Biology versus the Internet

Similarities

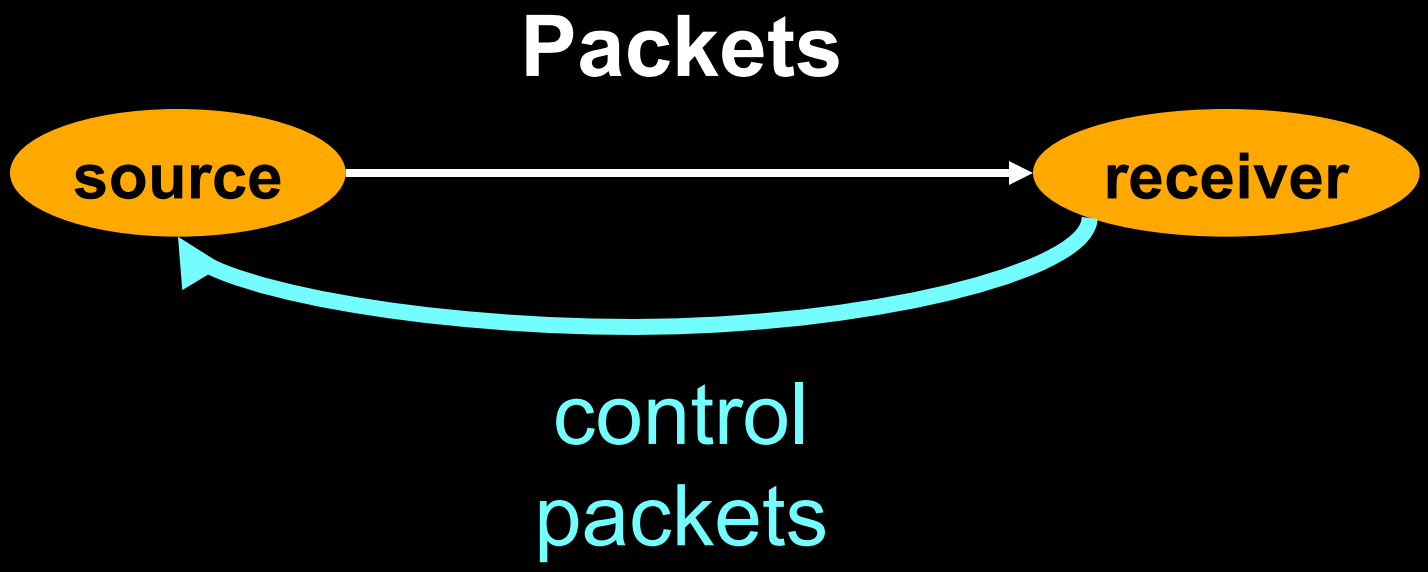
- Evolvable architecture
- **Robust yet fragile**
- **Constraints/deconstrain**
- **Layering, modularity**
- **Hourglass with bowties**
- Feedback
- Dynamics
- Distributed/decentralized
- ***Not*** scale-free, edge-of-chaos, self-organized criticality, etc

Differences

- Metabolism
- Materials and energy
- **Autocatalytic feedback**
- Feedback complexity
- Development and regeneration
- >4B years of evolution

Focus on bacterial biosphere

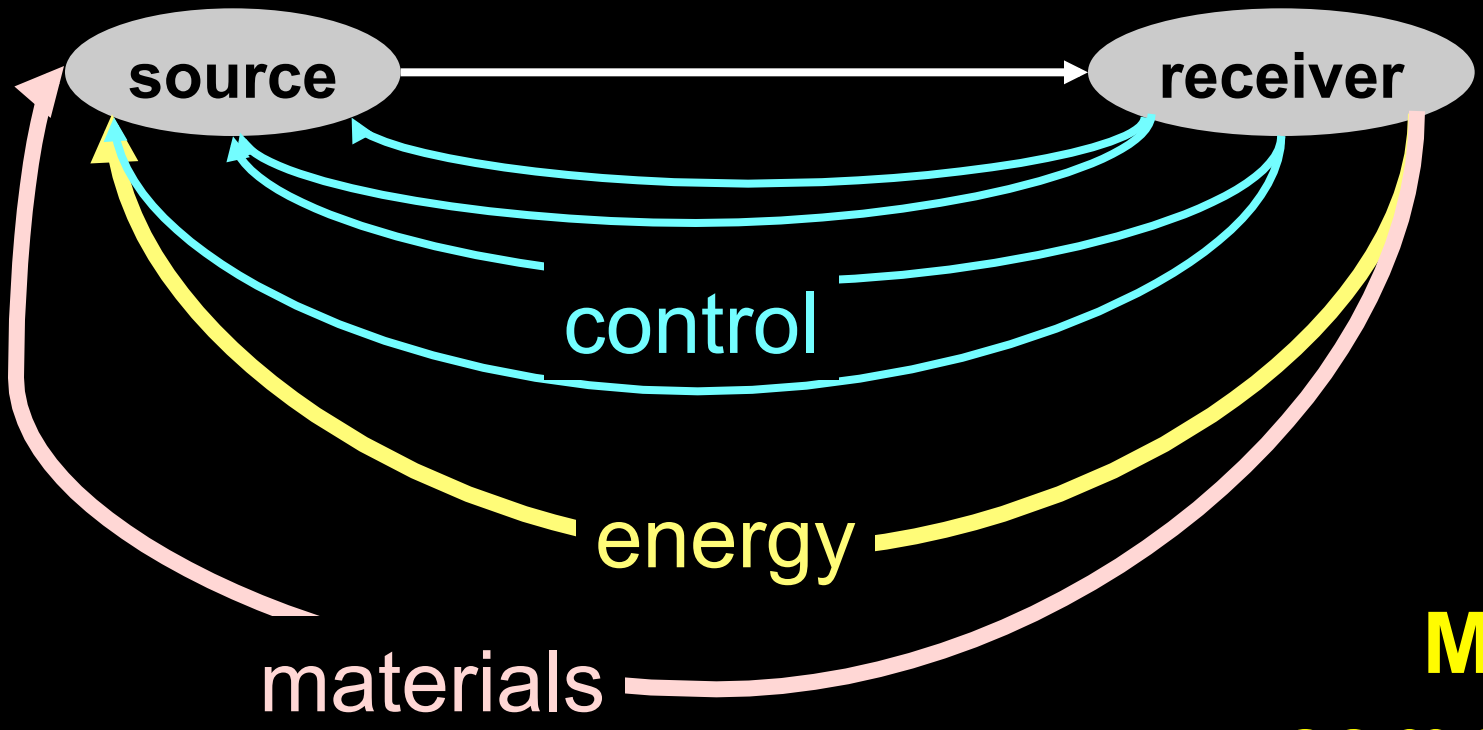
Control of the Internet



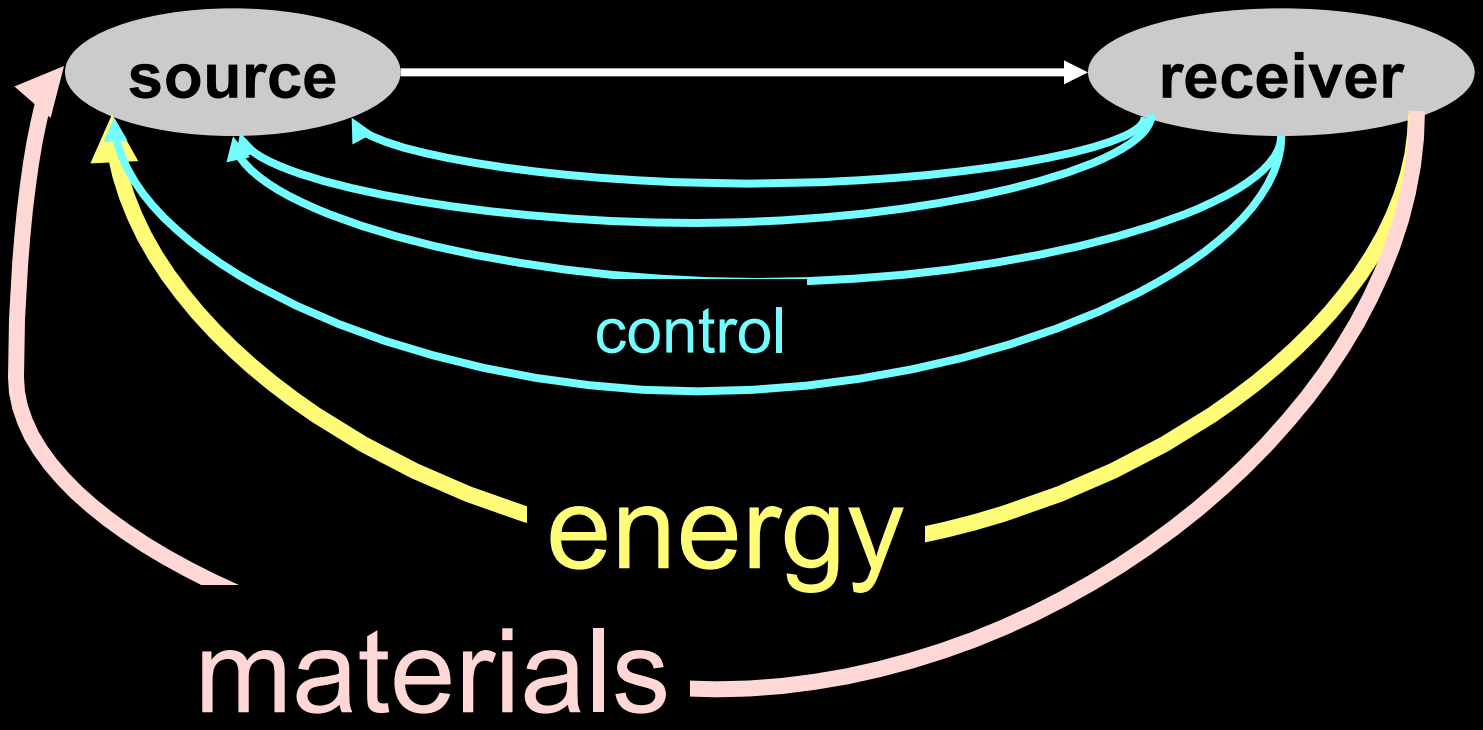
signaling
gene expression
metabolism
lineage

Biological pathways

signaling
gene expression
metabolism
lineage

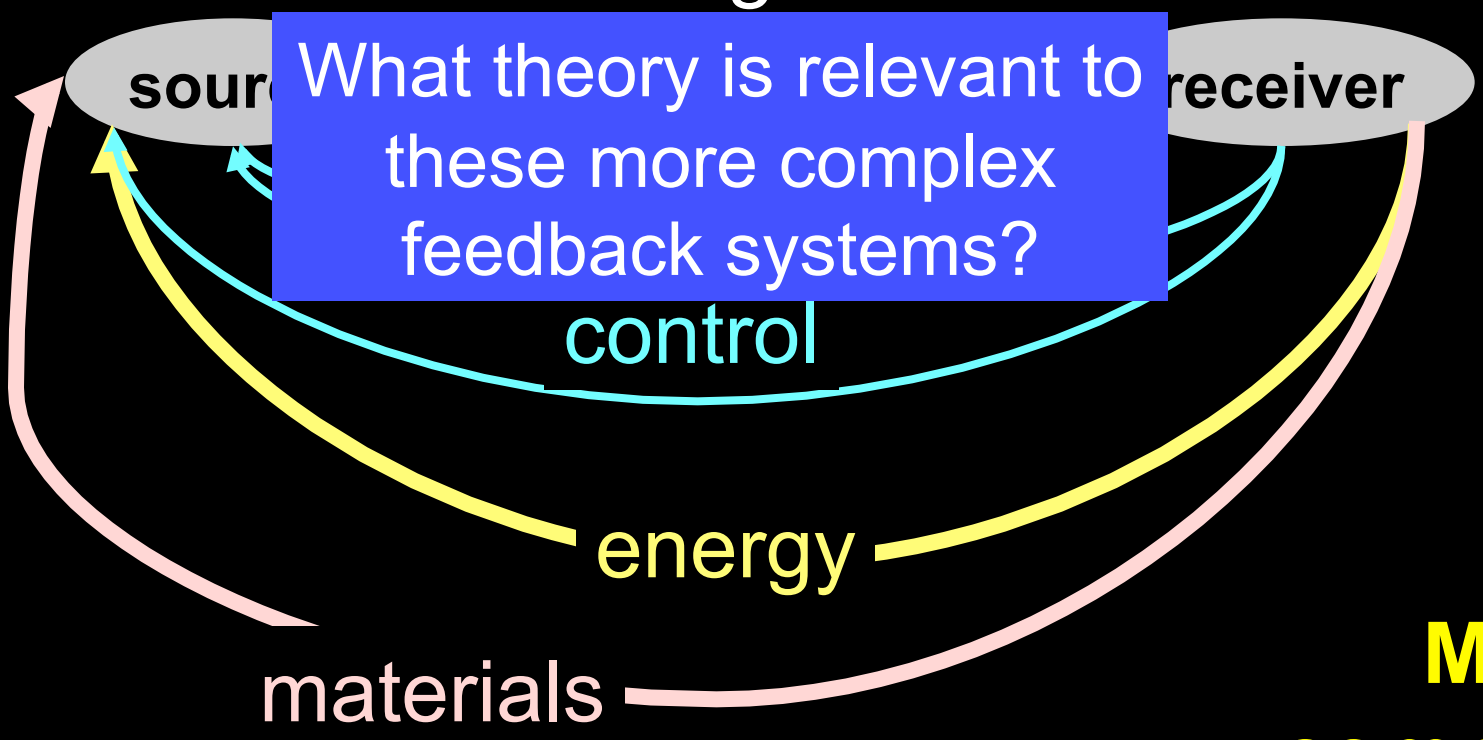


More complex feedback



Autocatalytic feedback

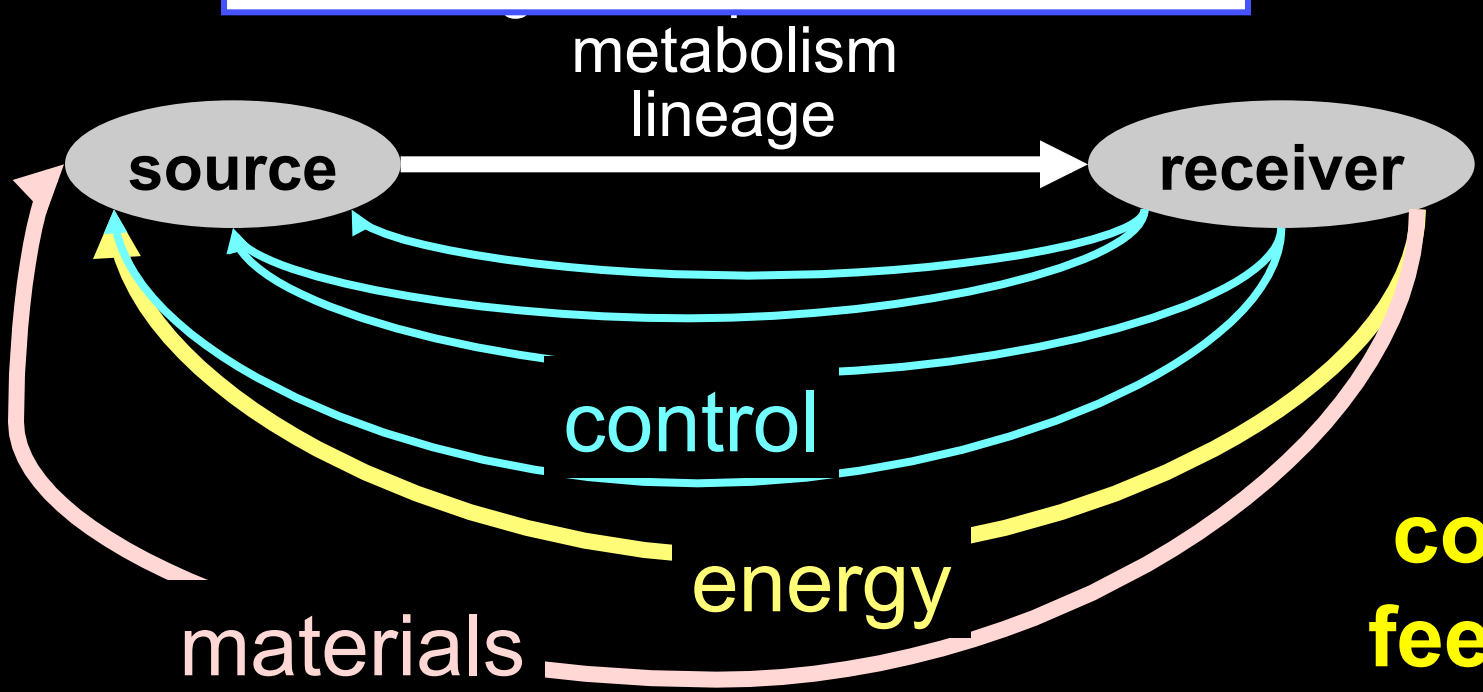
signaling
gene expression
metabolism
lineage



More complex feedback

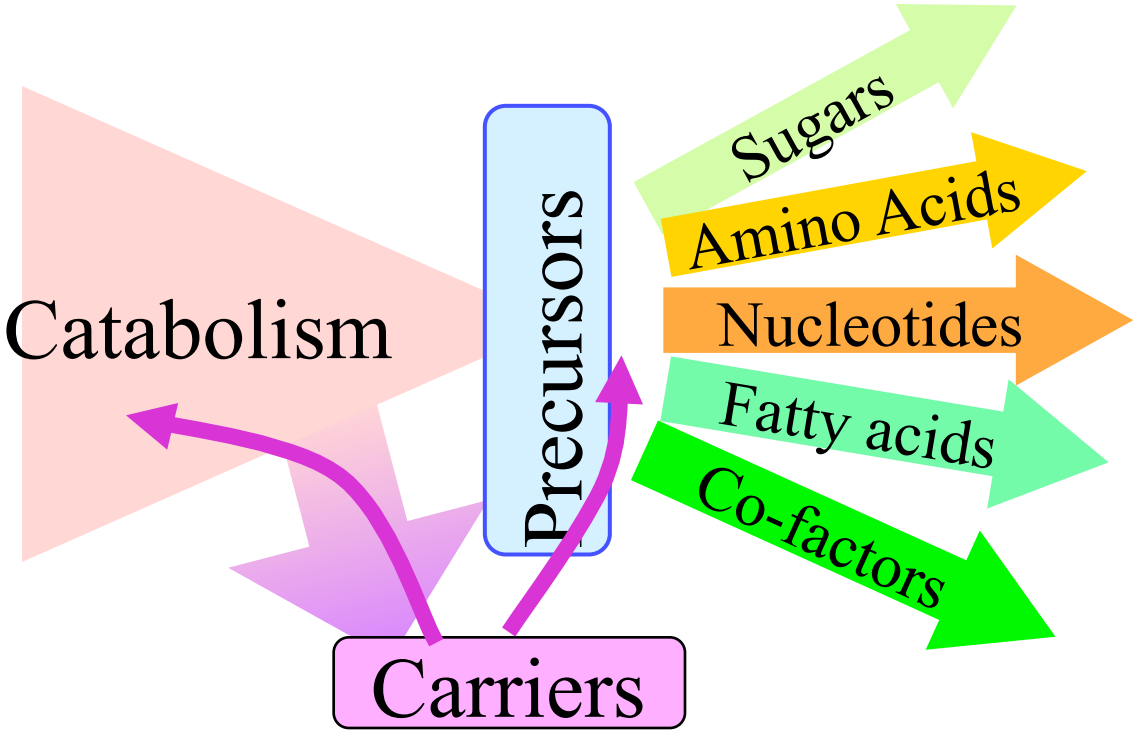
What theory is relevant to these more complex feedback systems?

