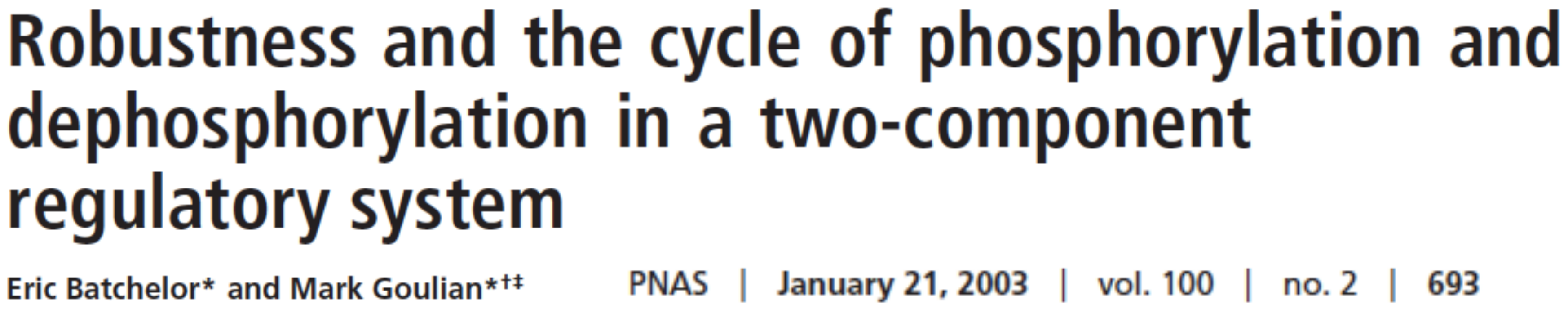
responds to extracellular osmolarity.

High osmolarity -> kinase
Low osmolarity -> phosphatase

Upon phosphorylation, the regulator dimerizes and binds DNA







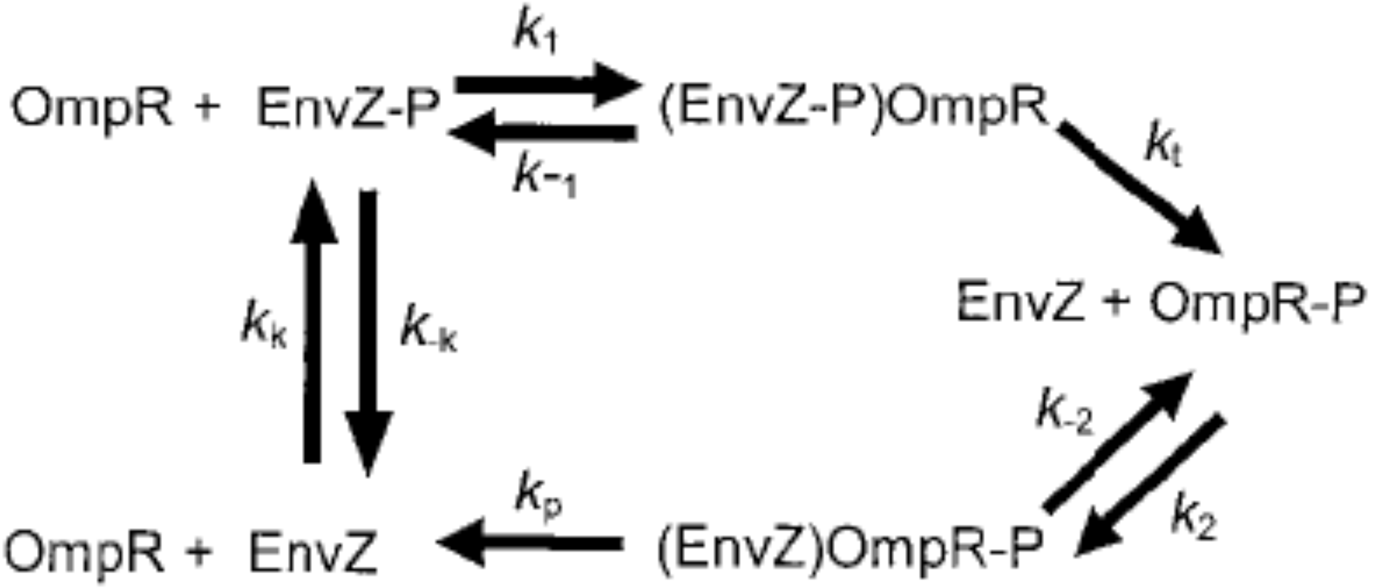
Robustness and the cycle of phosphorylation and dephosphorylation in a two-component regulatory system

