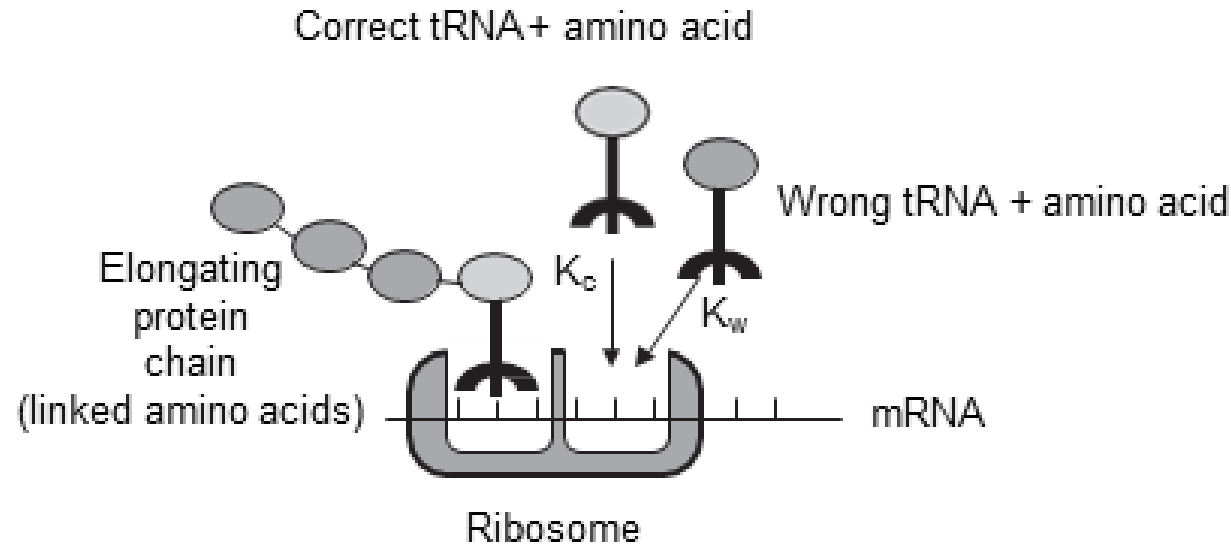


Kinetic Proofreading and robustness

The example of Picasso lovers

Ribosome as biological example



		Second letter									
		U		C		A		G			
First letter	U	UUU Phe	UUC	UCU	UCC Ser	UAU Tyr	UAC	UGU Cys	UGC	U	C
		UUA Leu	UUG	UCA	UCG	UAA STOP	UAG STOP	UGA STOP	UGG Trp	A	G
	C	CUU Leu	CUC	CCU	CCC Pro	CAU His	CAC	CGU Arg	CGC	U	C
		CUA	CUG	CCA	CCG	CAA Gln	CAG	CGA	CGG	A	G
First letter	A	AUU Ile	AUC	ACU	ACC Thr	AAU Asn	AAC	AGU Ser	AGC	U	C
		AUA Met	AUG	ACA	ACG	AAA Lys	AAG	AGA Arg	AGG	A	G
	G	GUU Val	GUC	GCU	GCC Ala	GAU Asp	GAC	GGU Gly	GGC	U	C
		GUA	GUG	GCA	GCG	GAA Glu	GAG	GGA	GGG	A	G

Problem: How to avoid wrong amino acid?
 (specificity of binding rates 1:100, incooperation of wrong AA, 1:10 000)