$$\frac{1}{\pi}\int_0^{\infty}\ln\left|S(j\omega)\right|\frac{z}{z^2+\omega^2}d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$



More complex feedback

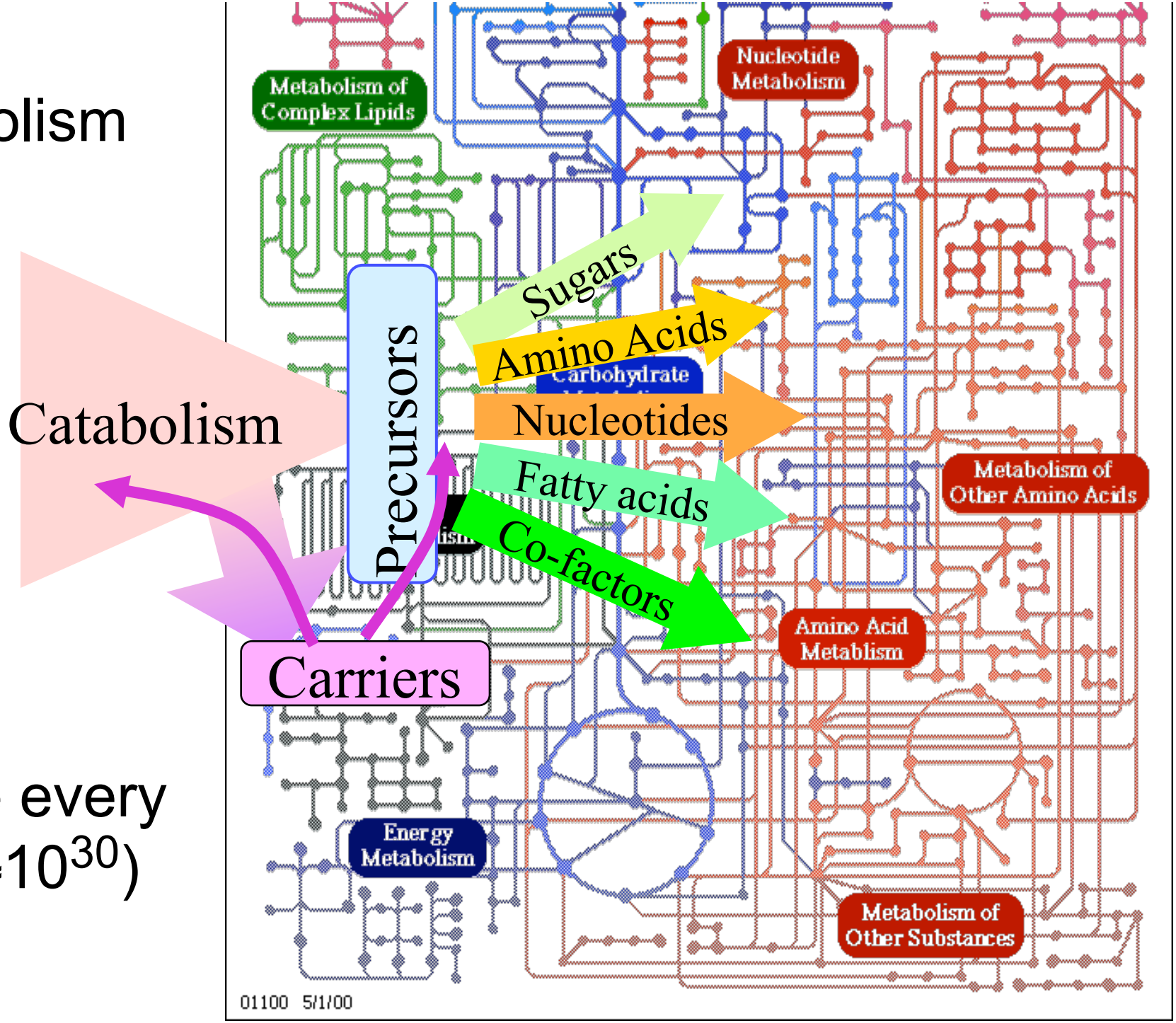
Inside every cell



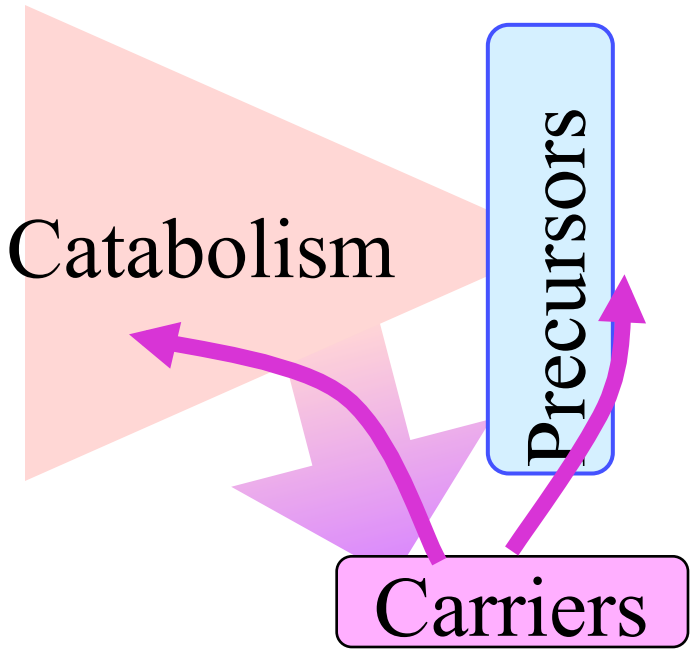
Core metabolic bowtie

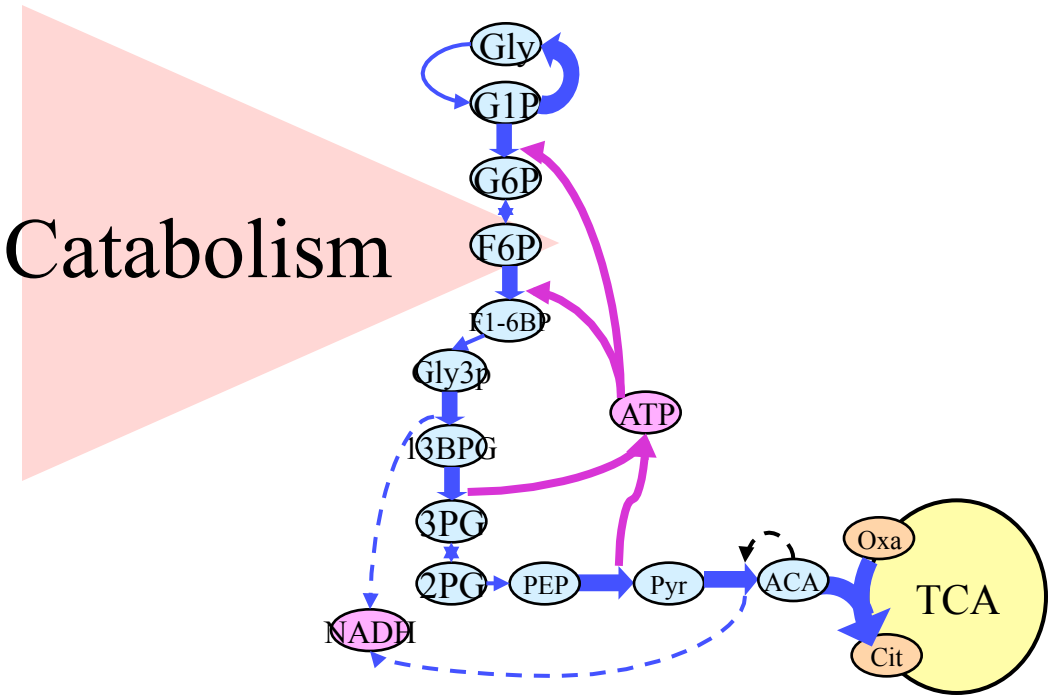
Skipping the “OS” story, right to networks

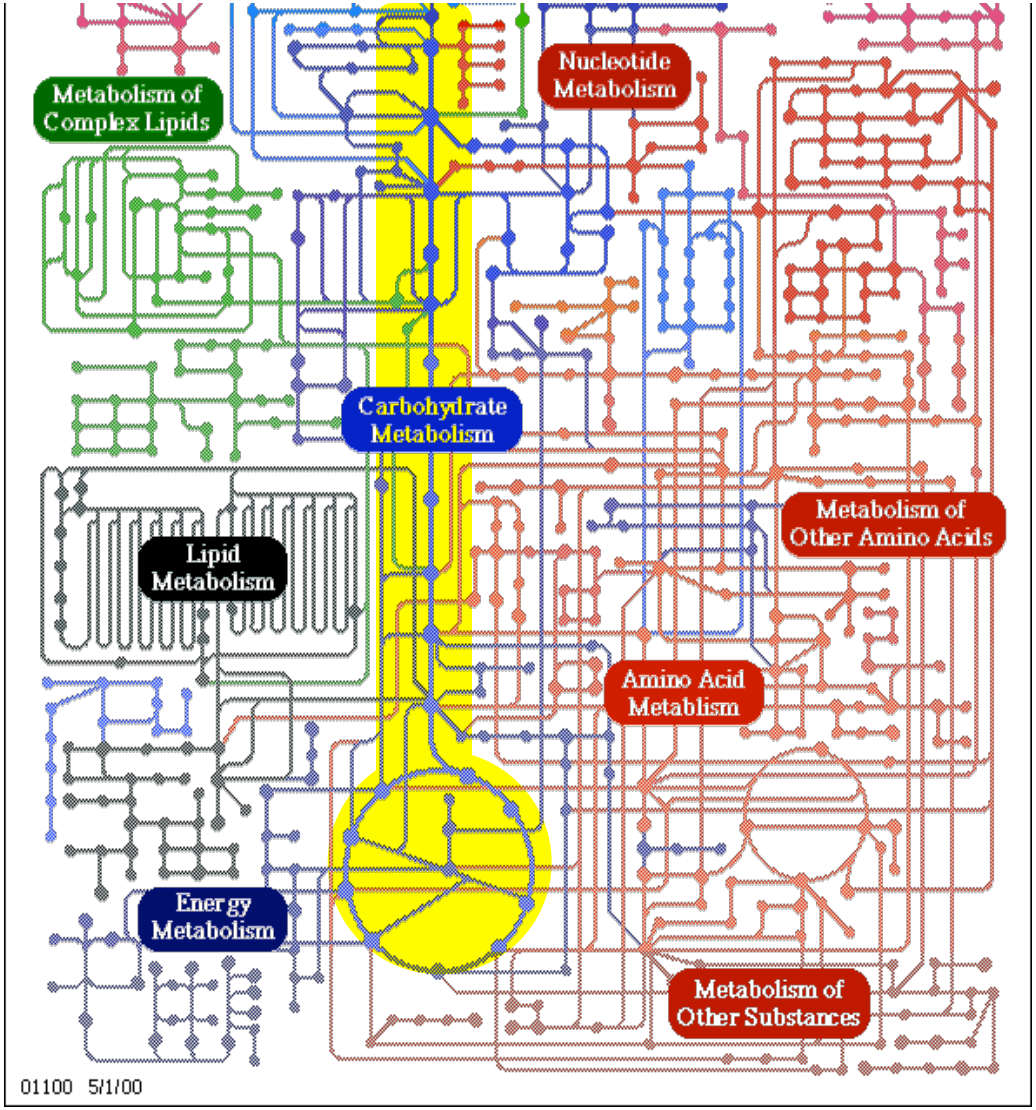
Core metabolism

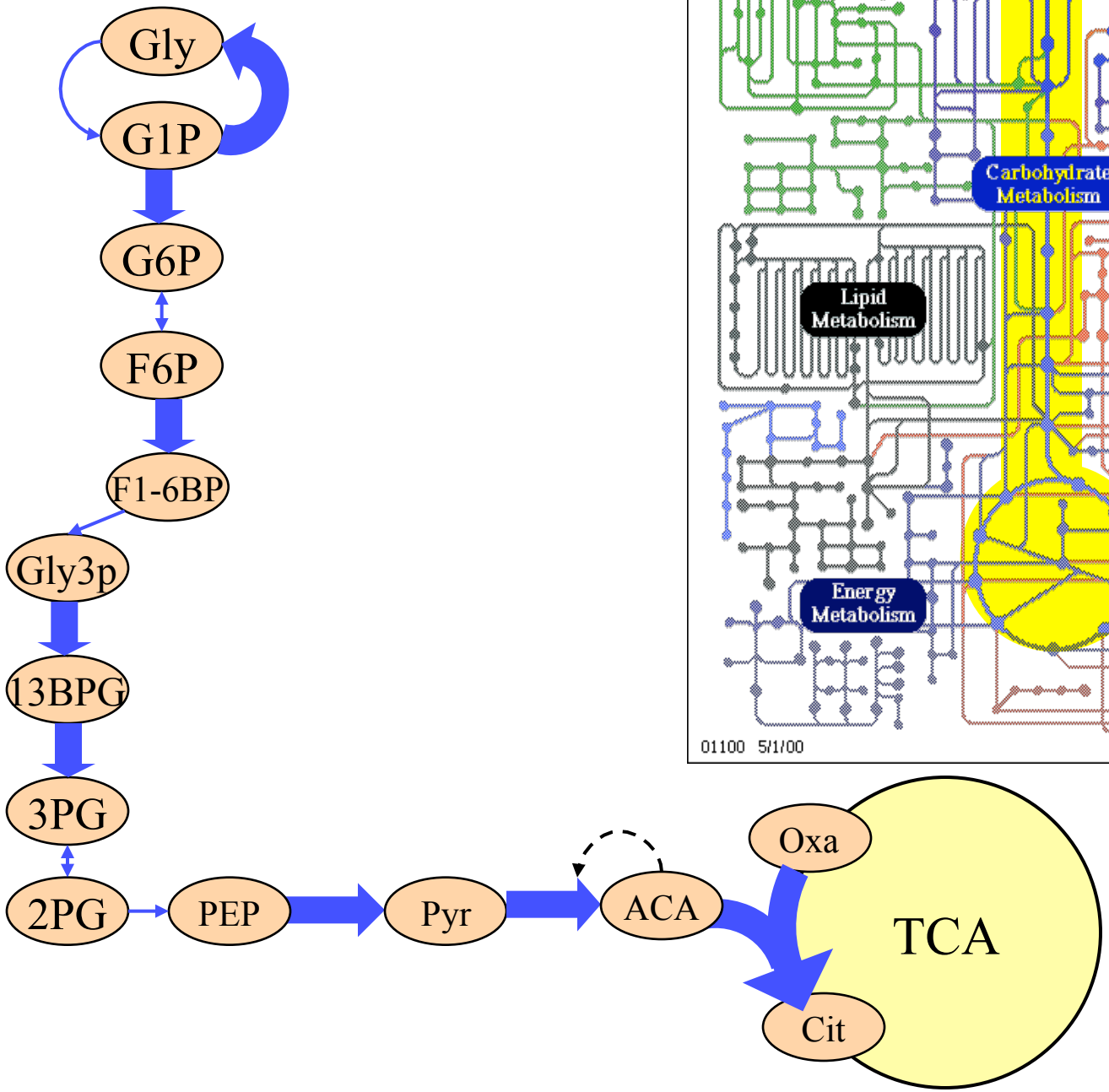


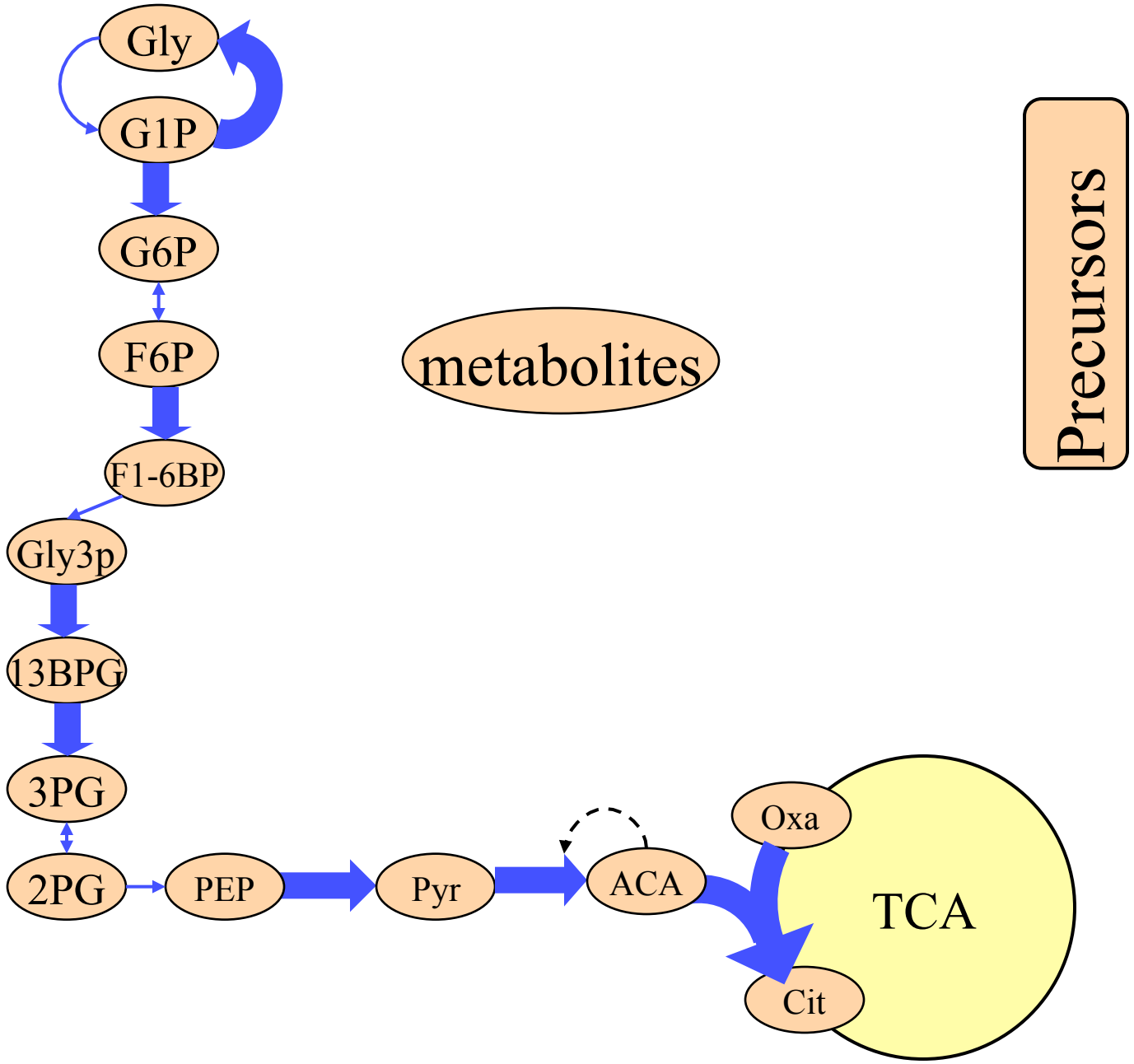
Inside every cell ($\approx 10^{30}$)