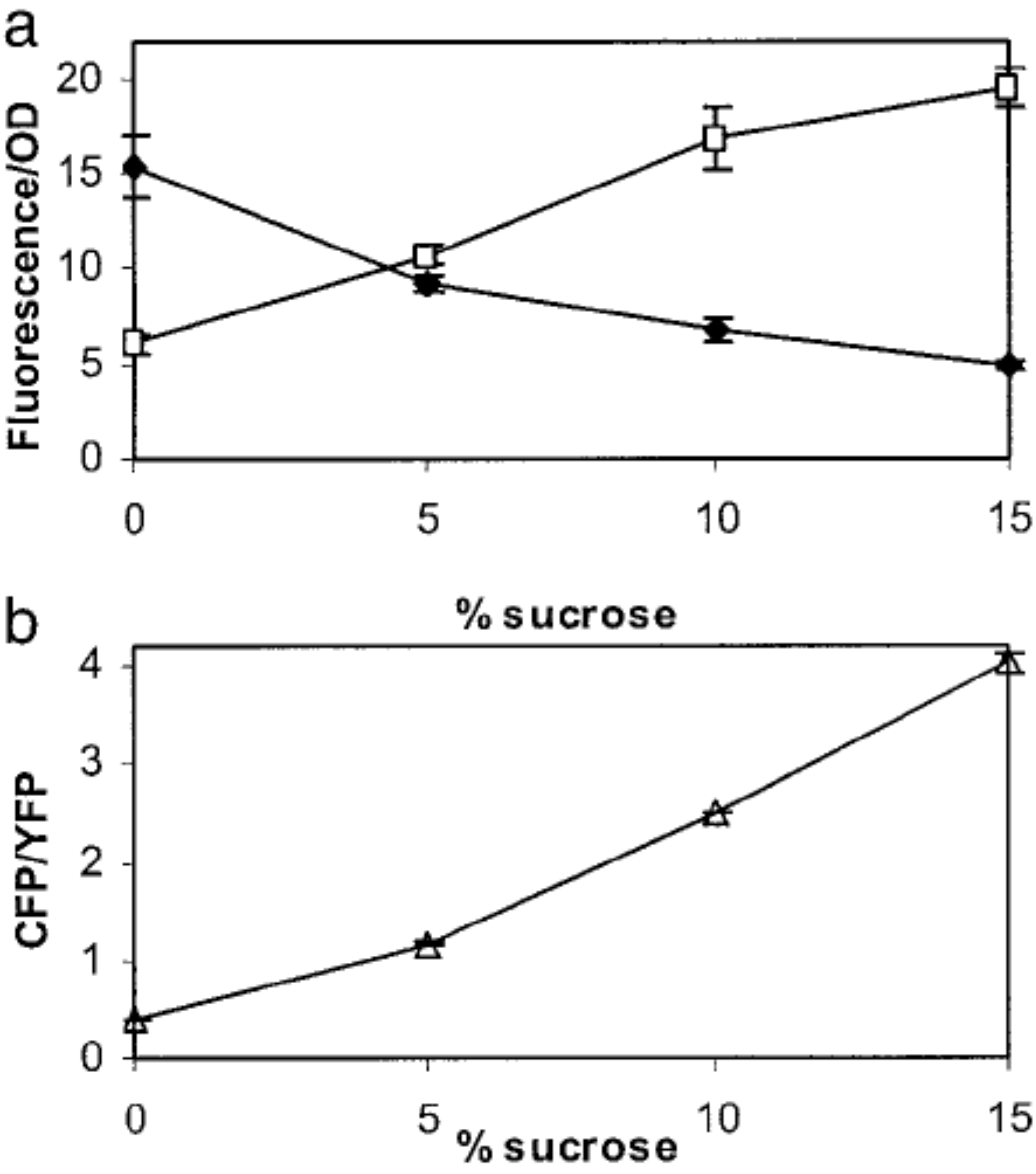
Eric Batchelor* and Mark Goulian*†‡

PNAS | January 21, 2003 | vol. 100 | no. 2 | 693

Specific goal: Explain the experimental observation that the response is robust to variations of the levels of the receptor EnvZ and the regulator OmpR.