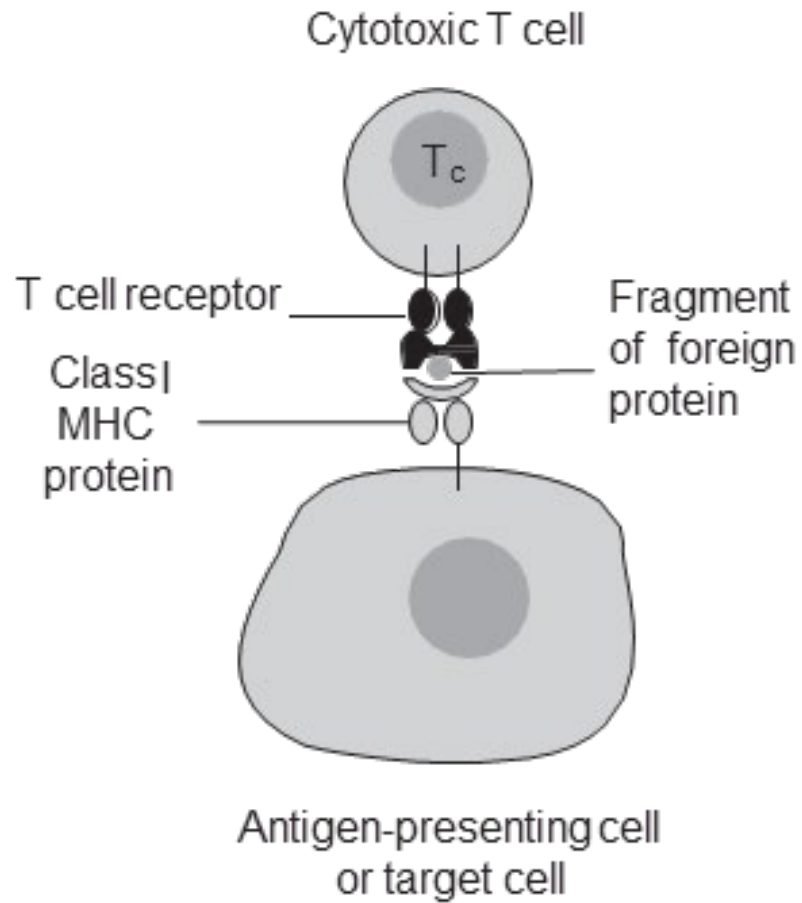
Why equilibrium approach does not explain this?

However, kinetic proofreading can improve drastically!

As it is a nonequilibrium process

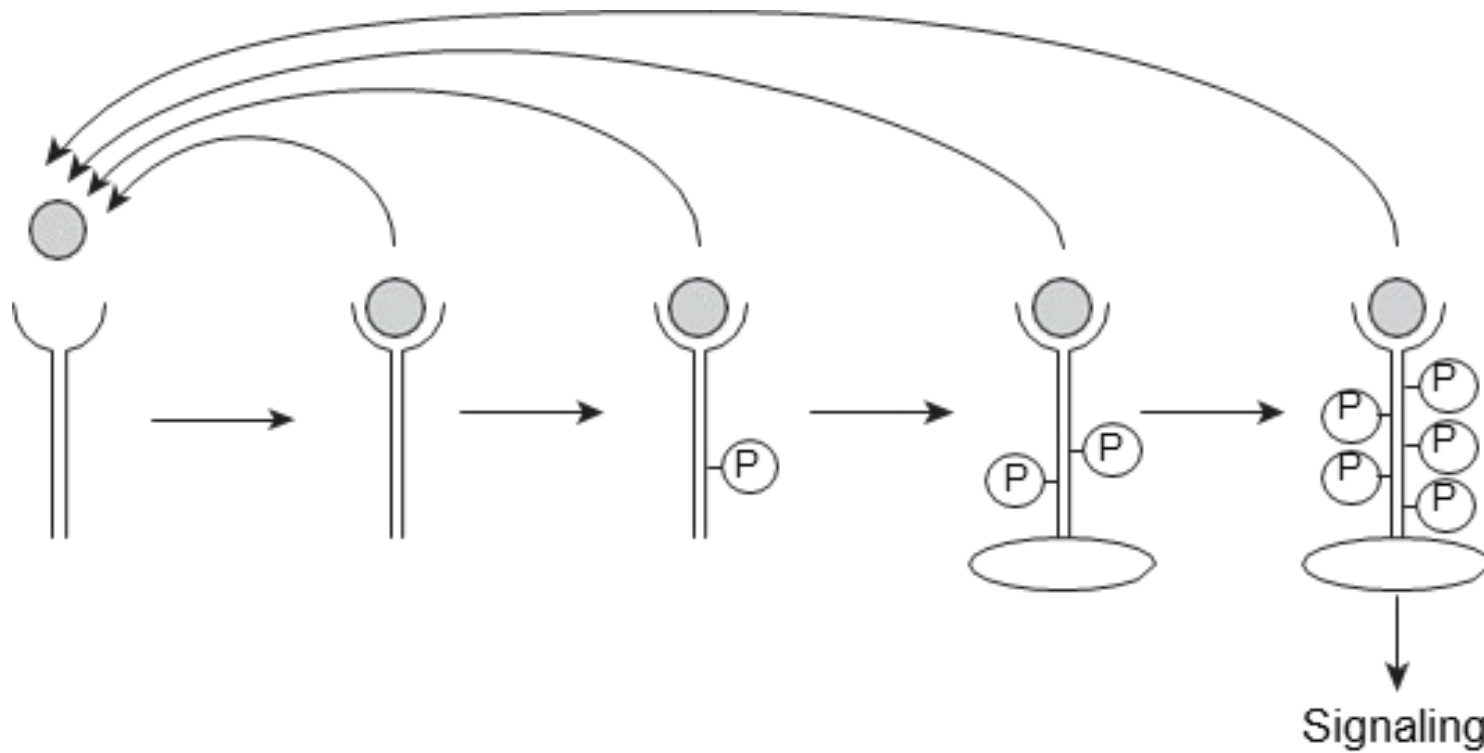
T-Cell Activation: Drastic effects when wrong!

