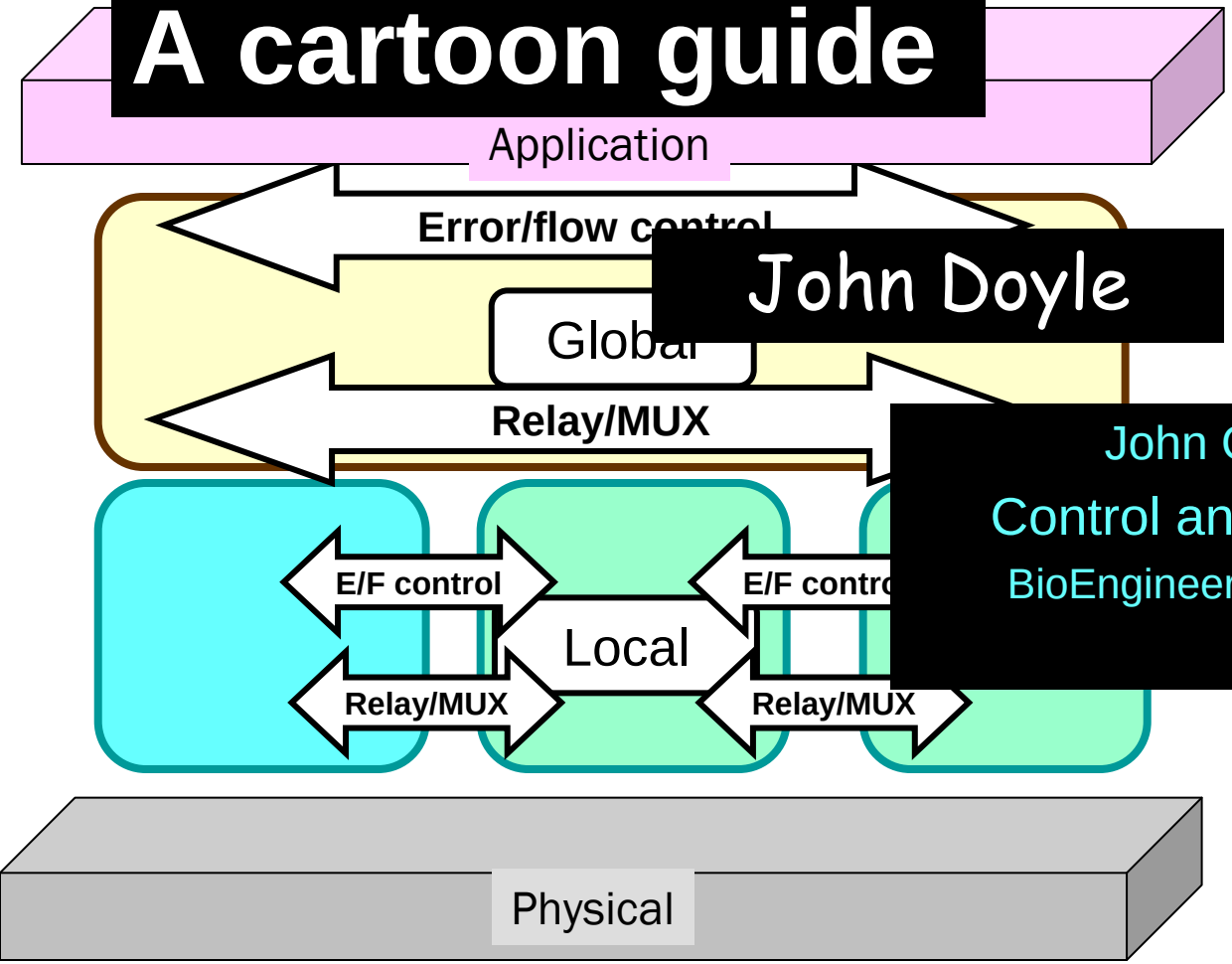
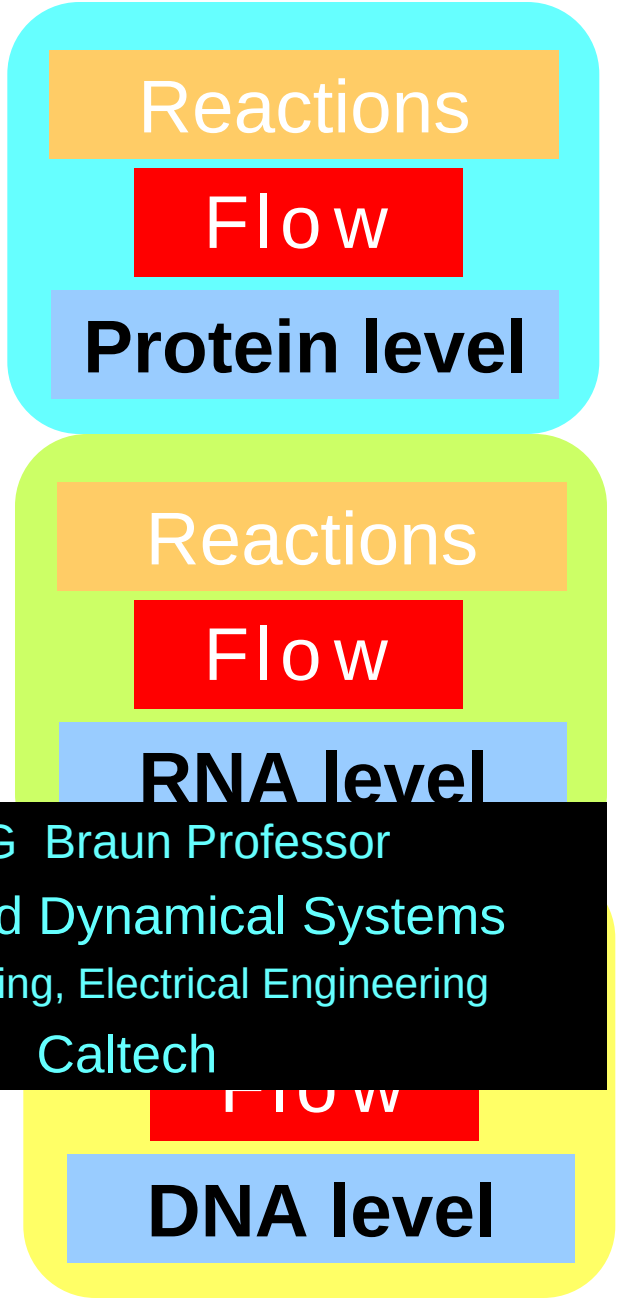
Complex Network Architecture: A cartoon guide