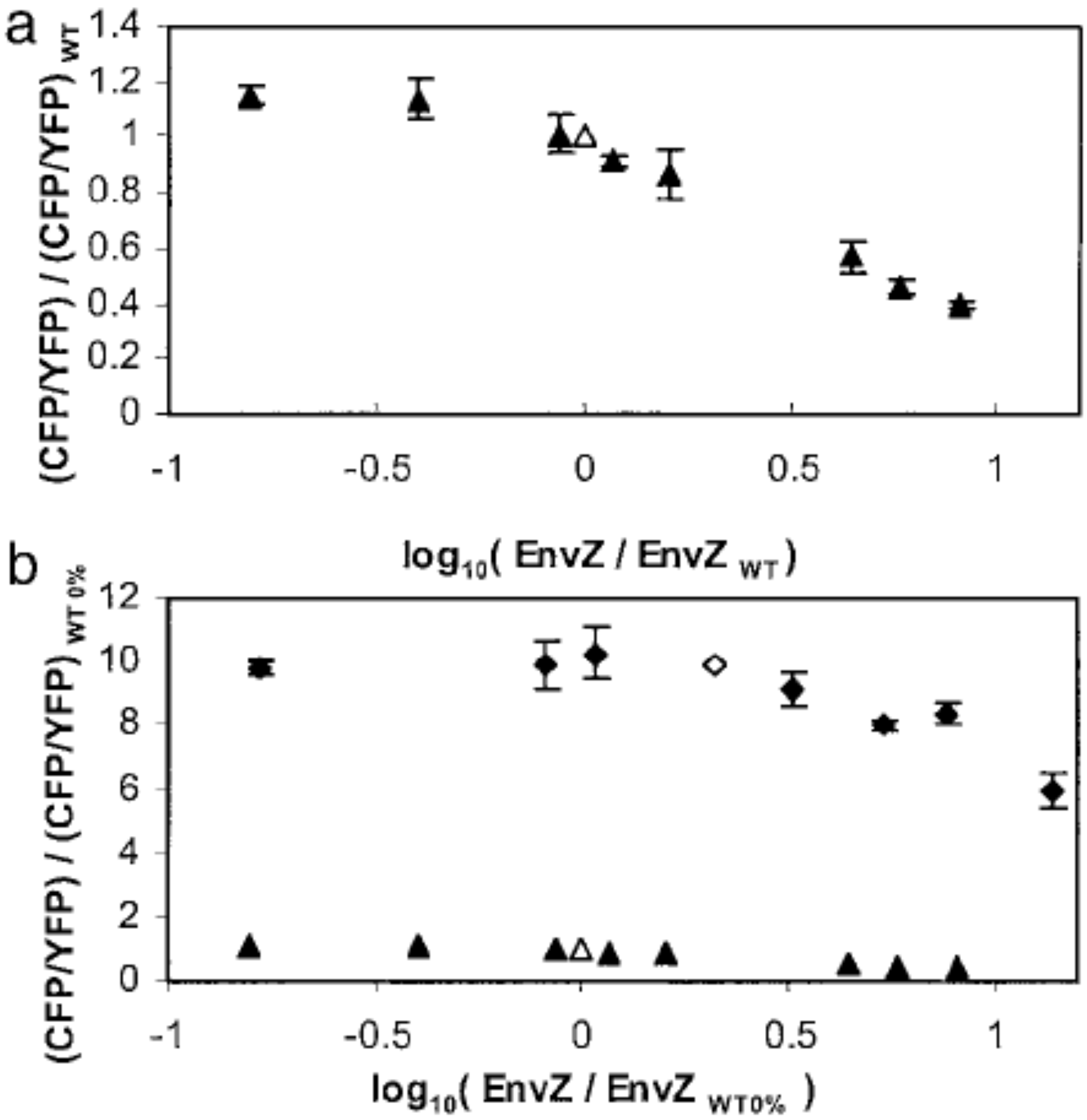
The histidine kinase is bi-functional



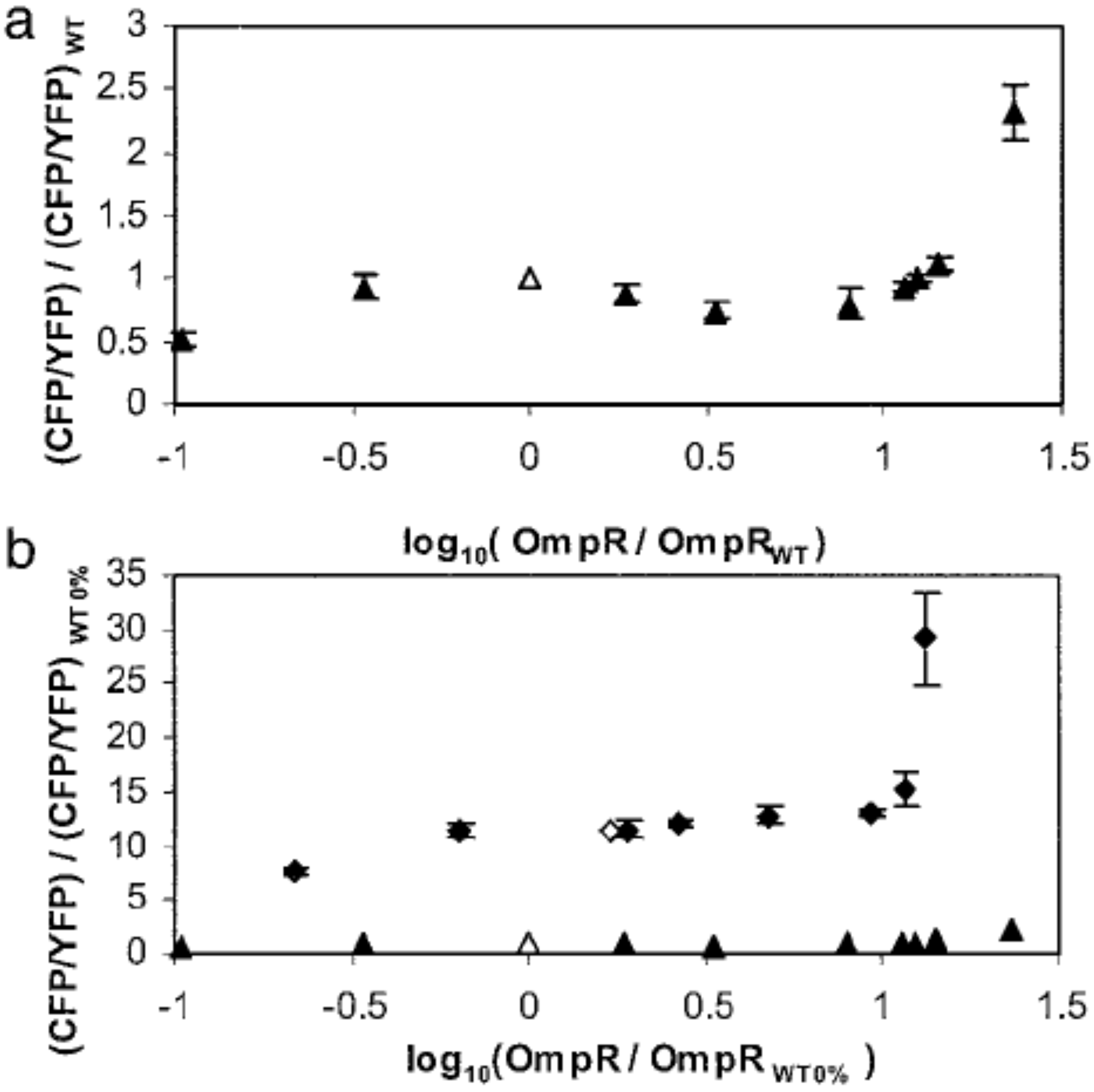


Experimental test of the theoretical predictions.
CFP: OmpC
YFP: OmpF

Experimental test of the theoretical predictions



Experimental test of the theoretical predictions



Goldbeter-Koshland push-and-pull model
Zero-th order ultrasensitivity

An amplified sensitivity arising from covalent modification in biological systems