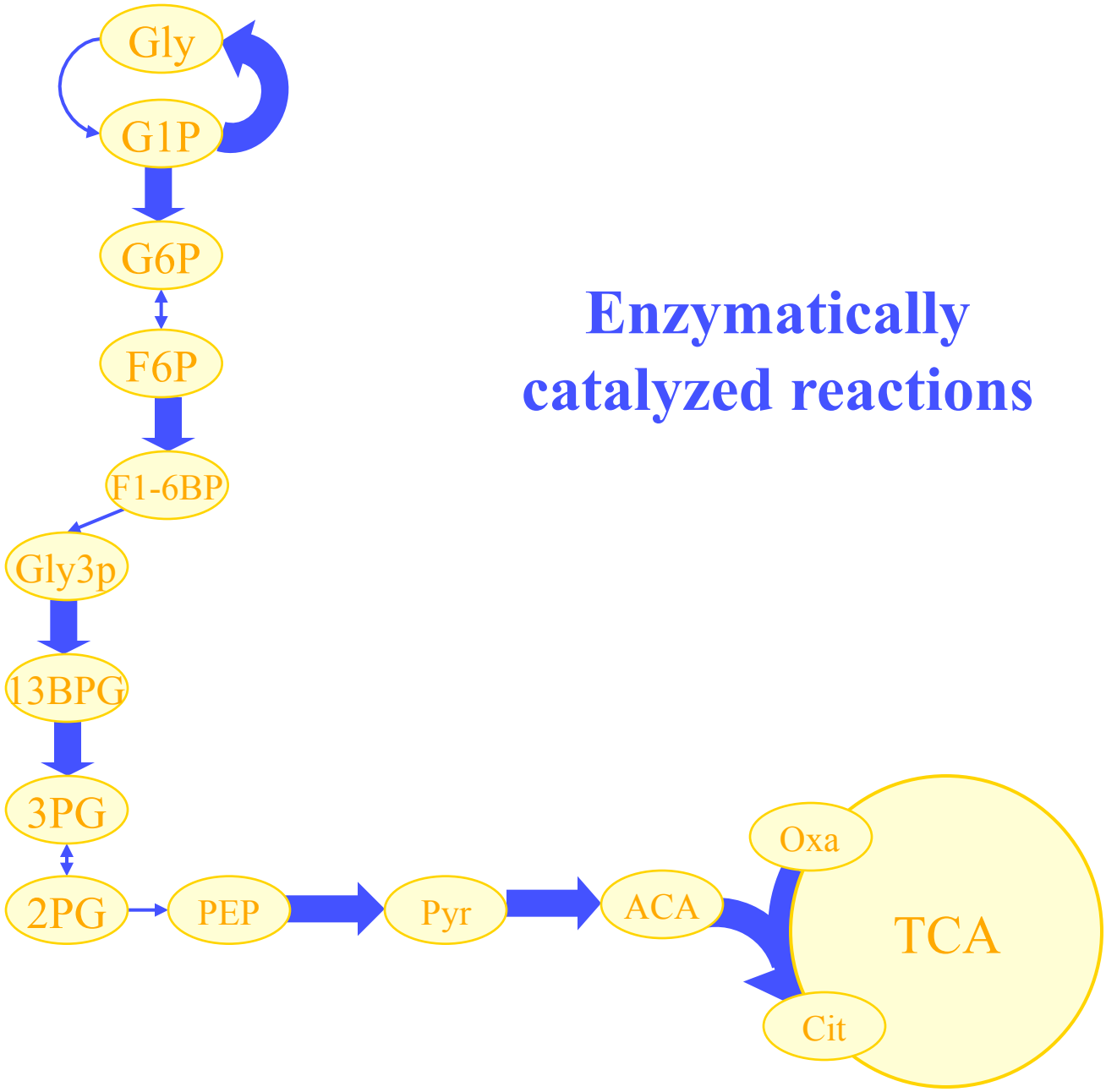

Catabolism
Precursors
Carriers


Catabolism
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit
ATP
NADH

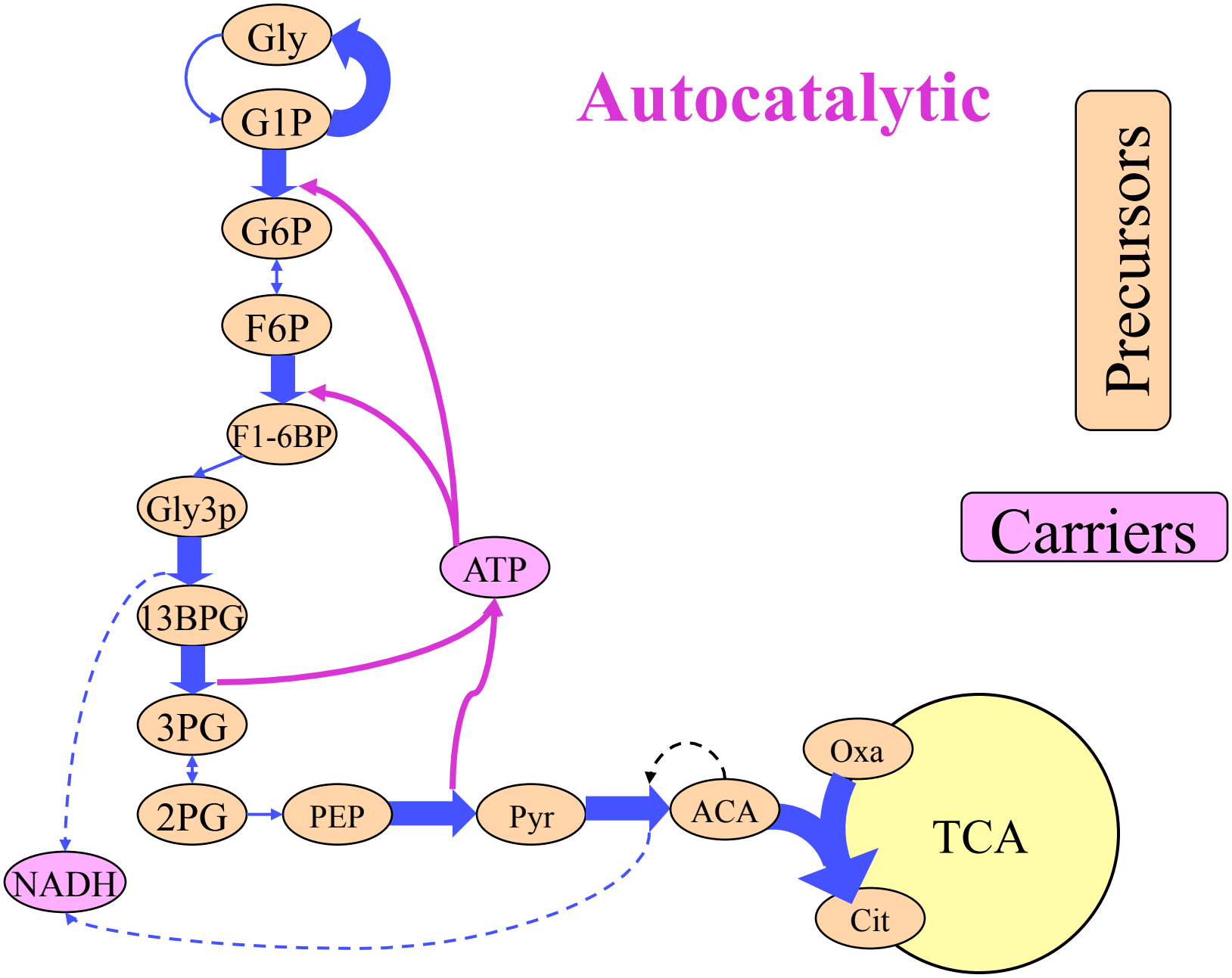

Metabolism of Complex Lipids
Nucleotide Metabolism
Carbohydrate Metabolism
Lipid Metabolism
Metabolism of Other Amino Acids
Amino Acid Metablism
Energy Metabolism
Metabolism of Other Substances
01100 5/1/00