John Doyle

John G Braun Professor
Control and Dynamical Systems
BioEngineering, Electrical Engineering
Caltech

Complex Network Architecture

Art
~~Science?~~
Engineering
Math

- Individually, these subjects are a mess.
- Together, a nightmare.
- “High impact” scientific literature has persistent errors and confusion. (Important symptom of “complexity.”)

For (lots) more slides see
http://www.cds.caltech.edu/~doyle/NetME101/AllDoylePPTFiles.zip

Complex Network Architecture

Connections to resilience, security?

- Complex networks have bewildering security and management challenges
- Architecture must better facilitate security
- Security must become more “architectural”

Essential ideas: Architecture

Robust yet fragile

Question

Constraints that deconstrain

Answer

Case studies?

Human systems?

- Important
- Great for anecdotes because of broad familiarity
- But hard to formalize. Why?
- Gratuitously complex and fragile
- Poorly understood “architectures” from metabolism to inflammation to brains to society
- Difficult to separate hard tradeoffs from frozen evolutionary accidents

Where do we look for “good” examples?

Cyber-physical networks?

- Water
- Waste
- Food
- Power
- Transportation
- Healthcare
- Finance

All examples of "bad" architectures:
- Unsustainable
- Hard to fix

Where do we look for "good" examples?

Essential ideas: Architecture

Robust yet fragile

Question

Constraints that deconstrain

Answer

Simplest case studies

Internet

Bacteria

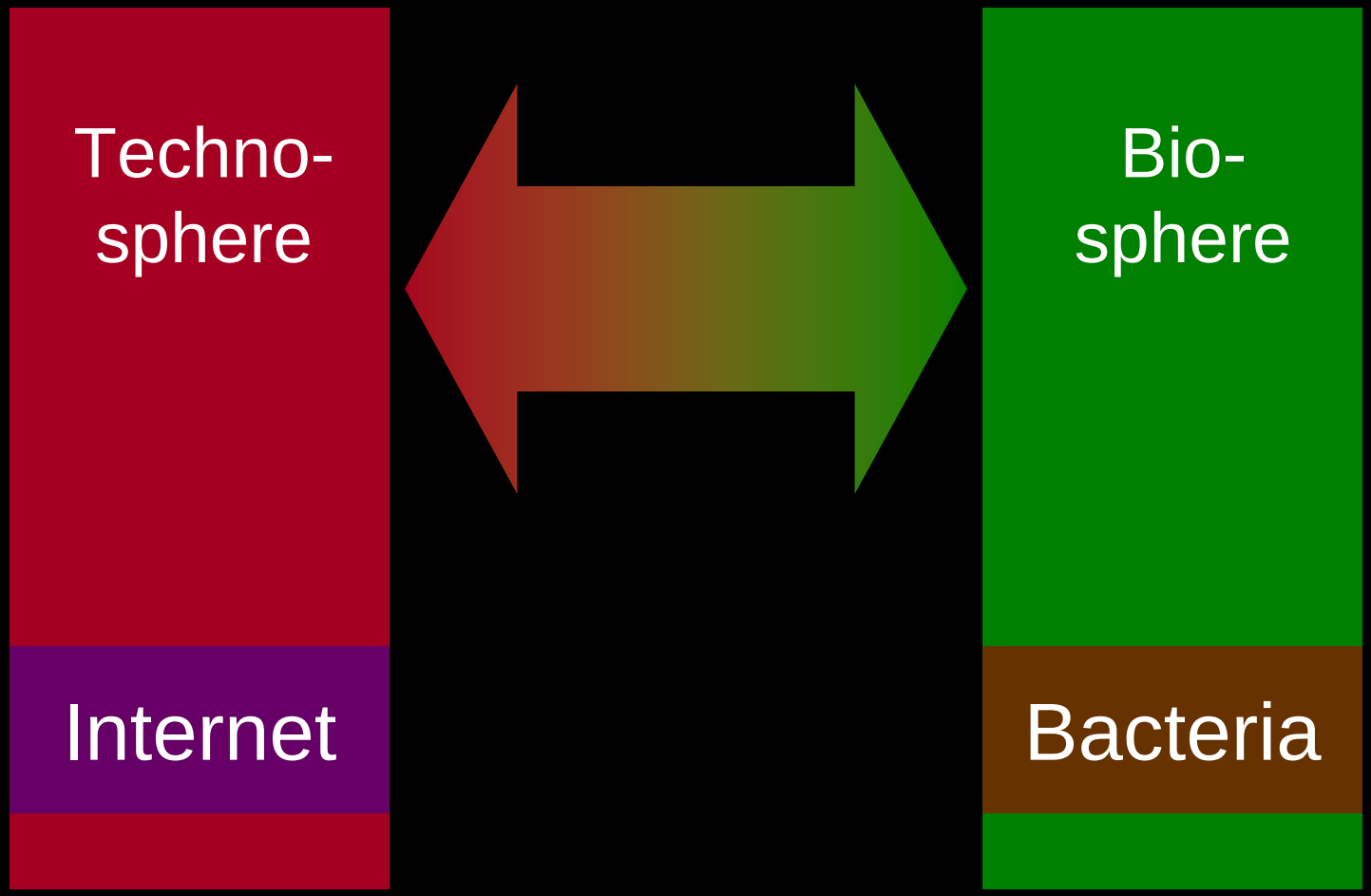
- Successful architectures
- Robust, evolvable
- Universal, foundational
- Accessible, familiar
- Unresolved challenges
- New theoretical frameworks
- Much easier than flies, oceans, humans
- Boringly retro?