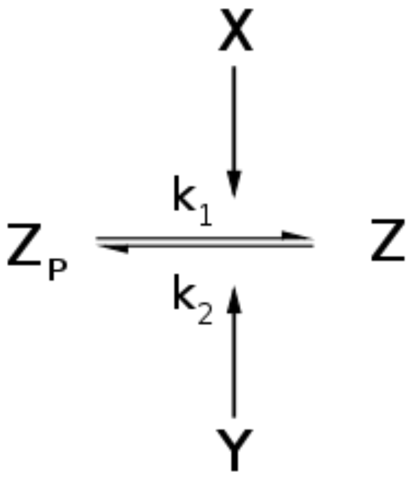
(protein modification/metabolic regulation/switch mechanism/enzyme cascades)

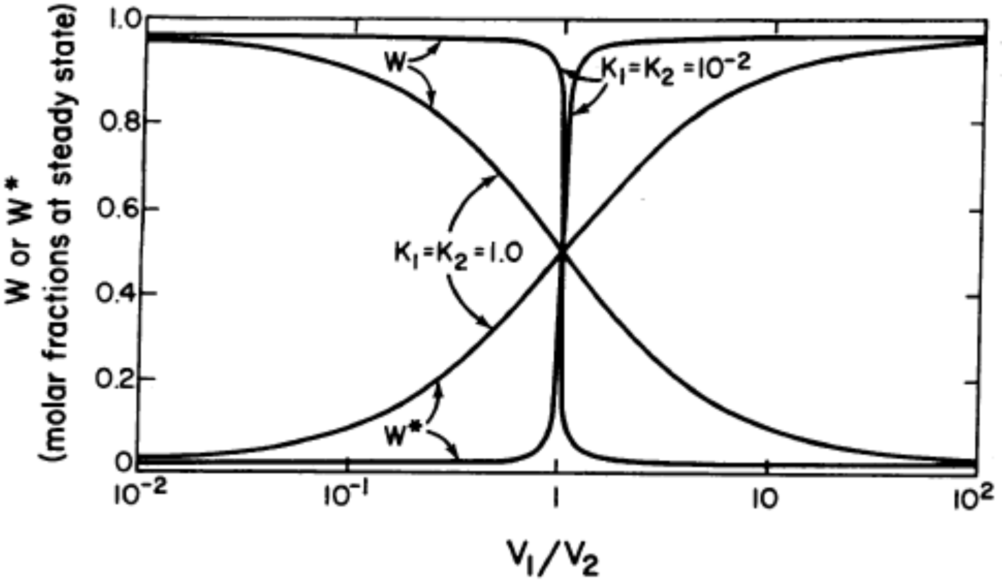
ALBERT GOLDBETER† AND DANIEL E. KOSHLAND, JR.

Proc. Natl. Acad. Sci. USA
Vol. 78, No. 11, pp. 6840–6844, November 1981

$$W + E_1 \underset{d_1}{\overset{a_1}{\rightleftarrows}} WE_1 \xrightarrow{k_1} W^* + E_1$$

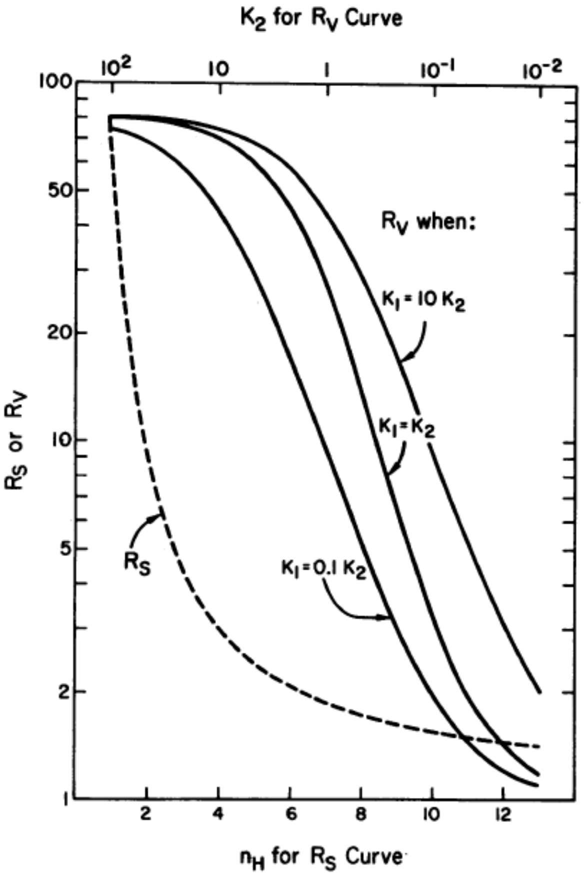
$$W^* + E_2 \underset{d_2}{\overset{a_2}{\rightleftarrows}} W^*E_2 \xrightarrow{k_2} W + E_2.$$