Problem, concentration of wrong ligands much larger than correct ligands



T-Cell Activation:

Requires time consuming receptor modifications



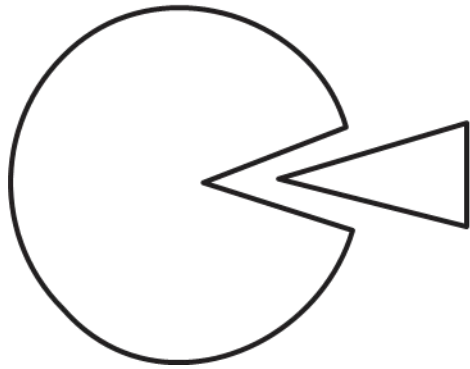
Costs: Loss of sensitivity, as also correct ligand can unbind!

Kinetic Proofreading happens in many situations:

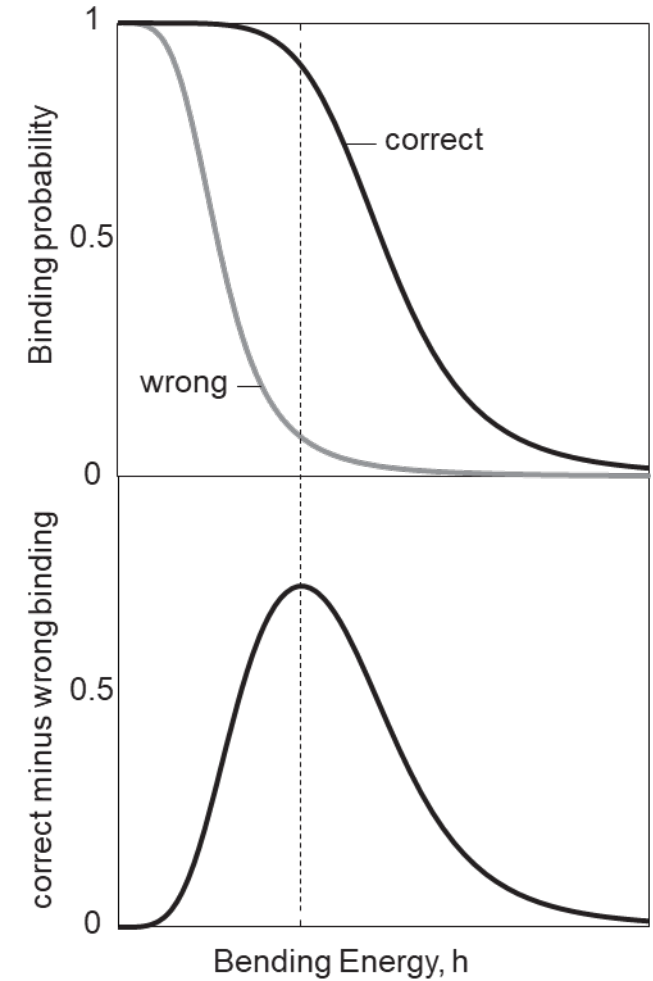
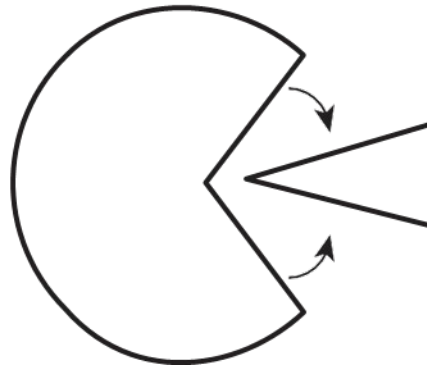
- DNA Repair: After binding of Protein A, phosphorylation required
- Synthesis of tRNA, high energy intermediate between RNA and AA, first modifying RNA -> covalent binding to AA
- Protein degradation by ubiquitination (multiple ubiquins added if correct. Constant removal on ubiquin in cells.