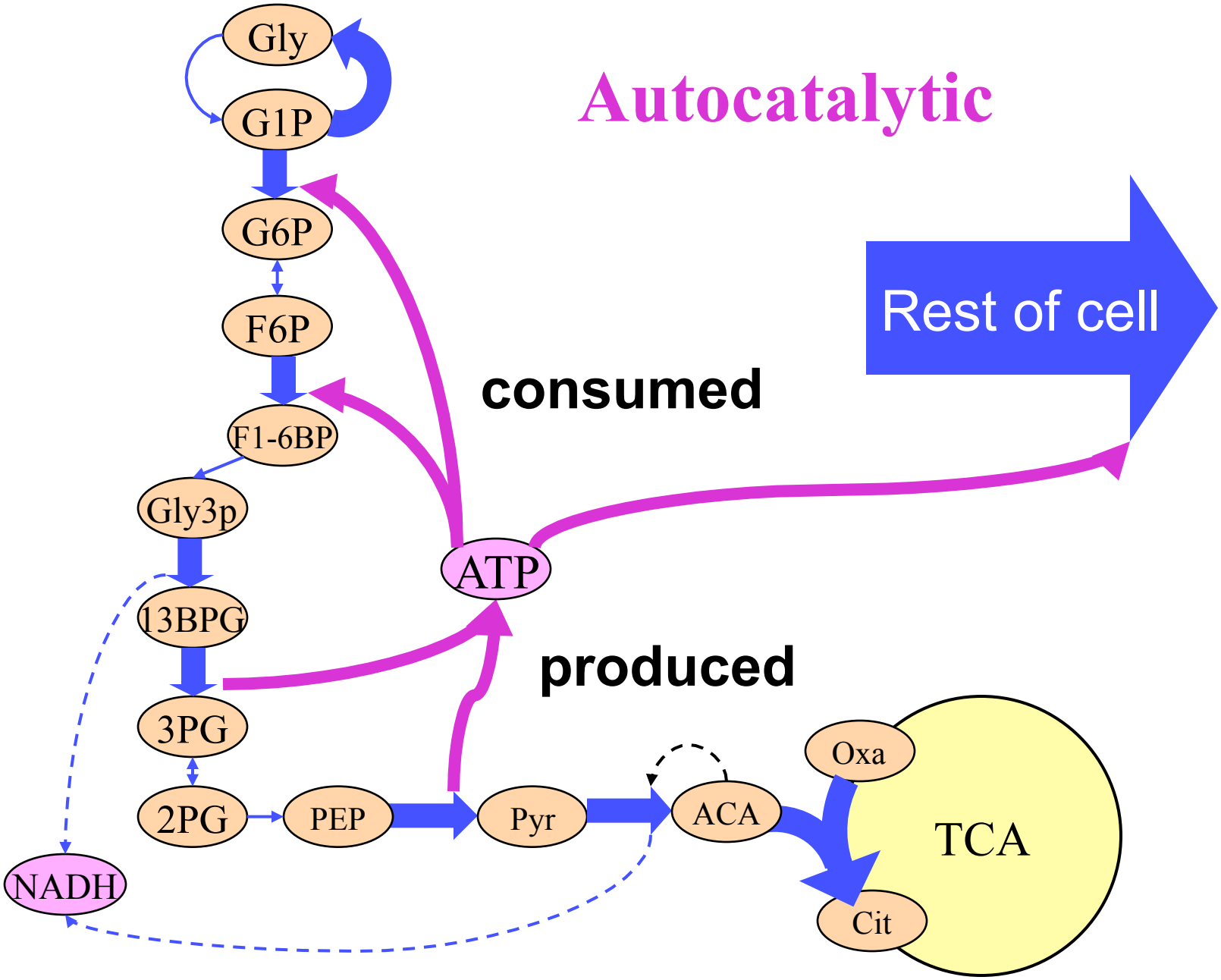

Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit

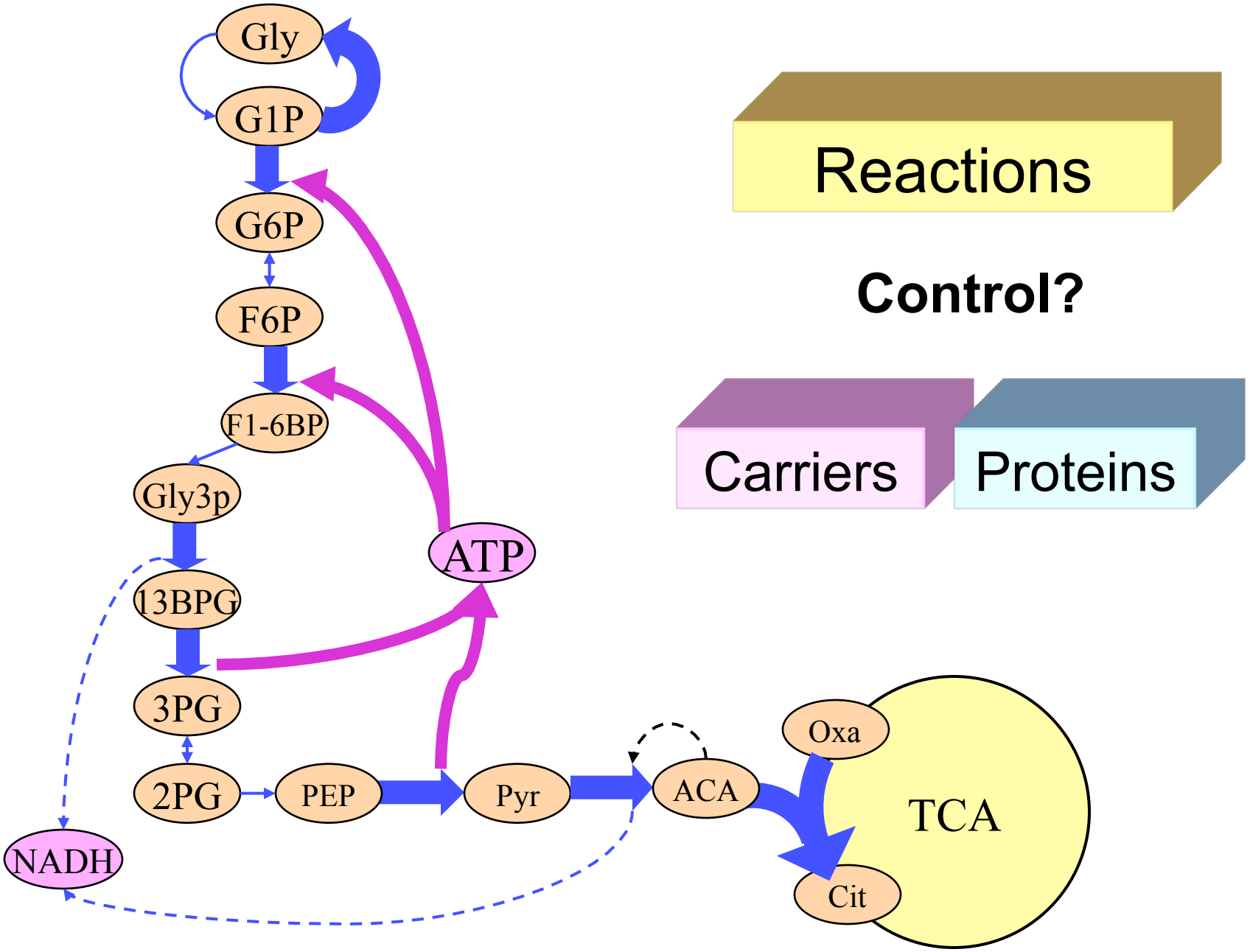

Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit
metabolites
Precursors

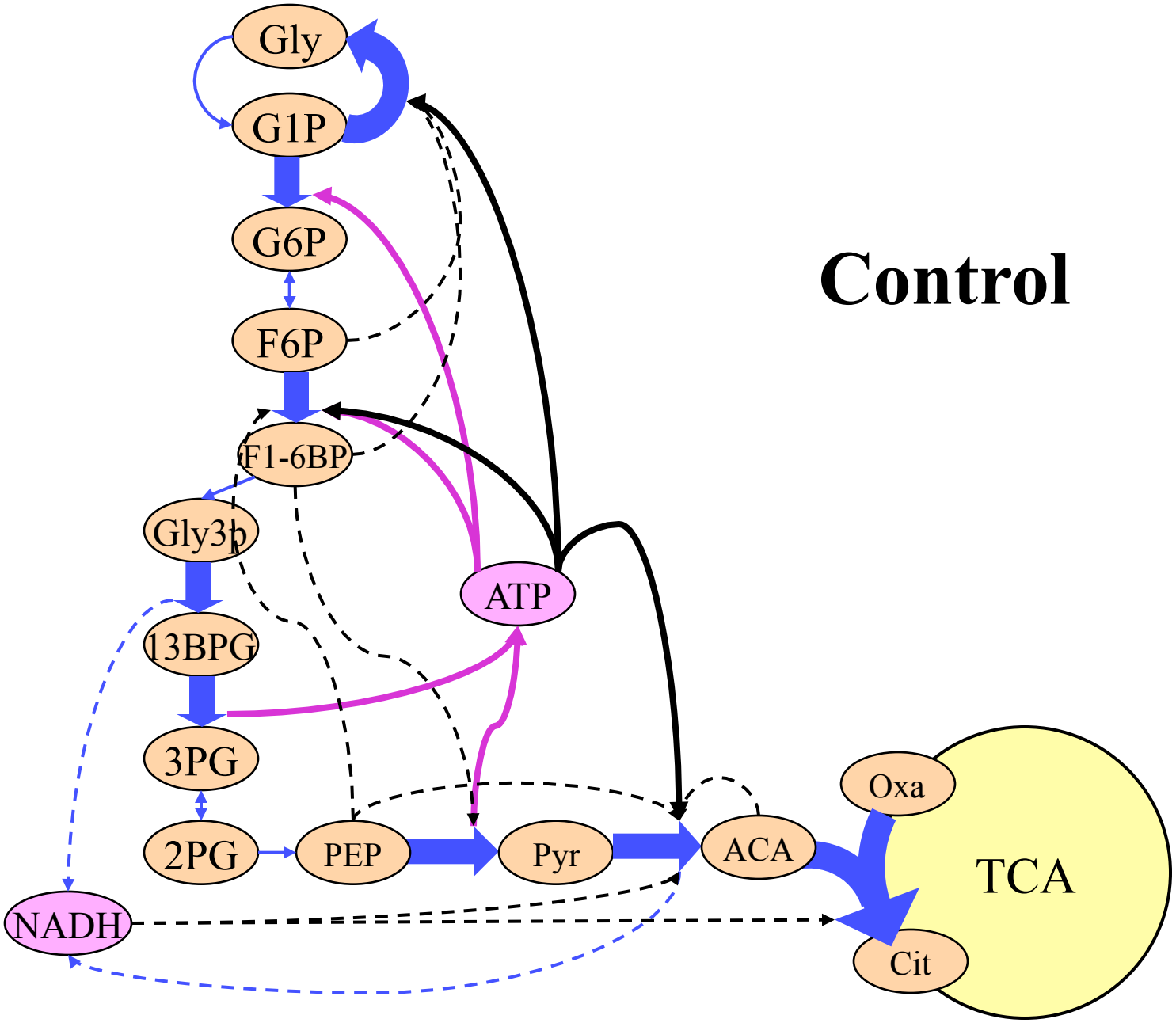


Enzymatically catalyzed reactions

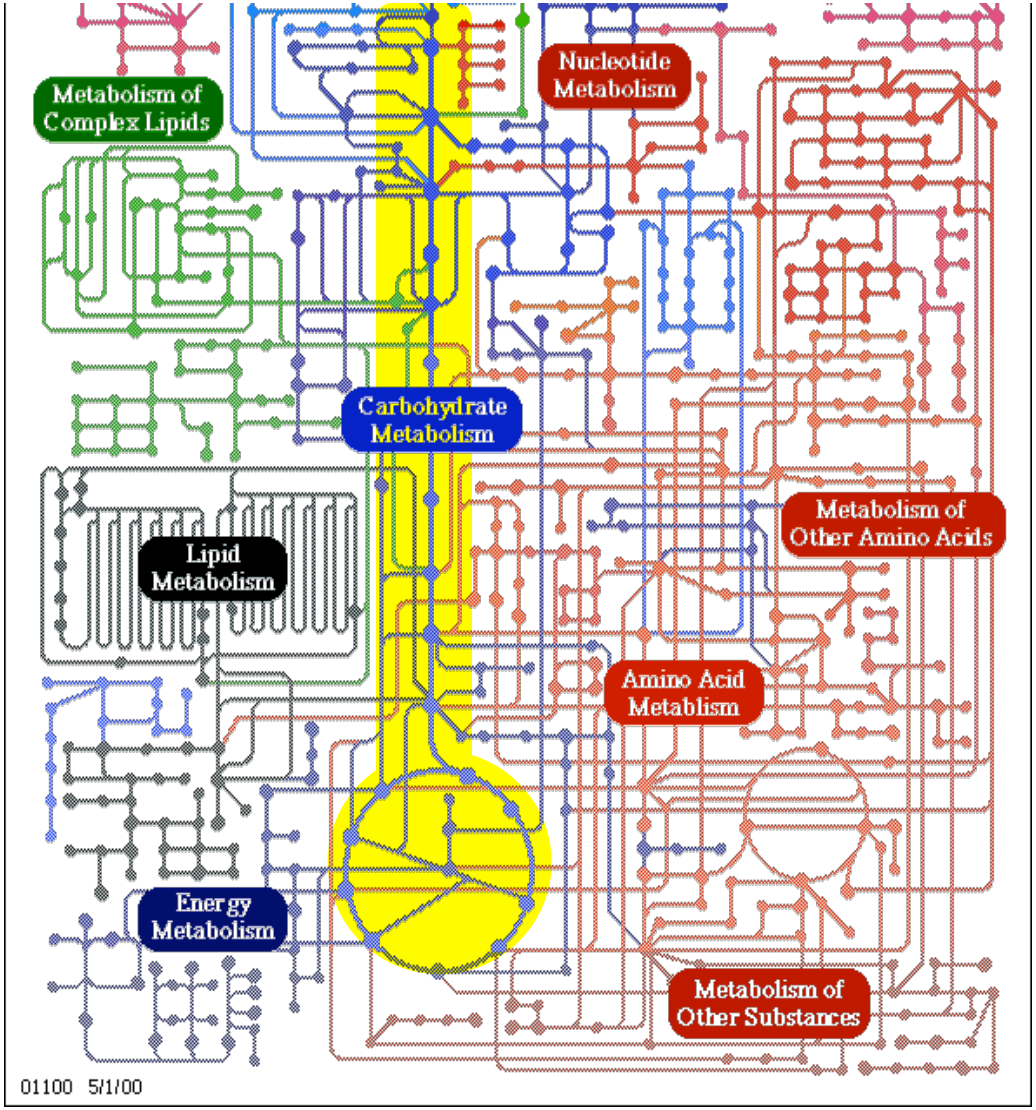

Autocatalytic
Precursors
Carriers
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
TCA
Cit

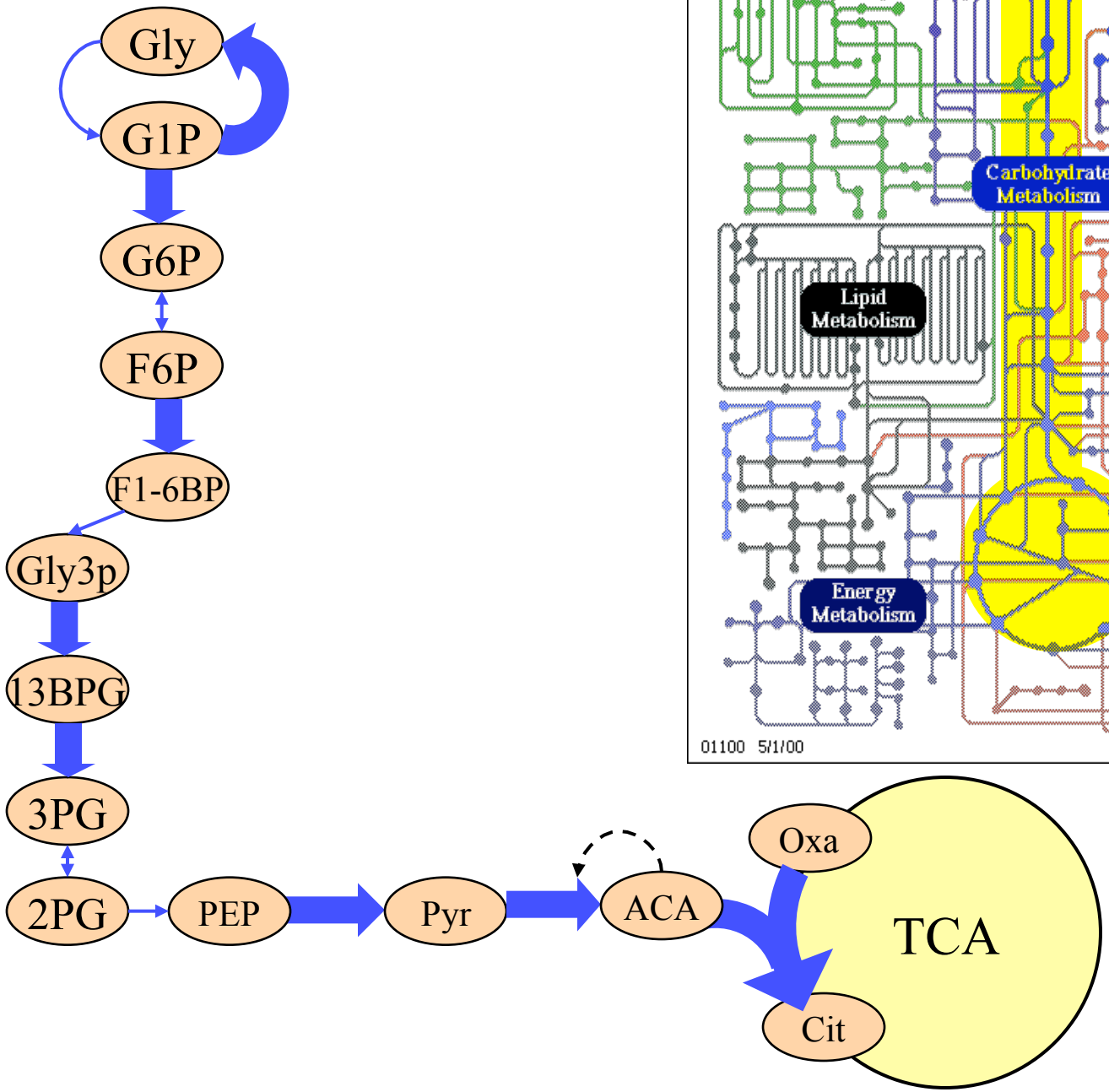

Autocatalytic
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
NADH
ATP
consumed
produced
Rest of cell
Oxa
TCA
Cit


Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
TCA
Cit
Reactions
Control?
Carriers
Proteins

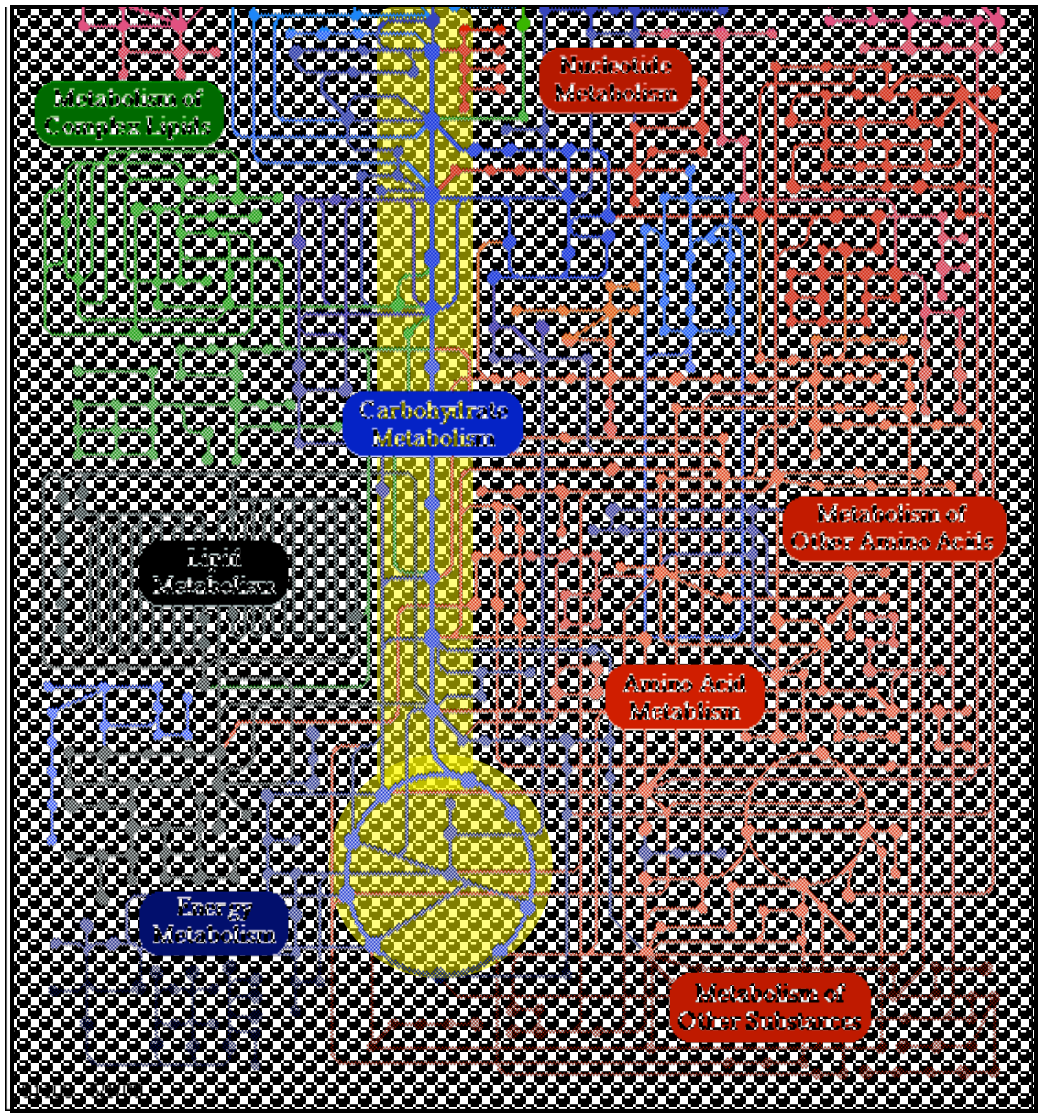

Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
TCA
Cit

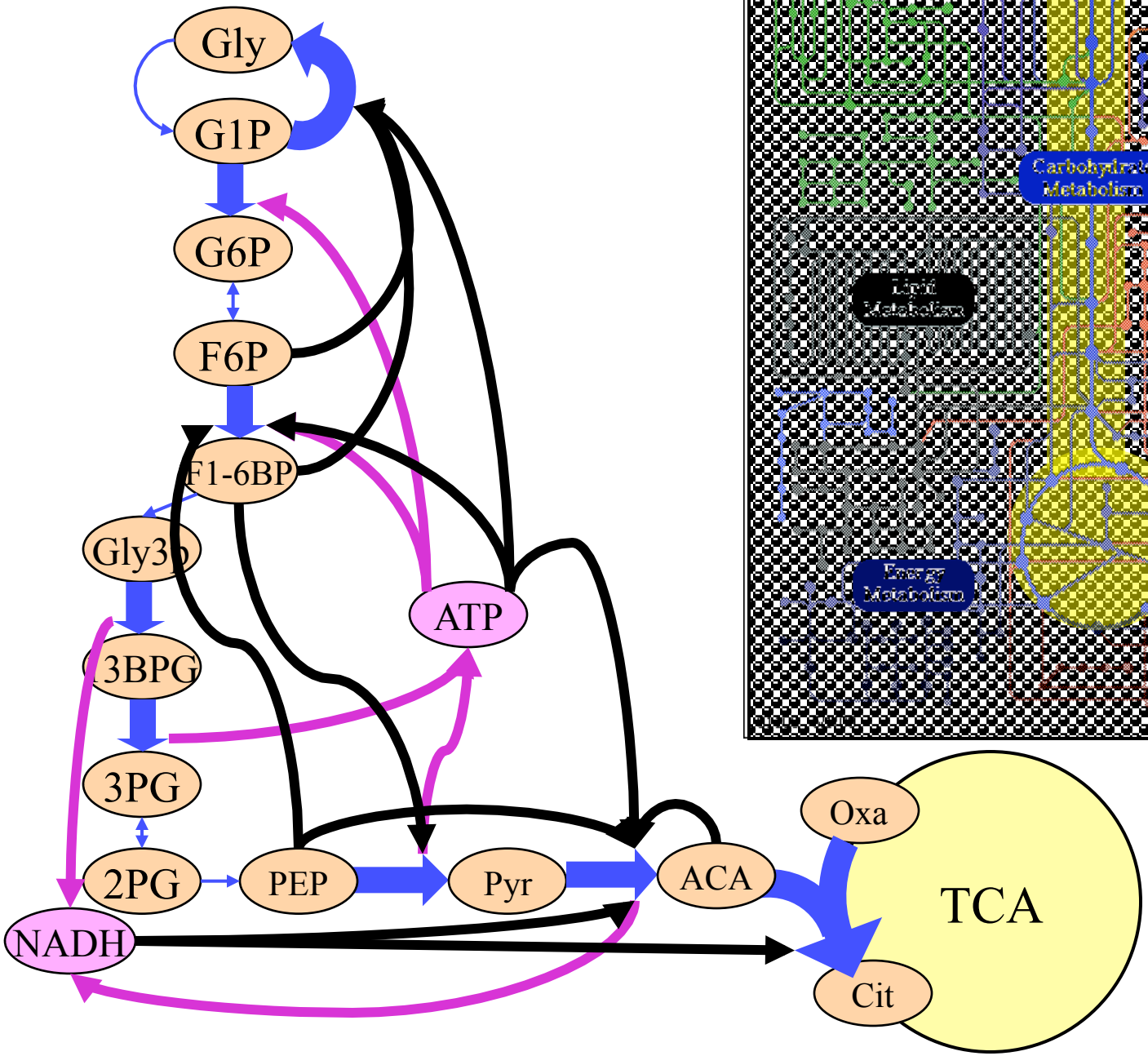
Control

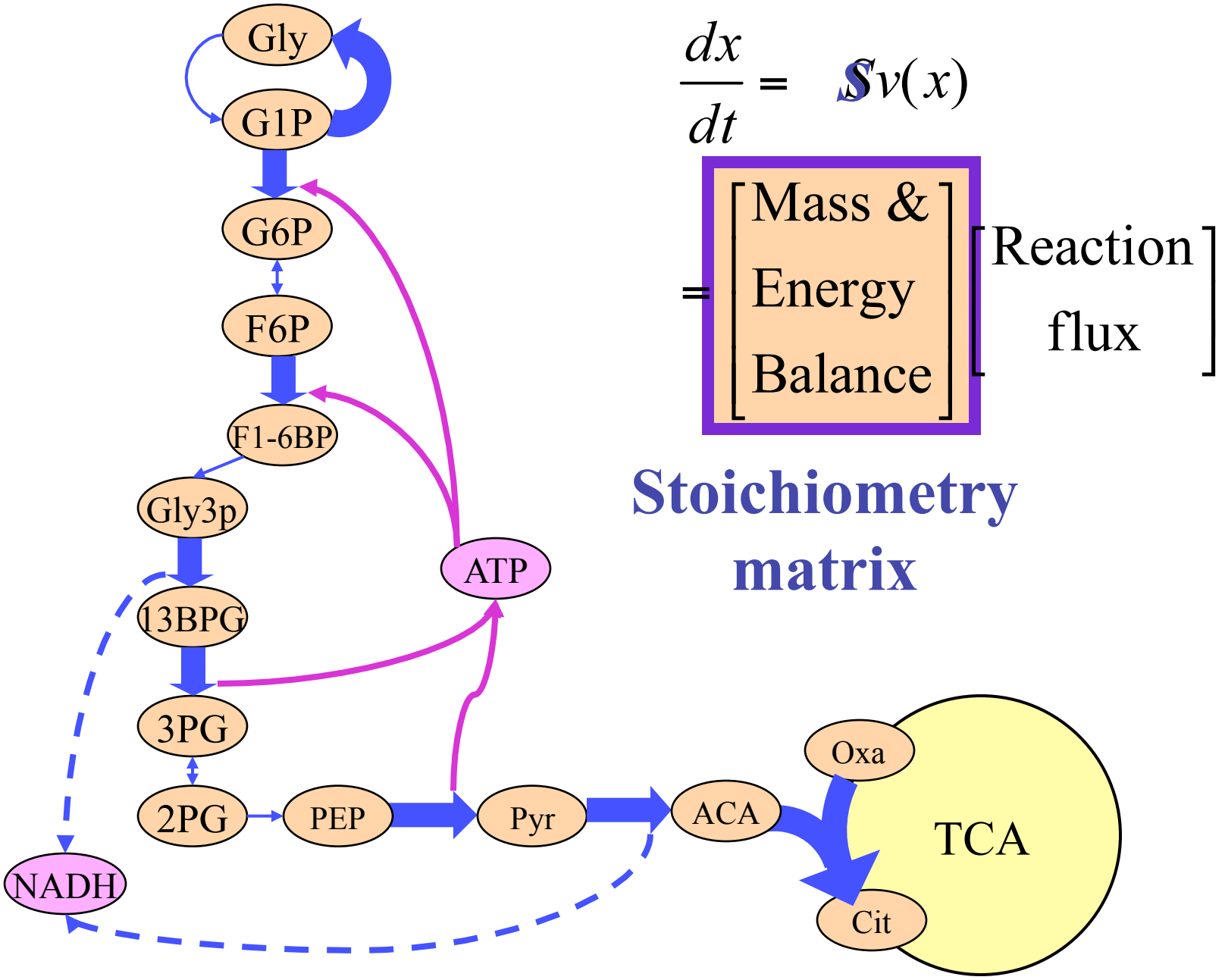

Metabolism of Complex Lipids
Nucleotide Metabolism
Carbohydrate Metabolism
Lipid Metabolism
Metabolism of Other Amino Acids
Amino Acid Metablism
Energy Metabolism
Metabolism of Other Substances
01100 5/1/00


Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit

If we drew the feedback loops the diagram would be unreadable.