Switch behavior in the 0-th order regime (and corrections)

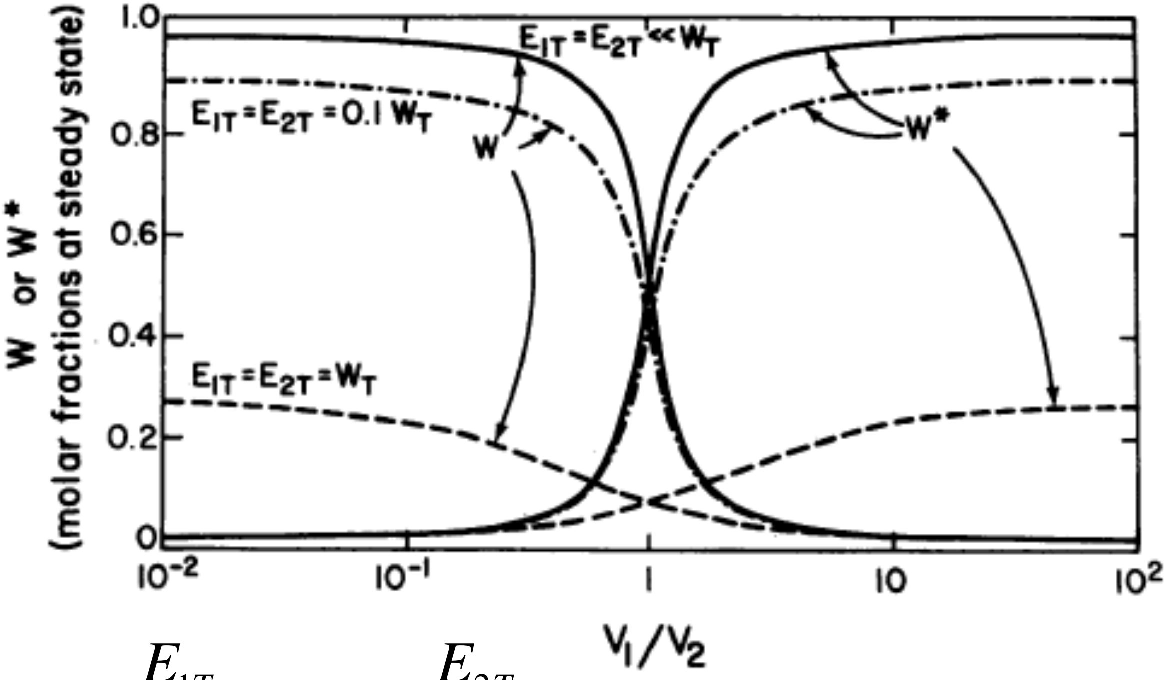
Steepness of the transition



Corrections when enzymes are not negligible wrt W_T

$$f_*^3\left(1-\beta\right)+f_*^2\left[\beta H_1+H_2+\left(1-\beta\right)\left(H_2-1+\beta\varepsilon_1+\varepsilon_2\right)\right]+$$

$$f_* H_2\left[\beta H_1+H_2+\varepsilon_2+\beta\varepsilon_1-2+\beta\right]-H_2^2=0$$



$$\beta=\frac{V_2}{V_1} \qquad \varepsilon_1=\frac{E_{1T}}{W_T} \qquad \varepsilon_2=\frac{E_{2T}}{W_T}$$

Adaptation

The amount of the enzyme is regulated by an external signal, e.g. via receptor binding

$$\frac{dE_1}{dt} = h_1 R - r_1 E_1 \qquad \frac{dE_2}{dt} = h_2 R - r_2 E_2$$

After a step the enzymes will saturate and the ratio of the velocity is the same as pre-stimulus