Conformational proofreading... no energy consumption!

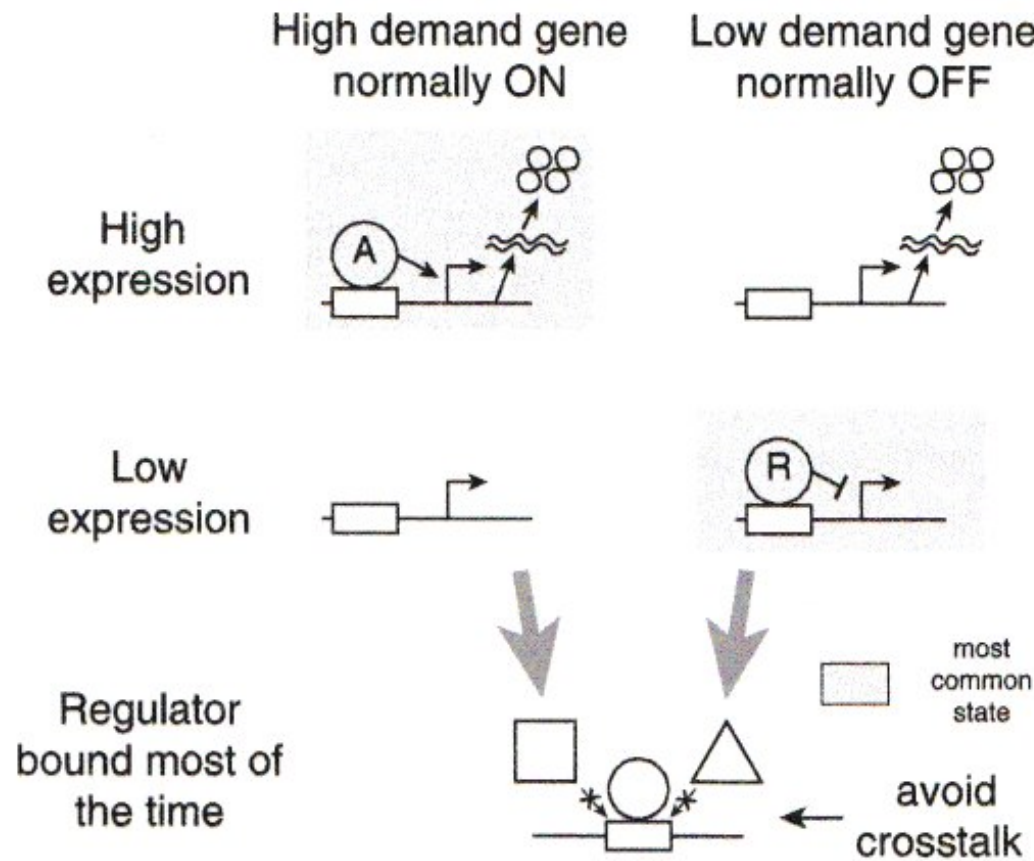
lock and key



induced fit



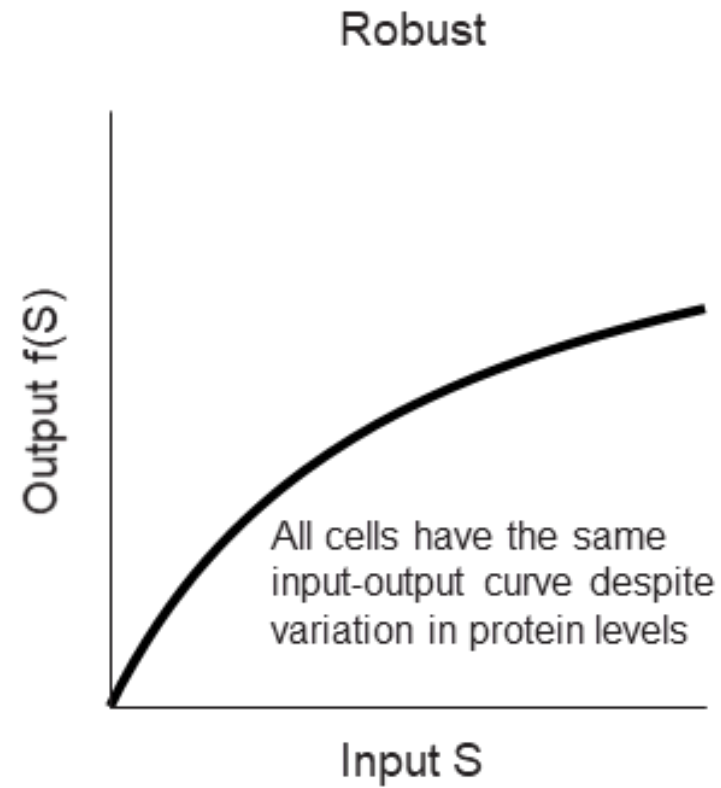