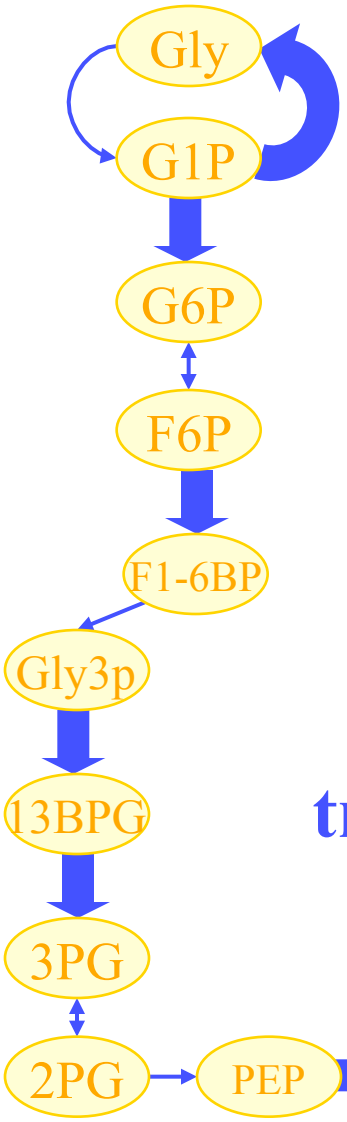




$$\frac{dx}{dt} = \mathbf{S}v(x)$$

$$= \begin{bmatrix} \text{Mass \&} \\ \text{Energy} \\ \text{Balance} \end{bmatrix} \begin{bmatrix} \text{Reaction} \\ \text{flux} \end{bmatrix}$$

Stoichiometry matrix

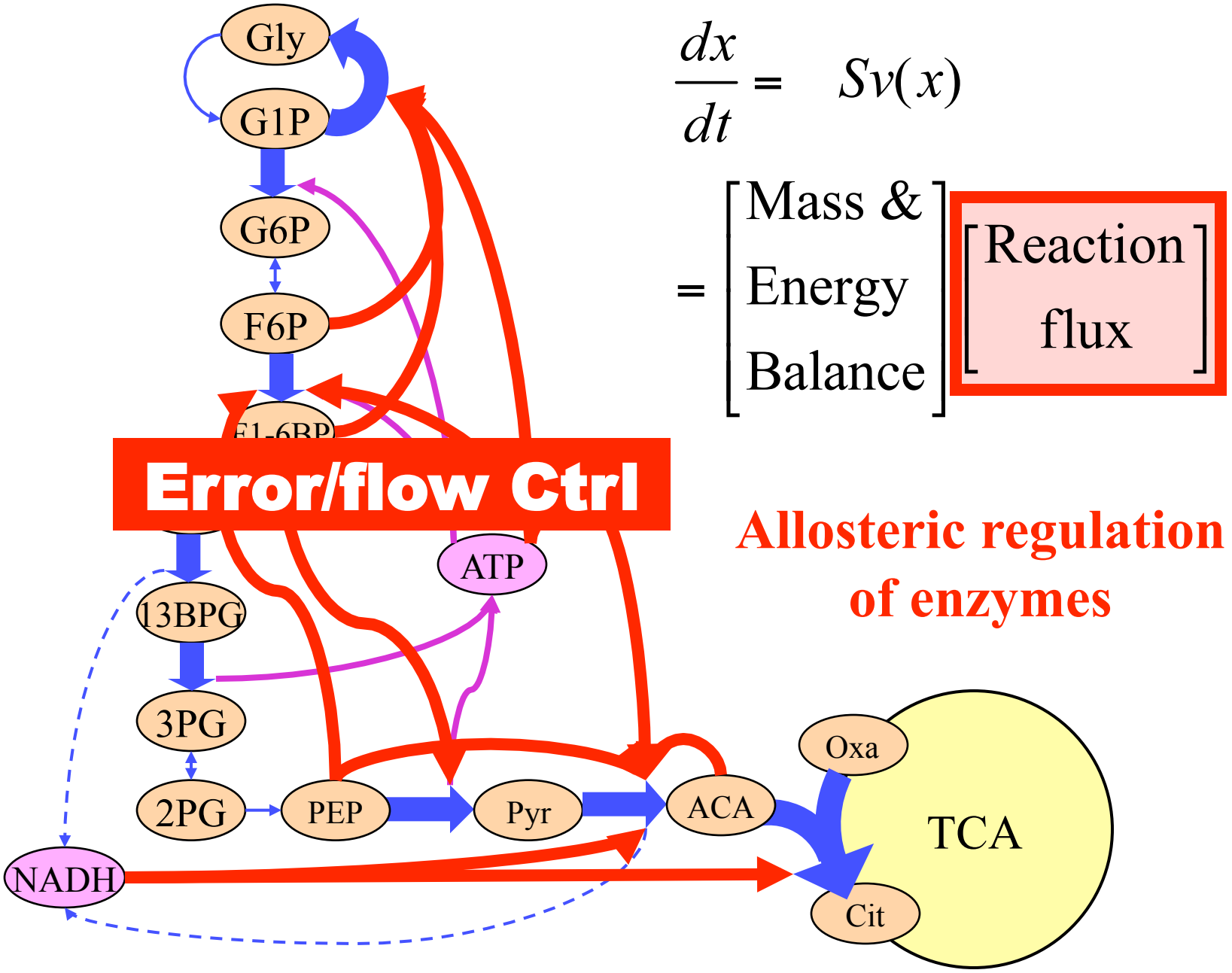


$$\frac{dx}{dt} = Sv(x)$$

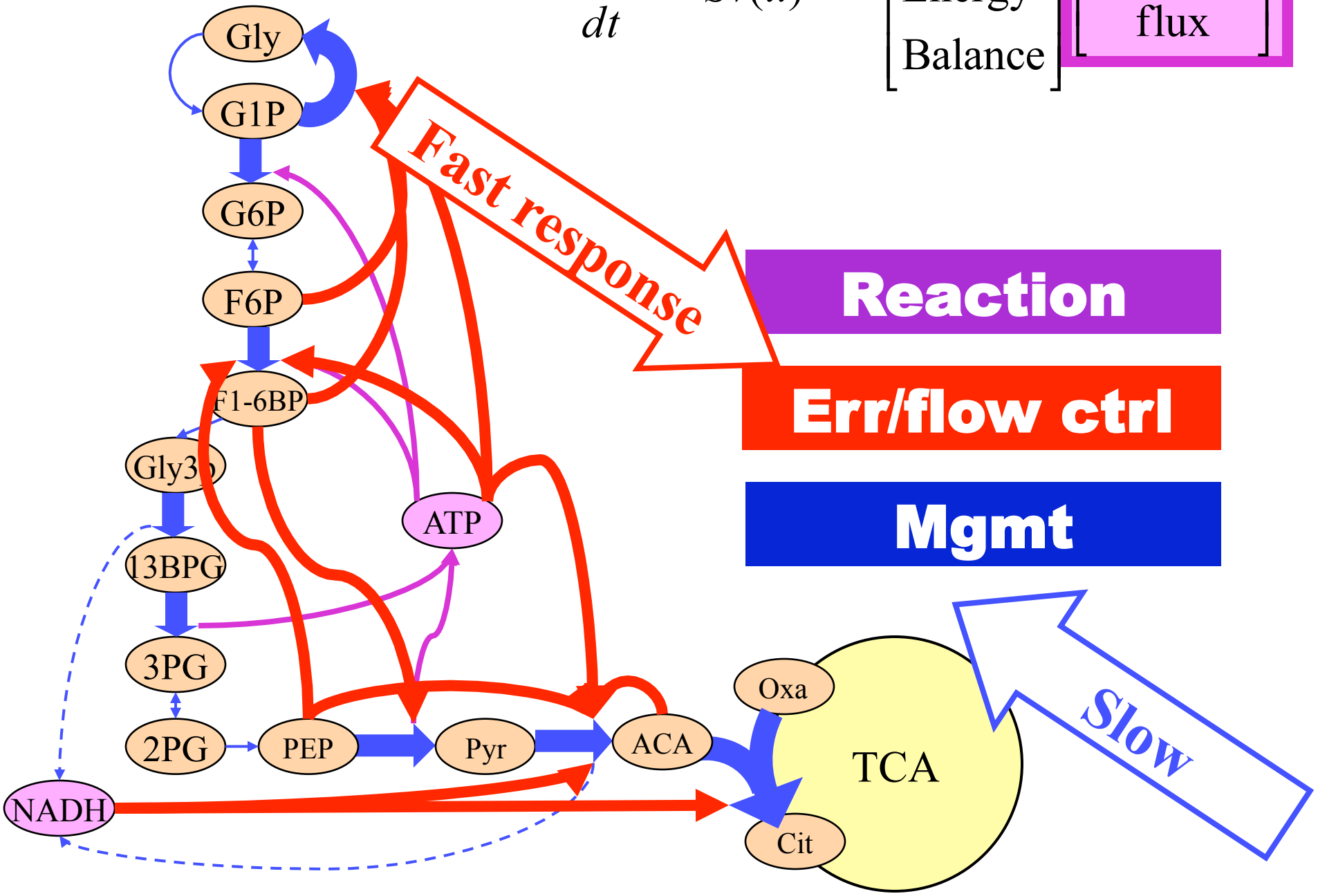
$$= \begin{bmatrix} \text{Mass \&} \\ \text{Energy} \\ \text{Balance} \end{bmatrix} \begin{bmatrix} \text{Reaction} \\ \text{flux} \end{bmatrix}$$

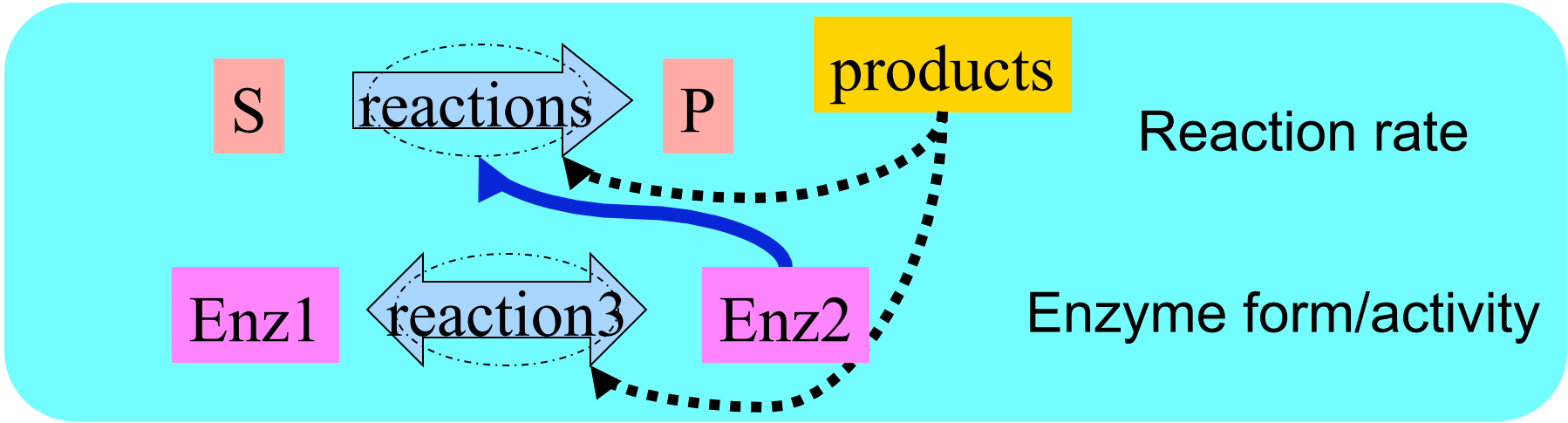
Regulation of enzyme levels by transcription/translation/degradation

Mgmt

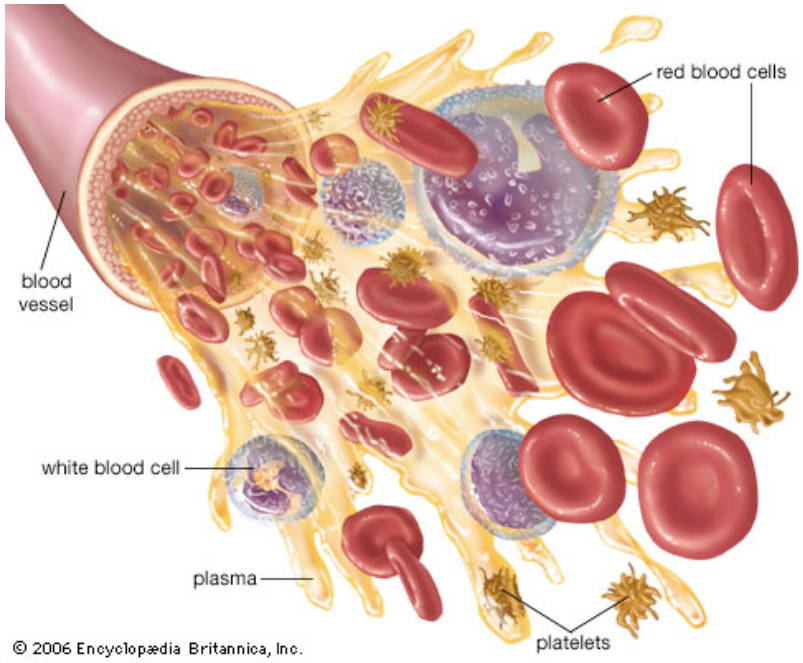

Gly
G1P
G6P
F6P
Error/flow Ctrl
ATP
13BPG
3PG
2PG
PEP
Pyr
ACA
NADH
Oxa
TCA
Cit
$\frac{dx}{dt} = Sv(x)$
$= \begin{bmatrix} \text{Mass \&} \\ \text{Energy} \\ \text{Balance} \end{bmatrix} \begin{bmatrix} \text{Reaction} \\ \text{flux} \end{bmatrix}$
Allosteric regulation
of enzymes

$$\frac{dx}{dt} = Sv(x) = \begin{bmatrix} \text{Mass \&} \\ \text{Energy} \\ \text{Balance} \end{bmatrix} \begin{bmatrix} \text{Reaction} \\ \text{flux} \end{bmatrix}$$



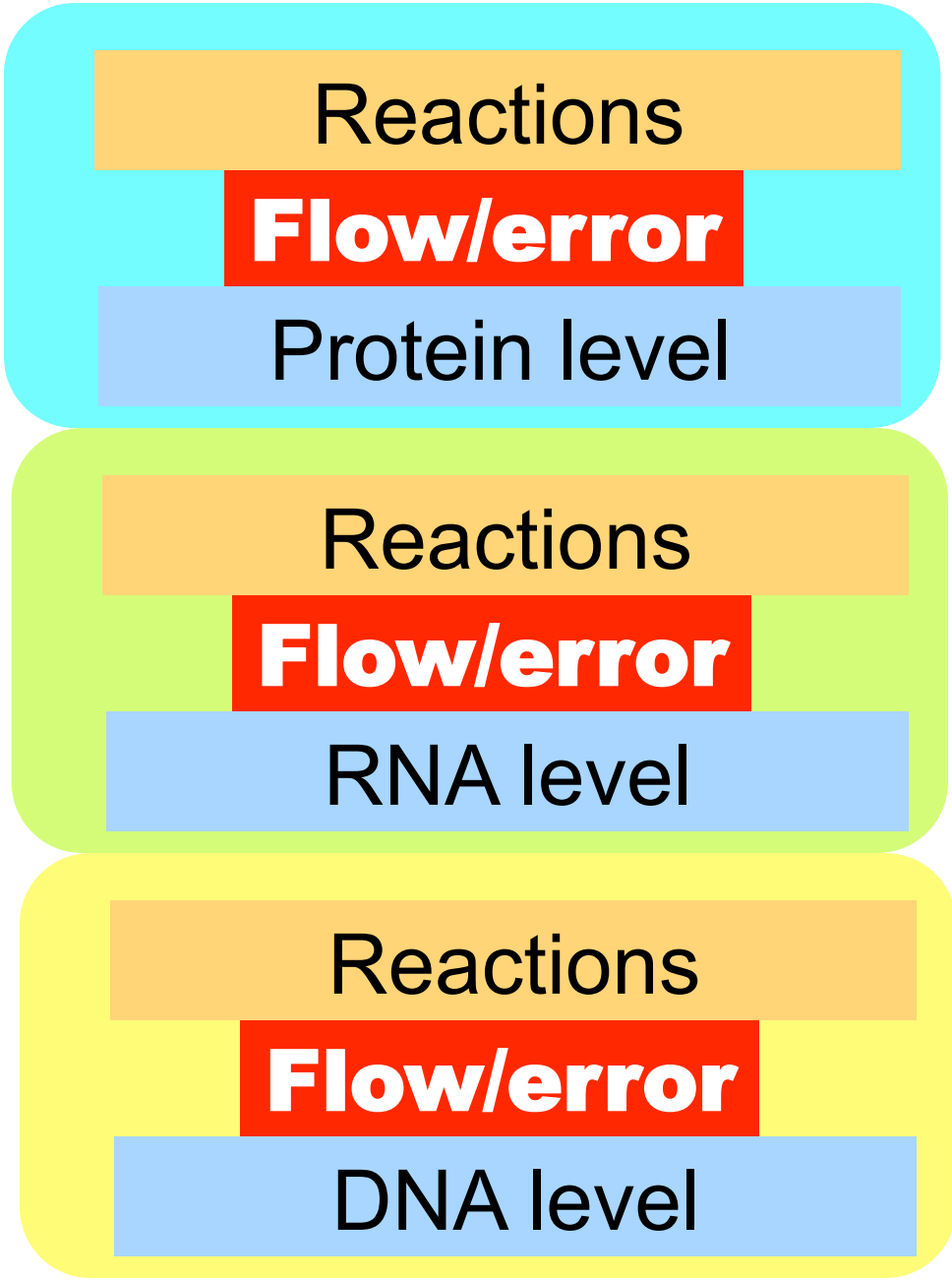


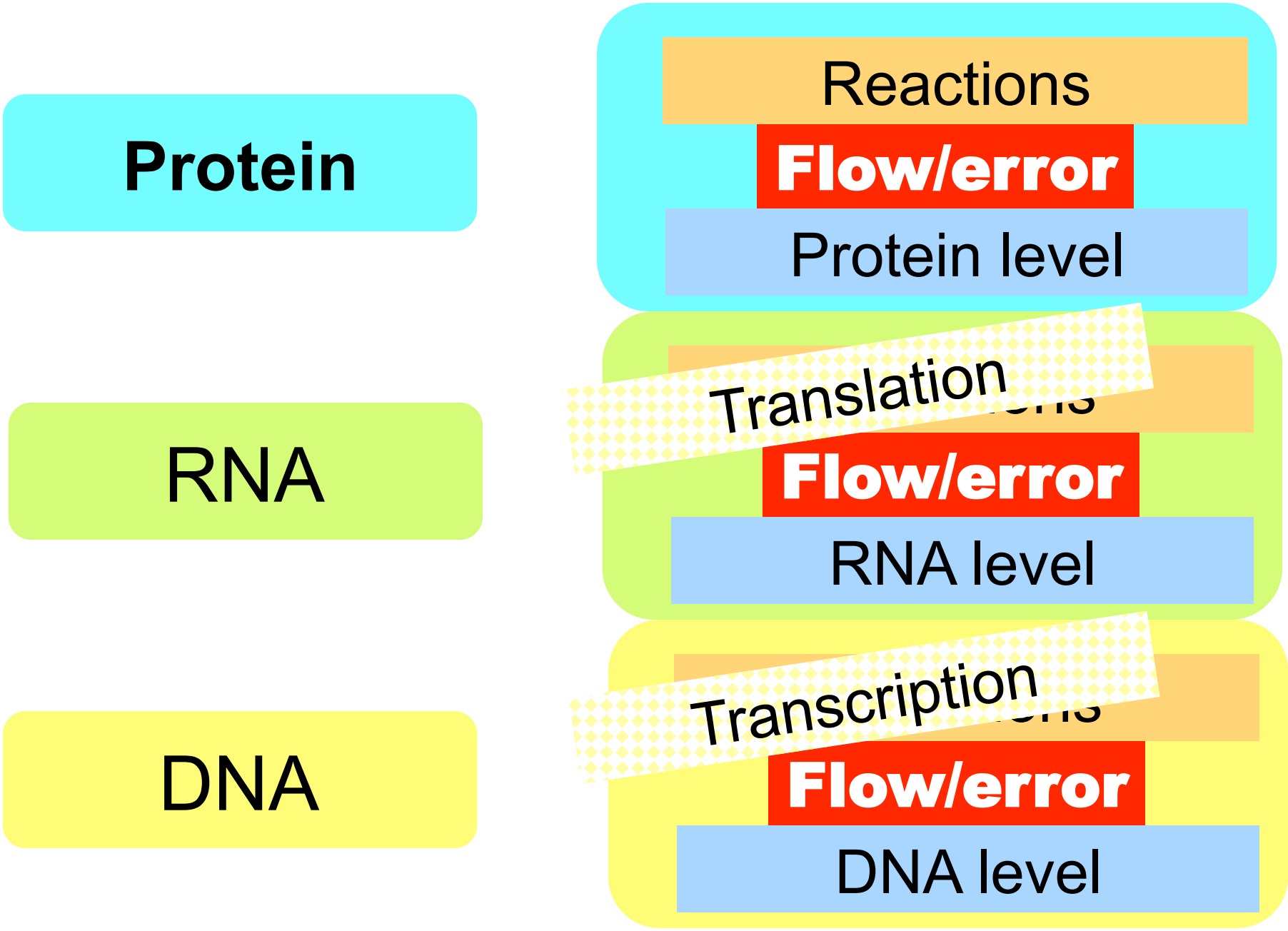
Running only the top layers

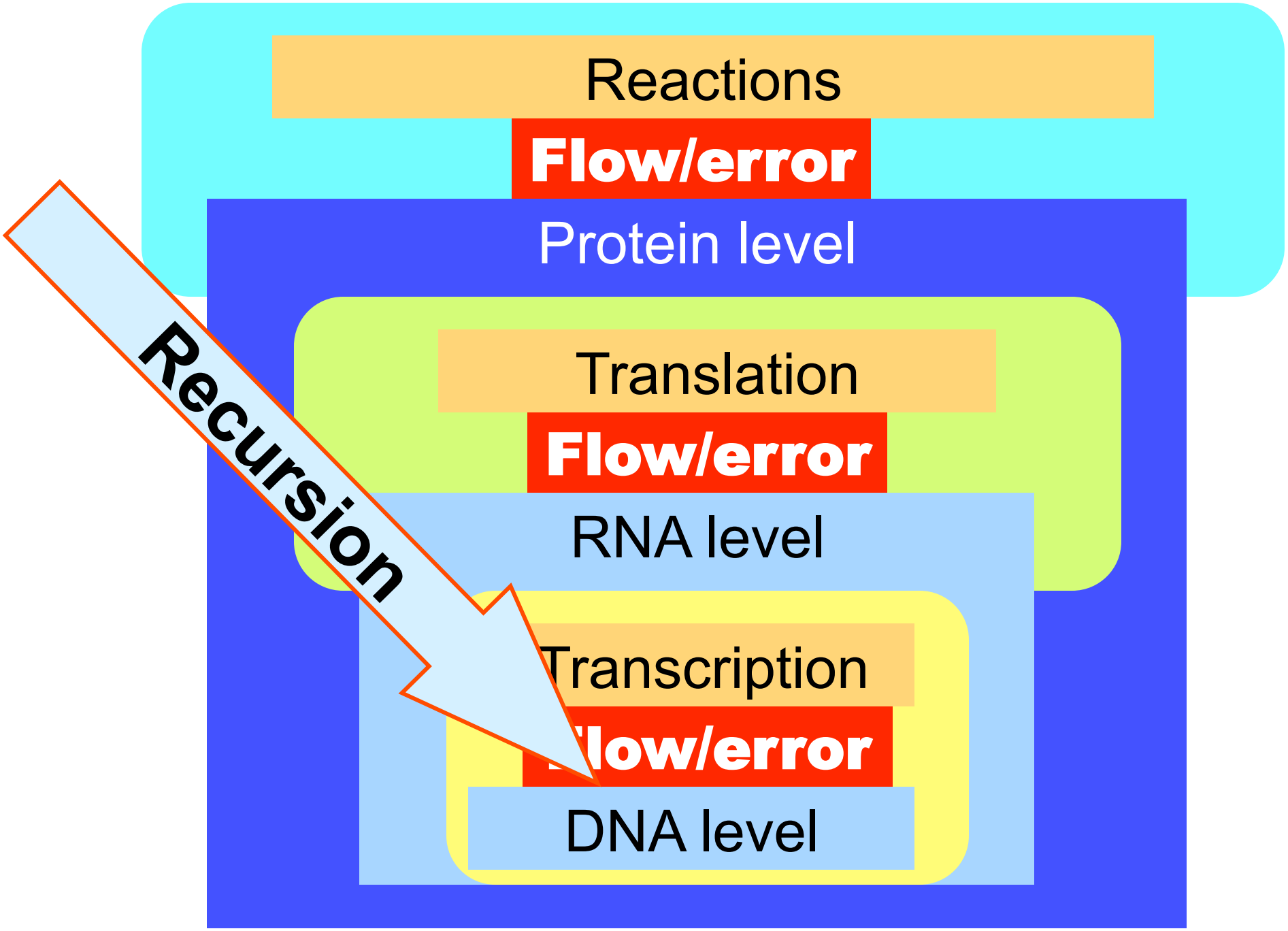


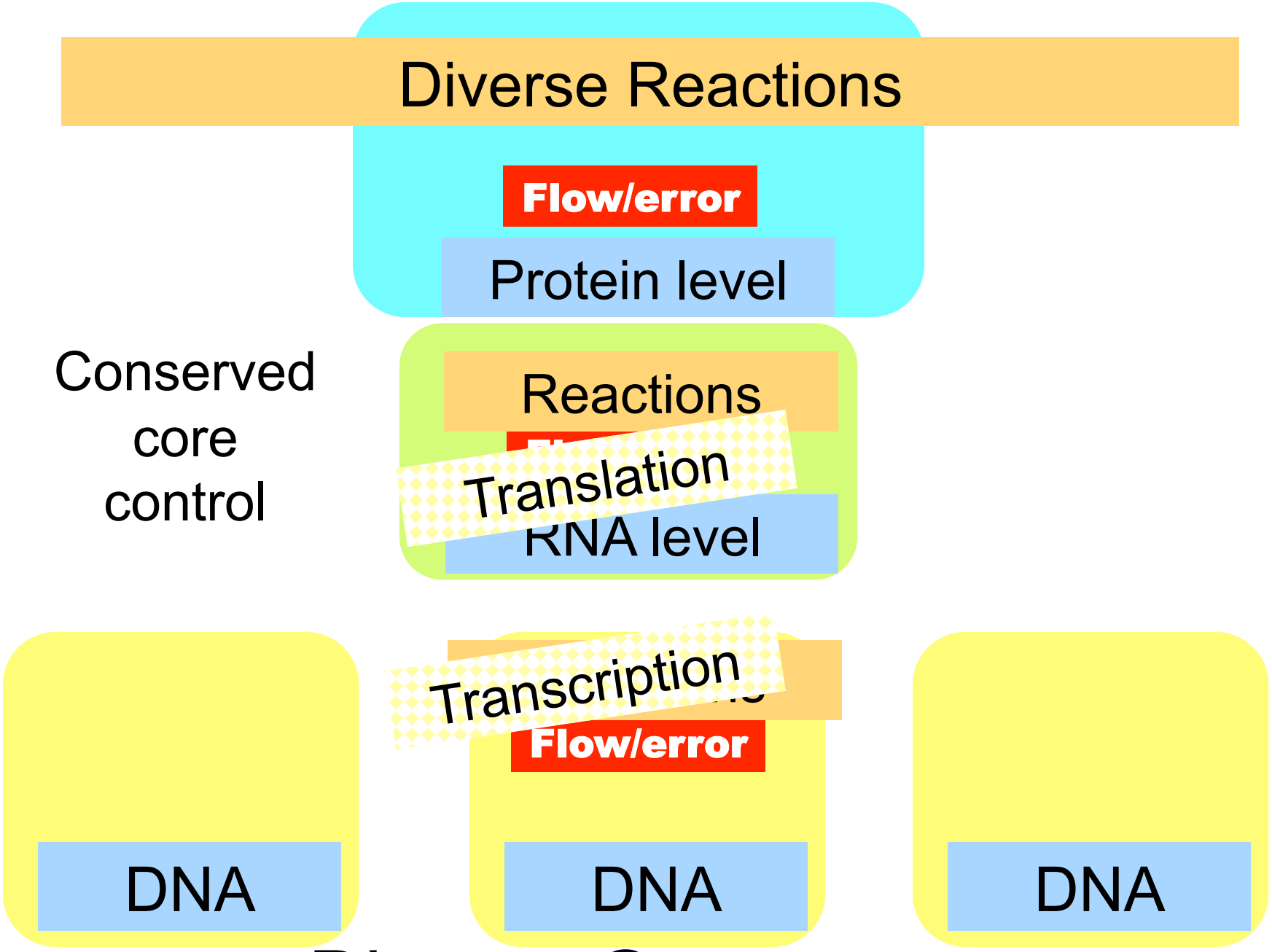
Mature red blood cells live 120 days

"metabolism first" origins of life?


Reactions
Flow/error
Protein level
Reactions
Flow/error
RNA level
Reactions
Flow/error
DNA level


Protein
RNA
DNA
Reactions
Flow/error
Protein level
Translation
Flow/error
RNA level
Transcription
Flow/error
DNA level

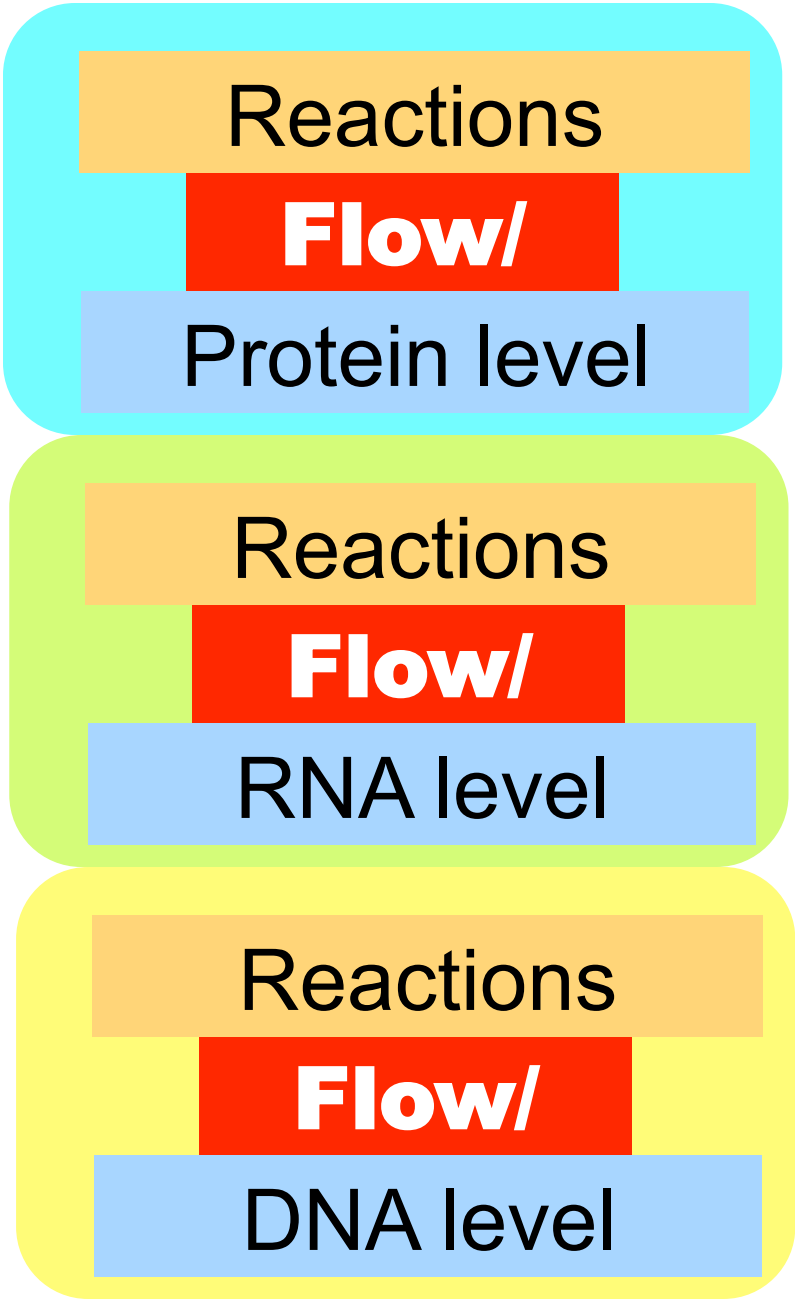

Reactions
Flow/error
Protein level
Translation
Flow/error
RNA level
Transcription
Flow/error
DNA level
Recursion