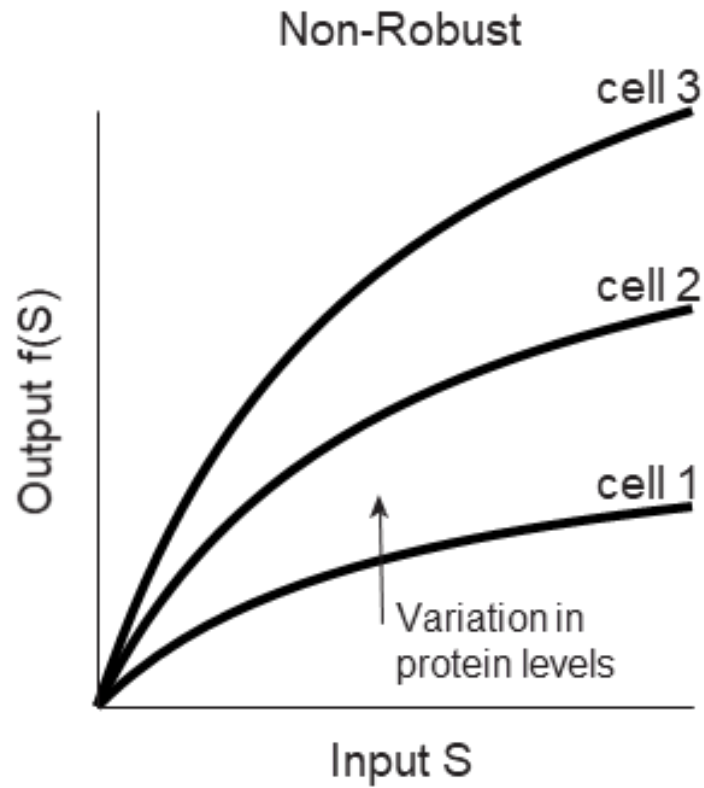
Demand rule for gene regulation:



gene expression	AA	AR	RR
High			
Mid			
Low			

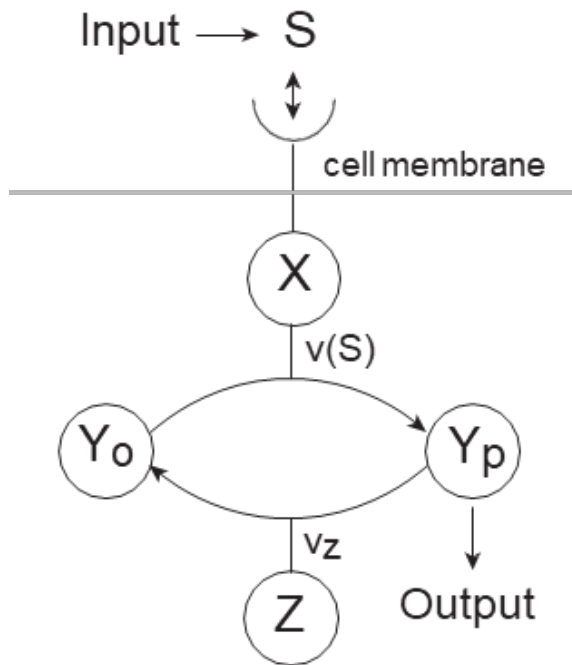
Robust Signaling...