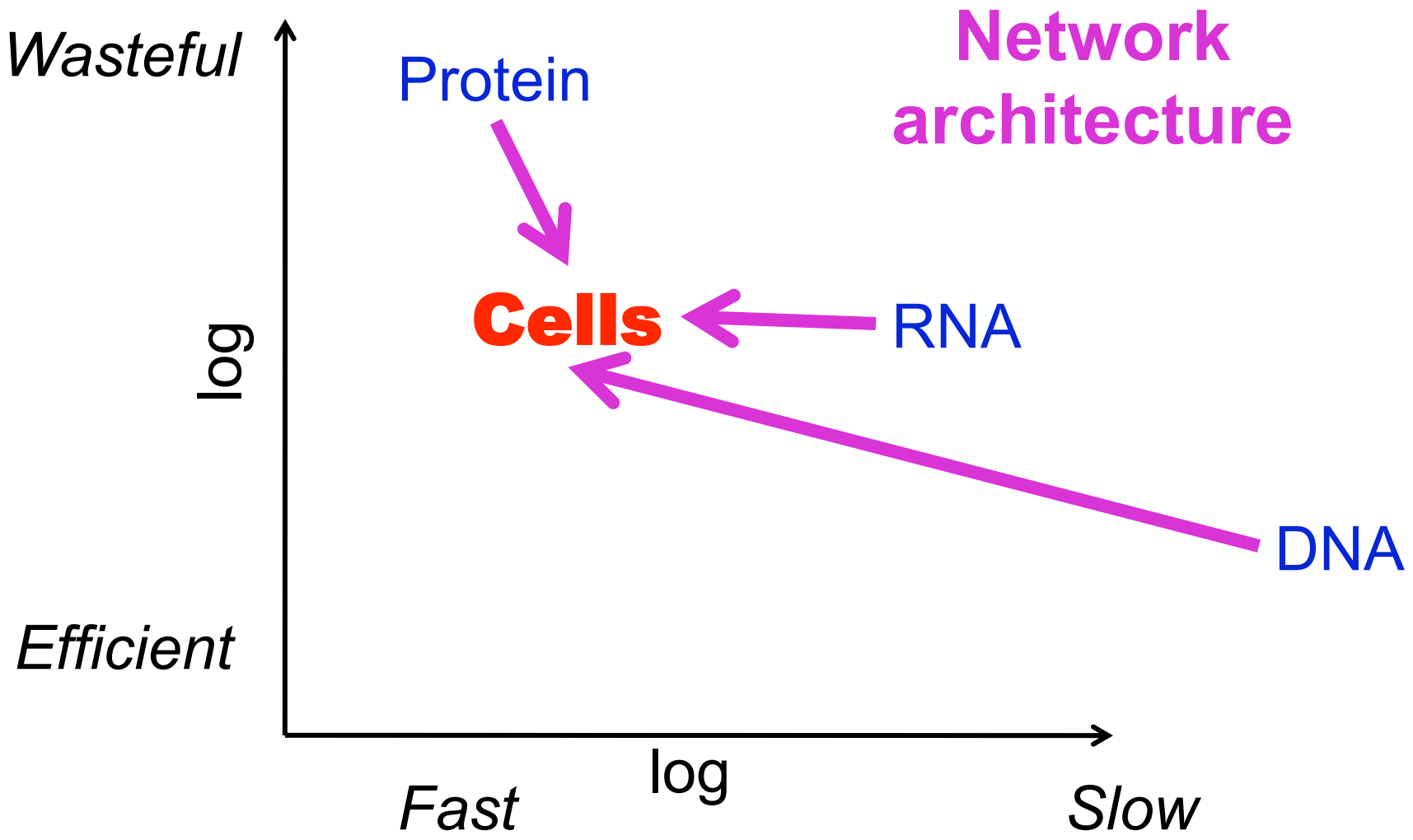

Diverse Reactions
Flow/error
Protein level
Conserved
core
control
Reactions
Translation
RNA level
Transcription
Flow/error
DNA
DNA
DNA
Diverse Genomes

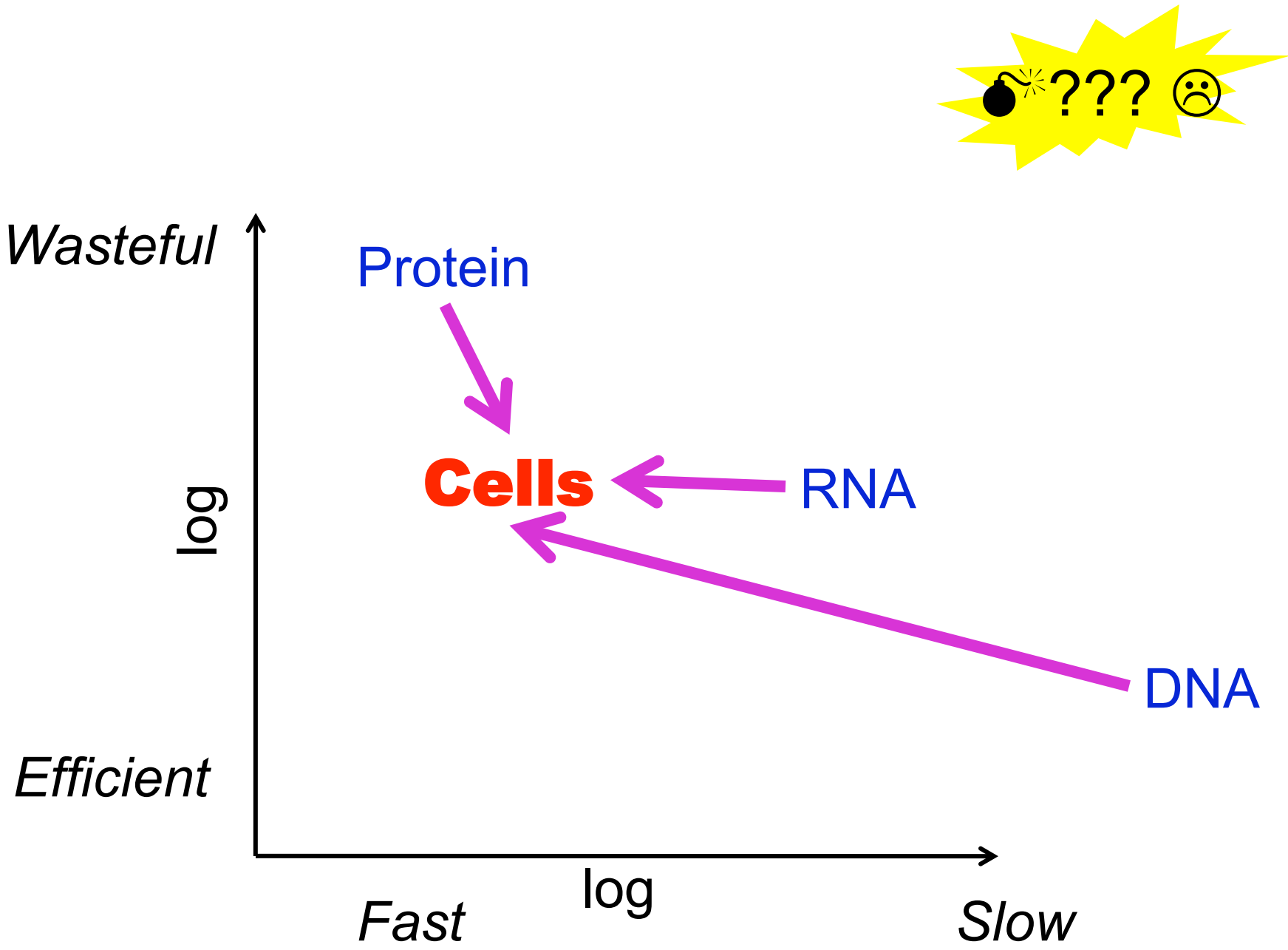
Top to bottom

- Metabolically costly but fast to cheap but slow
- Special enzymes to general polymerases
- Allostery to regulated recruitment
- Analog to digital
- High molecule count to low (noise)

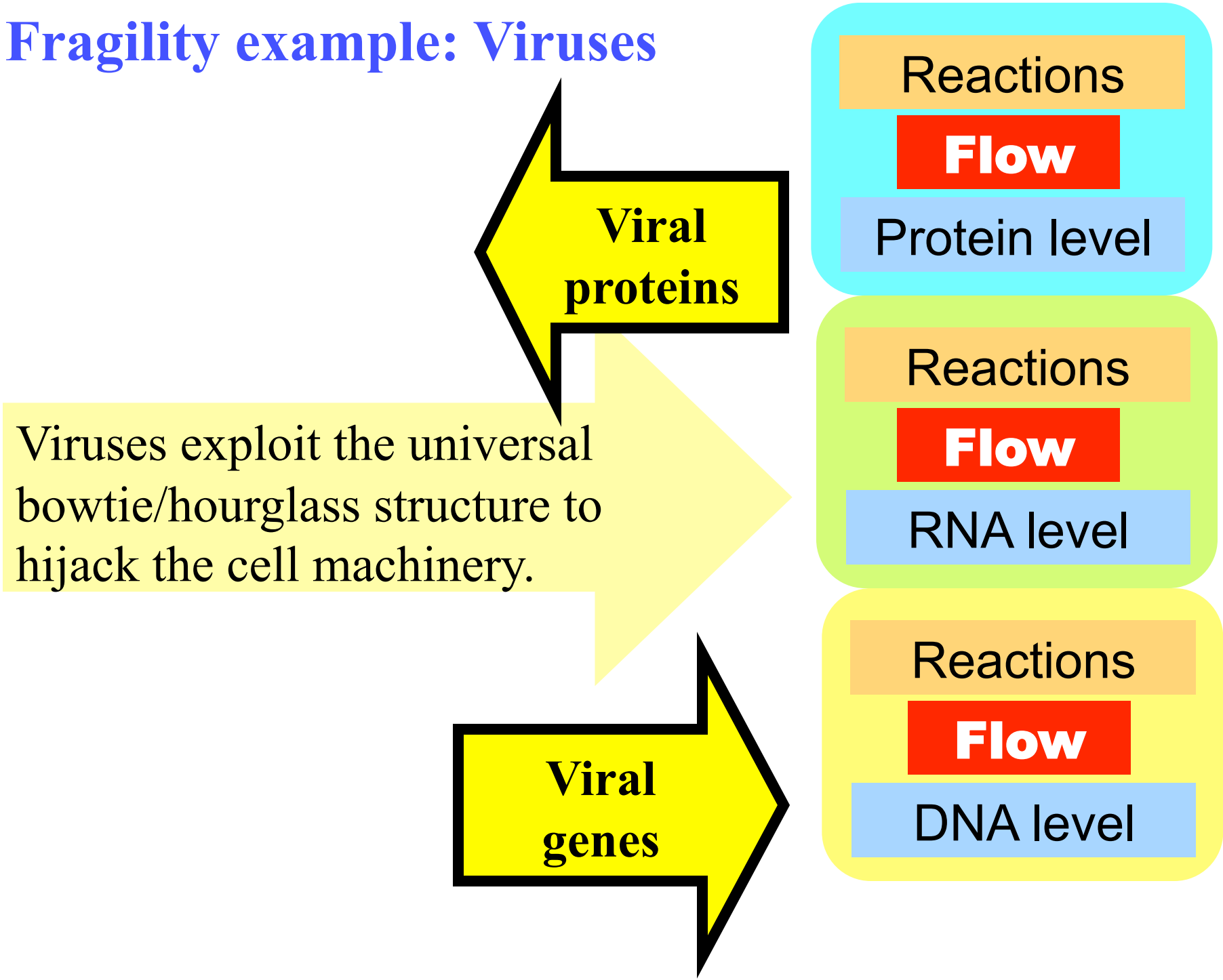
Rich Tradeoffs



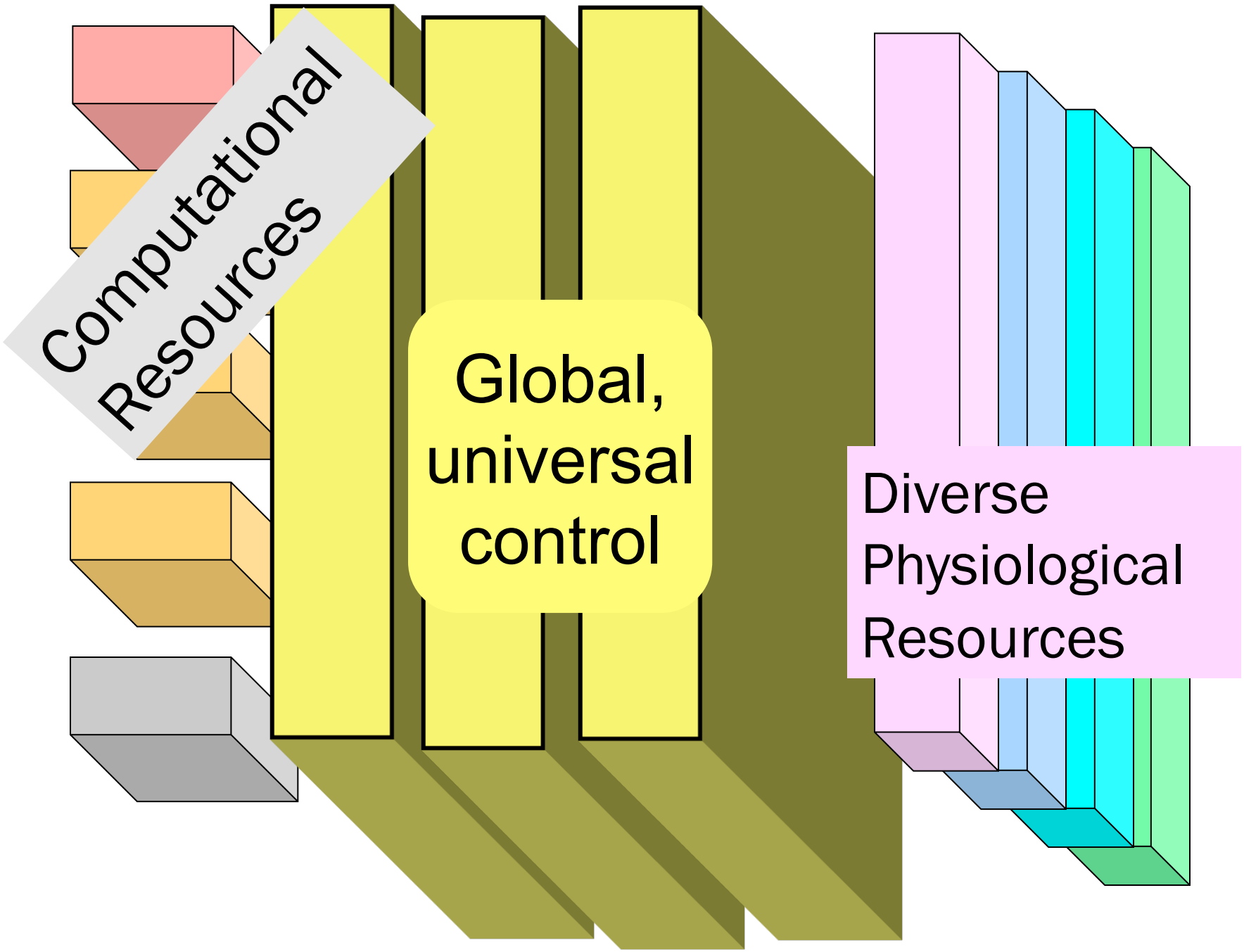

Wasteful
Efficient
log
Protein
Network
architecture
Cells
RNA
DNA
Fast
log
Slow


???
Wasteful
Protein
log
Cells
RNA
DNA
Efficient
log
Fast
Slow

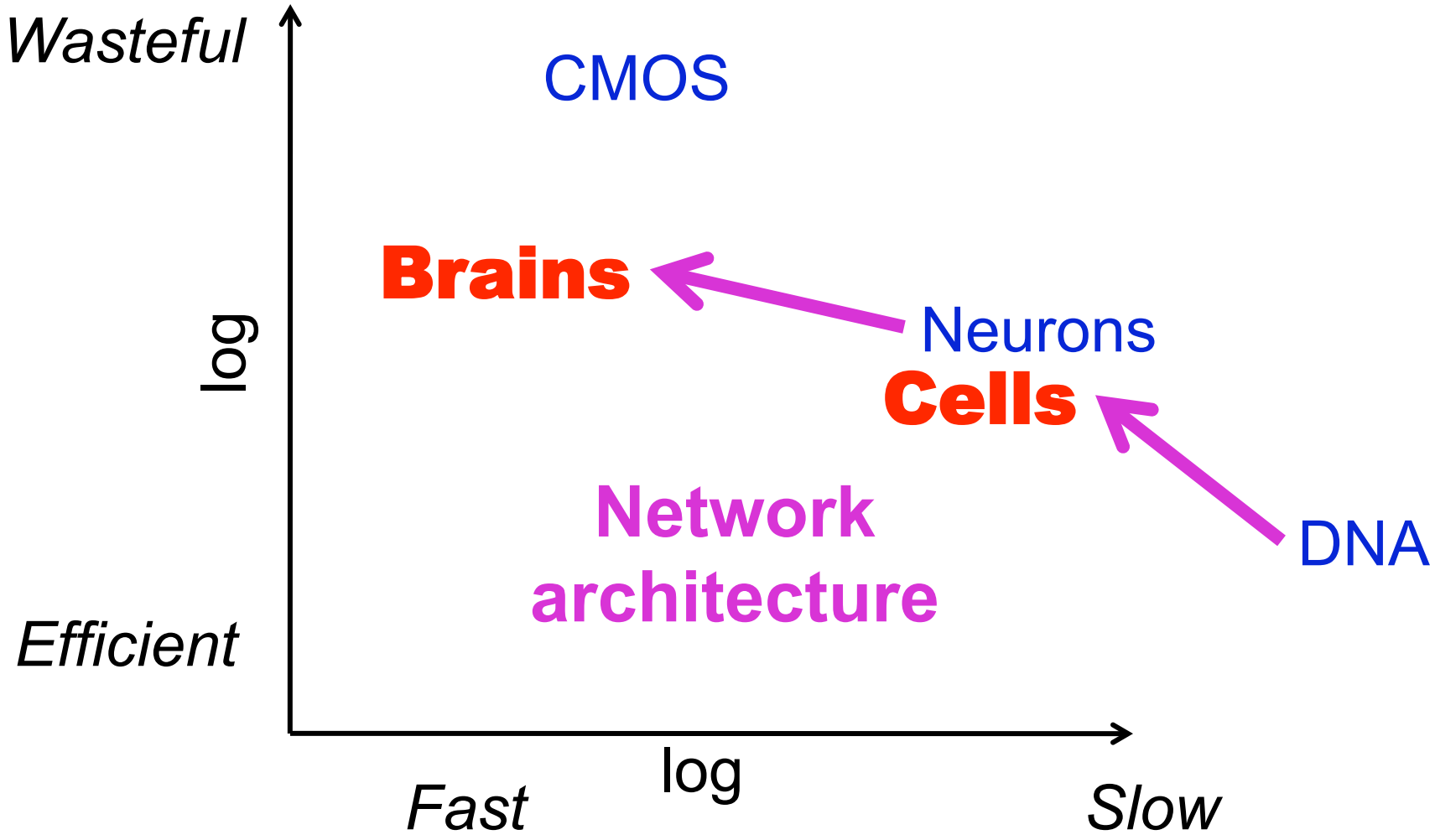
Fragility example: Viruses



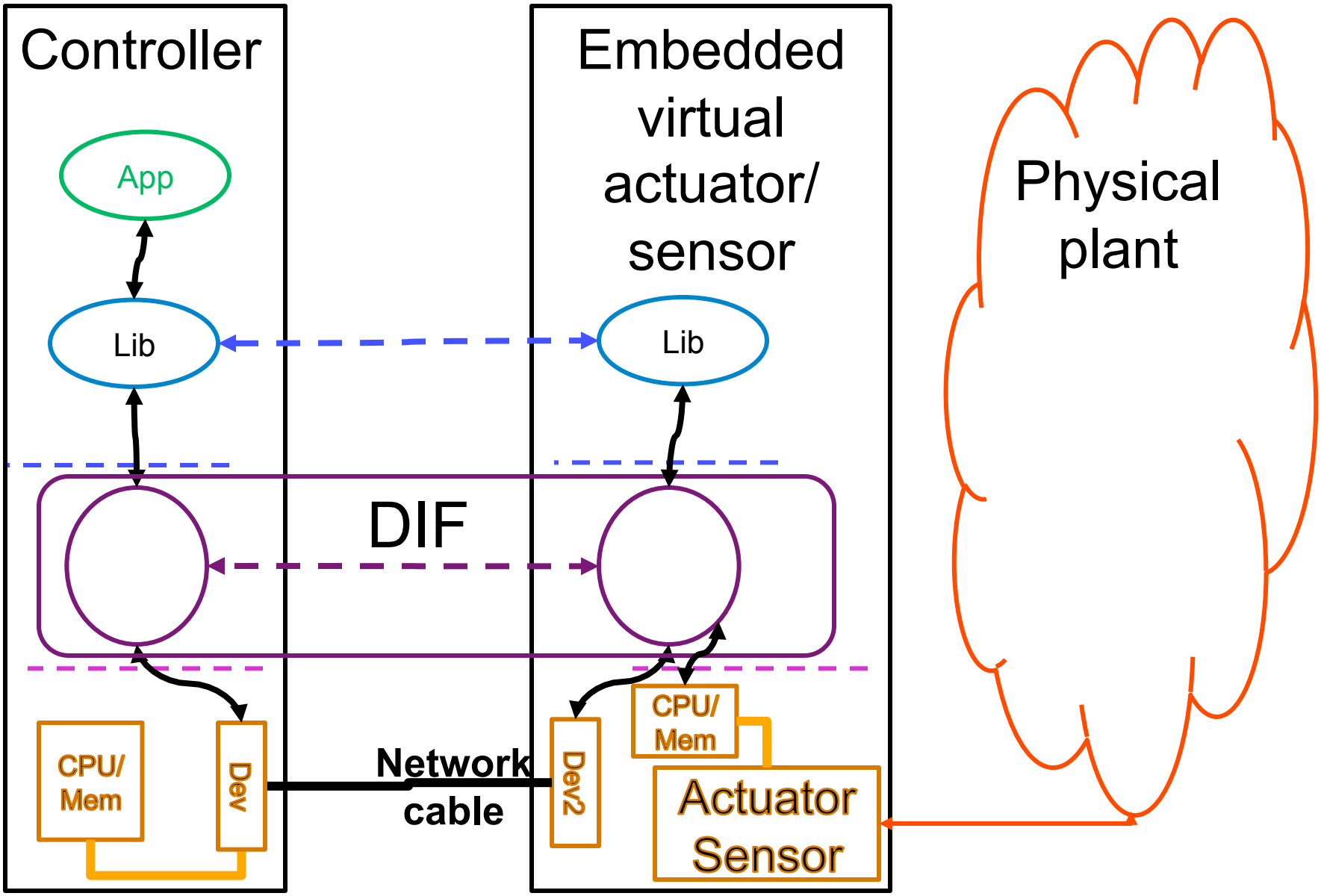
Layered Brain (Hawkins)?