should be independent of protein concentration

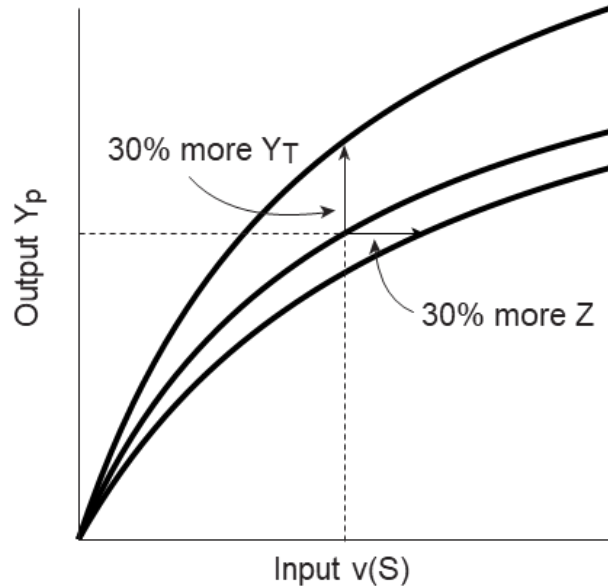


Robust Signaling...

should be independent of protein concentration



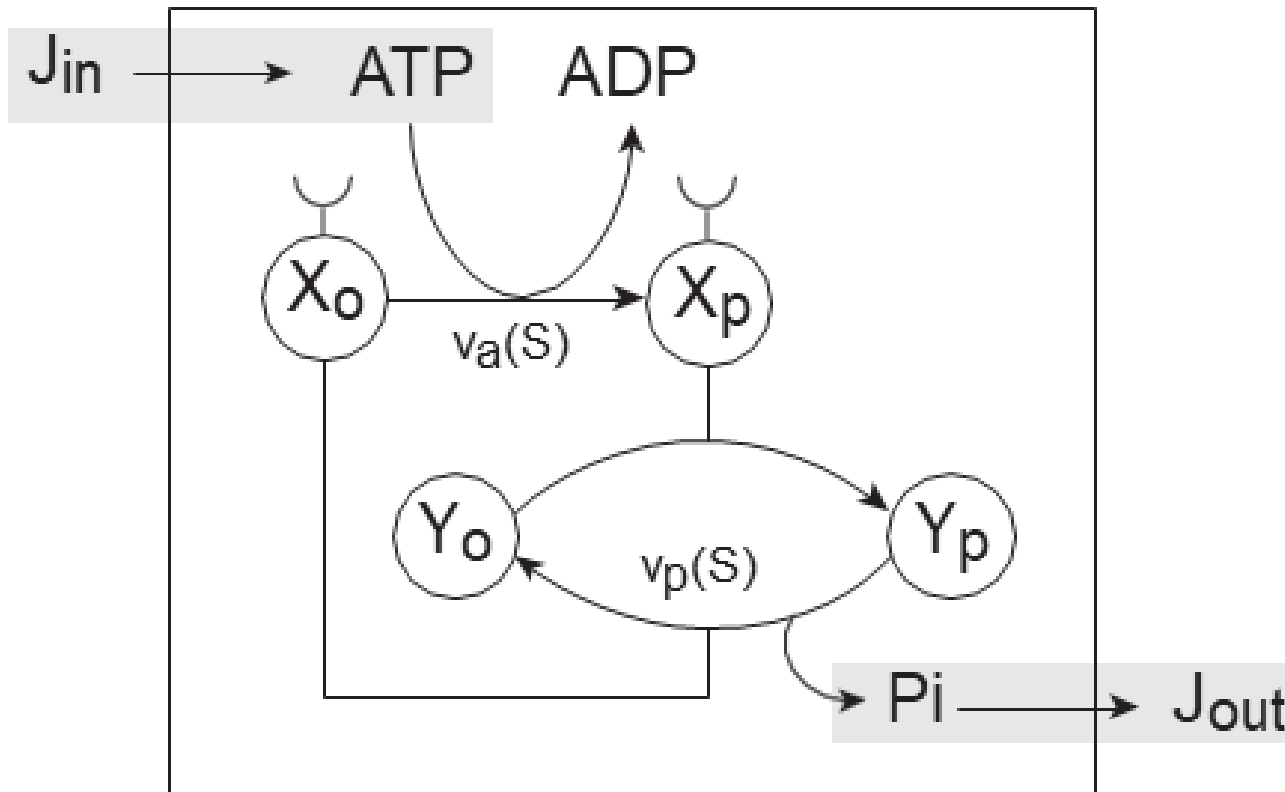
Non-Robust



Robust Signaling...

Impossible, right?

Bifunctional components: Phosphorilates AND dephosphorylates!



Limit of robustness... obviously Y total