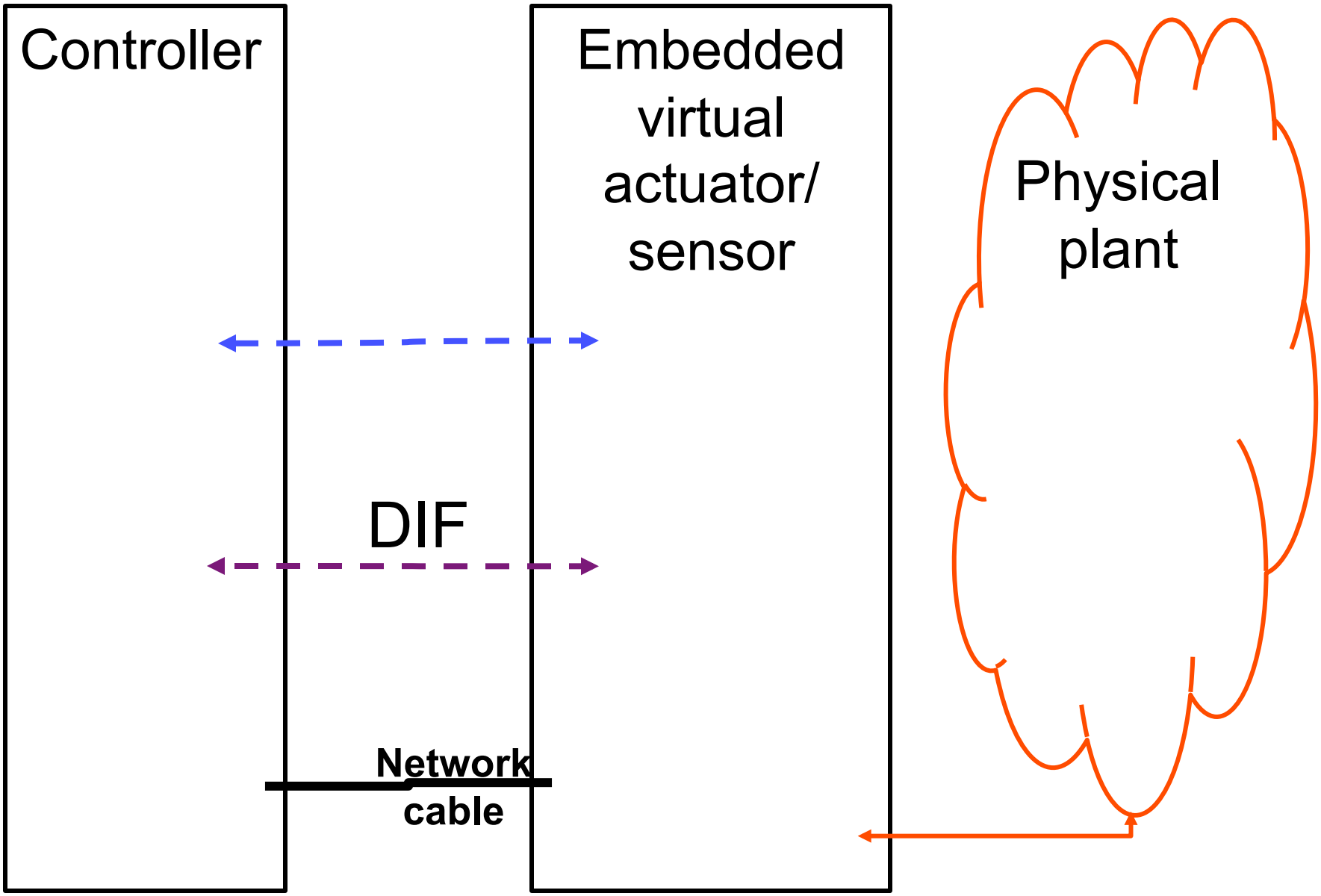
What makes this possible?



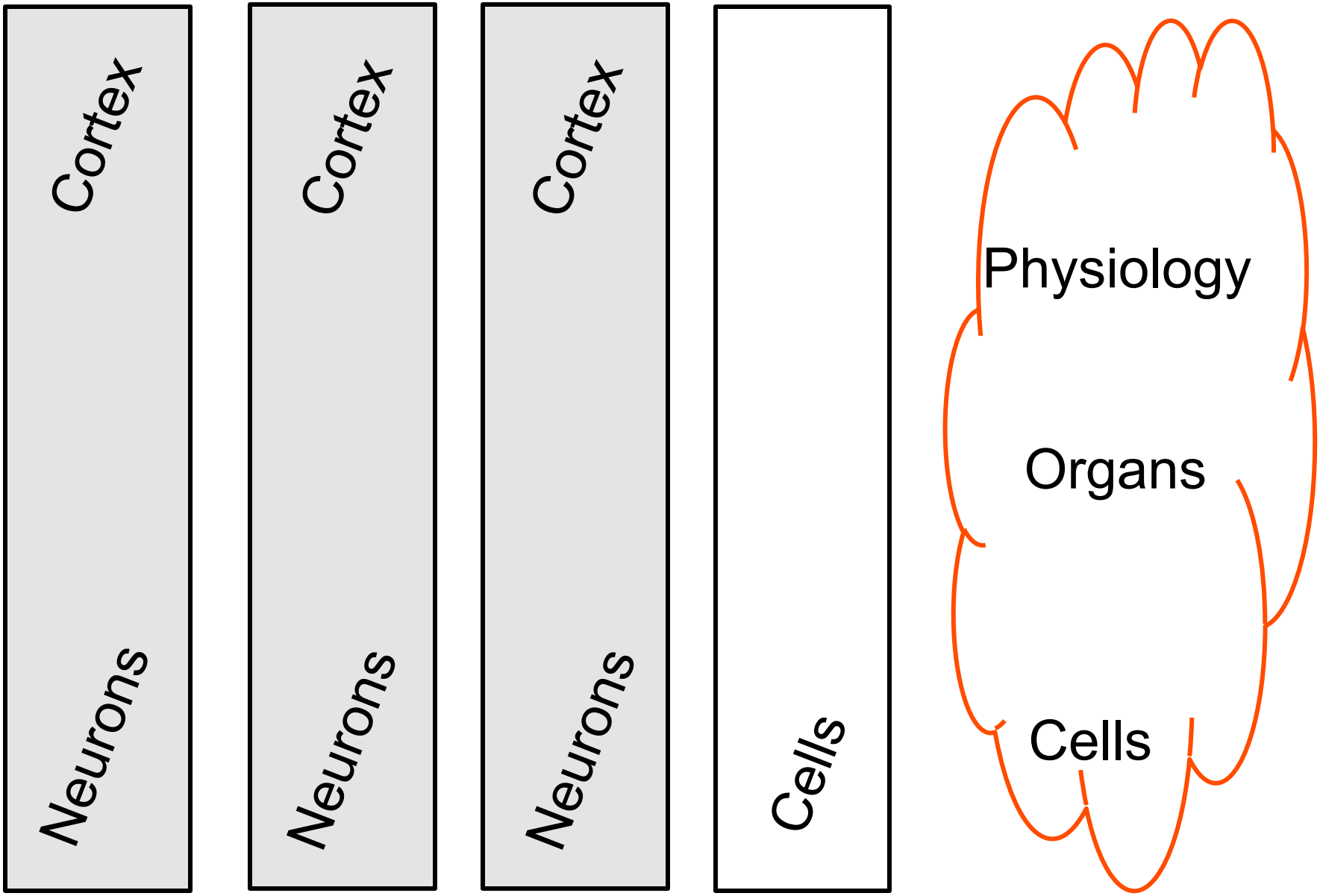
Networked embedded

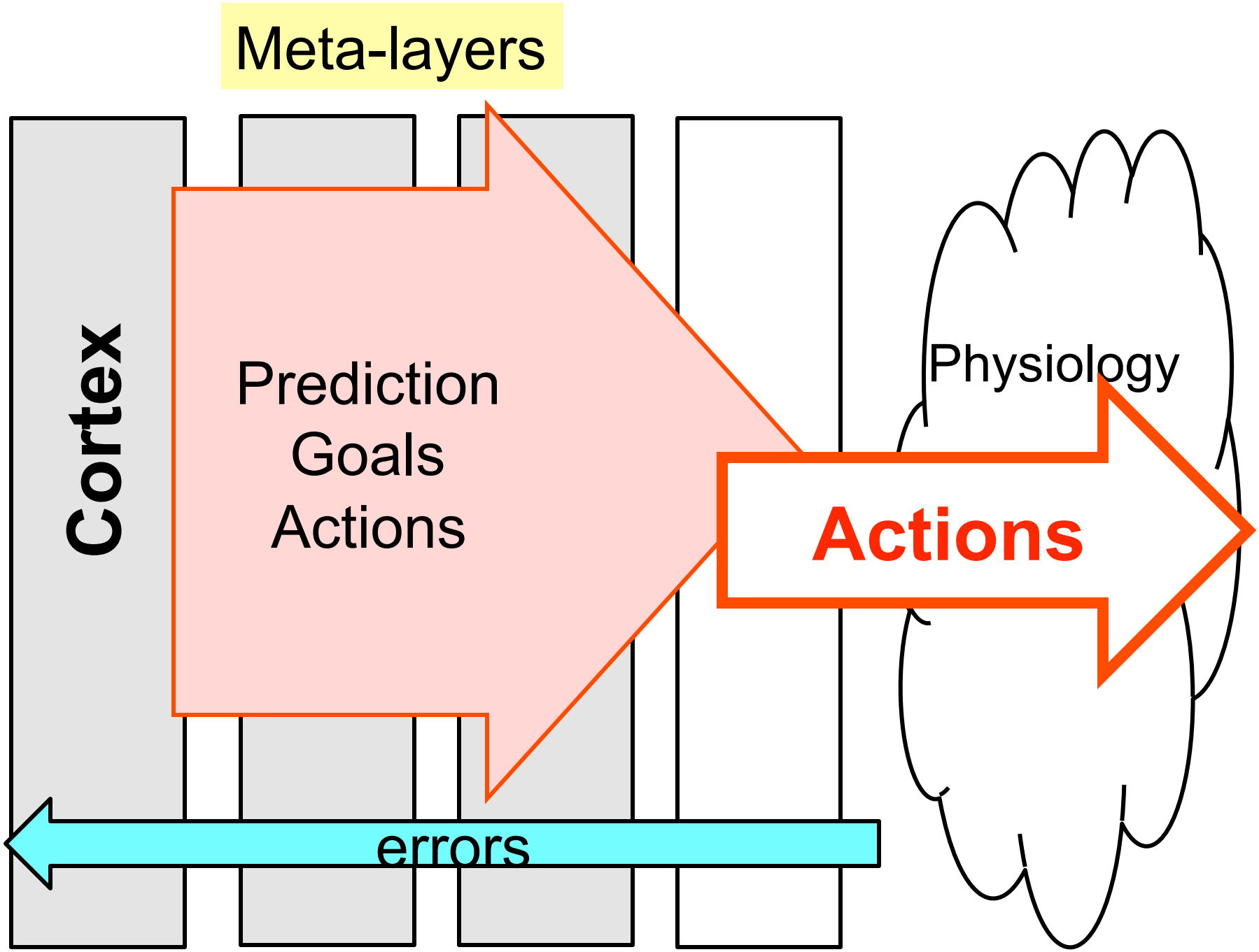


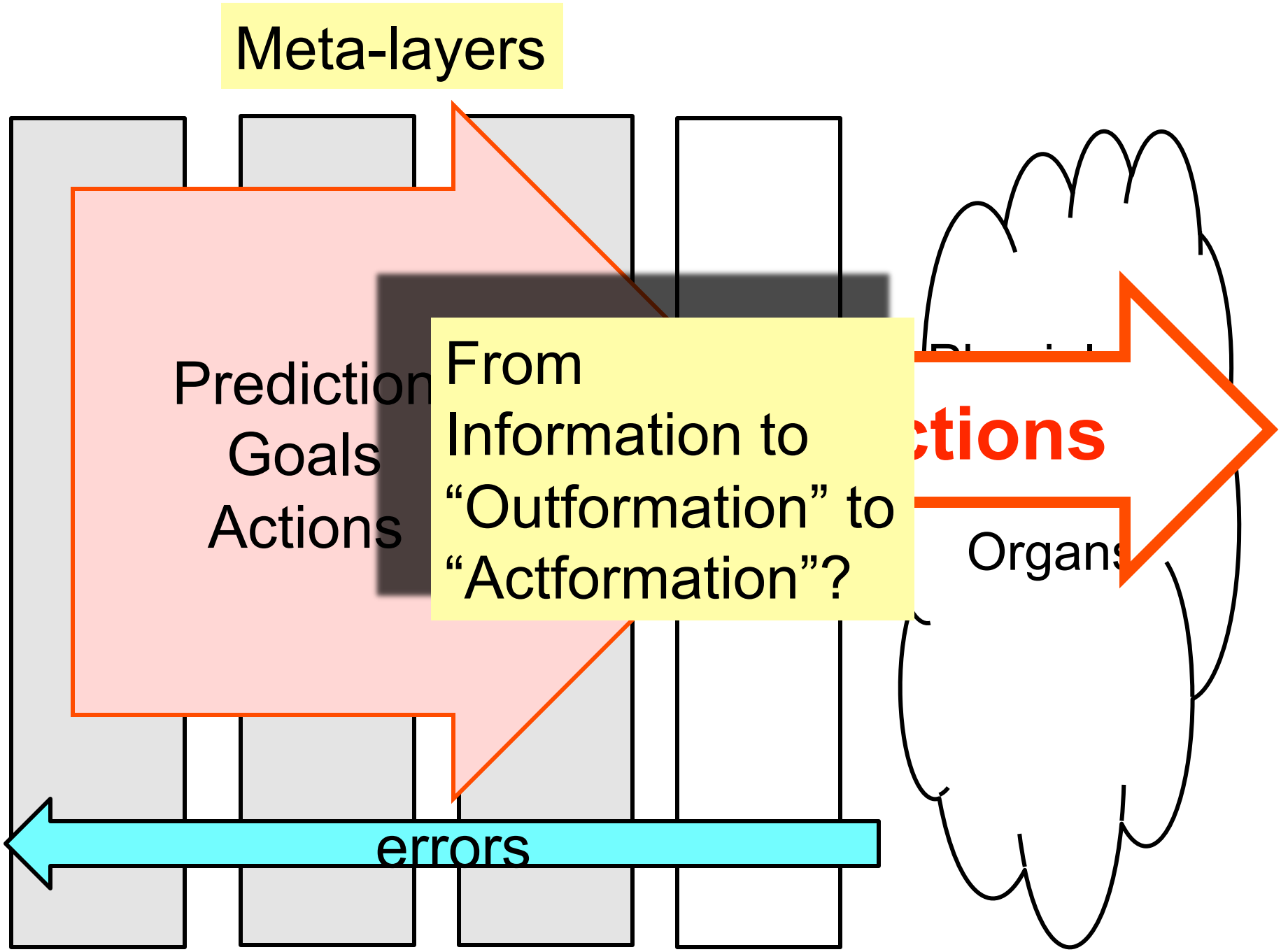
Meta-layering of cyber-phys control



Meta-layers


Cortex
Neurons
Cortex
Neurons
Cortex
Neurons
Cells
Physiology
Organs
Cells


Meta-layers
Cortex
Prediction
Goals
Actions
Physiology
Actions
errors


Meta-layers
Prediction
Goals
Actions
From
Information to
“Outformation” to
“Actformation”?
ctions
Organs
errors

"Architecture" in practice

- Internet, biology, energy, manufacturing, transportation, water, food, waste, law, etc
- Many architectures are unsustainable/hard to fix

What does "architecture" mean here?

- Persistent, ubiquitous, global features
- Constrains the possible (for good or bad)
- Enables/prevents innovation, sustainability, etc,
- Theory is fragmented, incoherent, incomplete
- Needs rigor and relevance
- "Constraints that deconstrain" and "facilitated variation" (Gerhart and Kirschner)