Simplest case studies

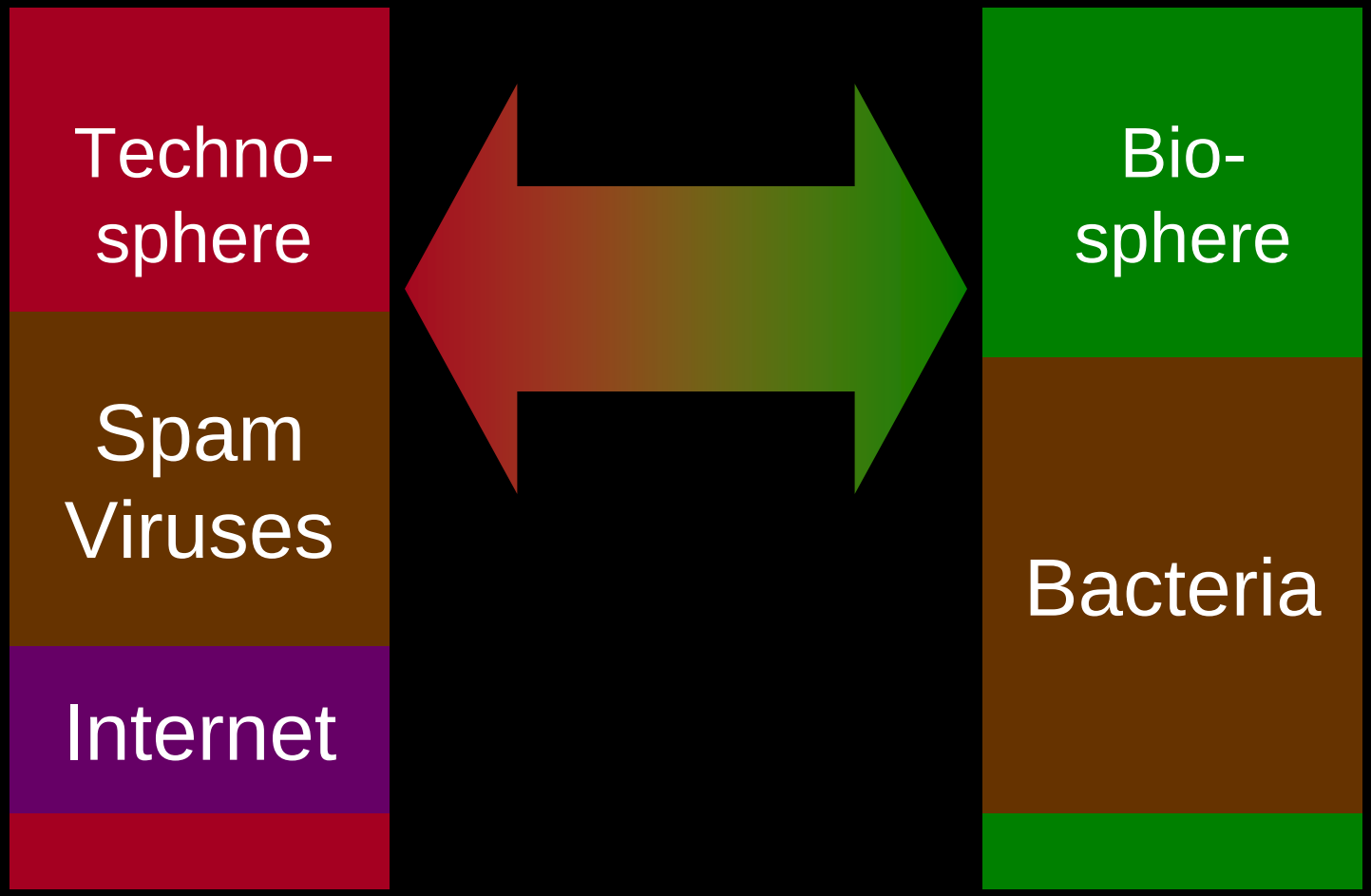
Internet

Bacteria

- Universal, foundational



- Universal, foundational



Collaborators and contributors (partial list)

Biology: Csete,Yi, El-Samad, Khammash, Tanaka, Arkin, Savageau, Simon, AfCS, Kurata, Smolke, Gross, Kitano, Hucka, Sauro, Finney, Bolouri, Gillespie, Petzold, F Doyle, Stelling, Caporale,…

Theory: Parrilo, Carlson, Murray, Vinnicombe, Paganini, Mitra Papachristodoulou, Prajna, Goncalves, Fazel, Liu, Lall, D'Andrea, Jadbabaie, Dahleh, Martins, Recht, many more current and former students, …

Web/Internet: Li, Alderson, Chen, Low, Willinger, Kelly, Zhu,Yu, Wang, Chandy, …

Turbulence: Bamieh, Bobba, McKeown, Gharib, Marsden, …

Physics: Sandberg, Mabuchi, Doherty, Barahona, Reynolds,

Disturbance ecology: Moritz, Carlson,…

Finance: Martinez, Primbs, Yamada, Giannelli,…

Current Caltech Former Caltech Longterm Visitor Other

Thanks to

- NSF ITR
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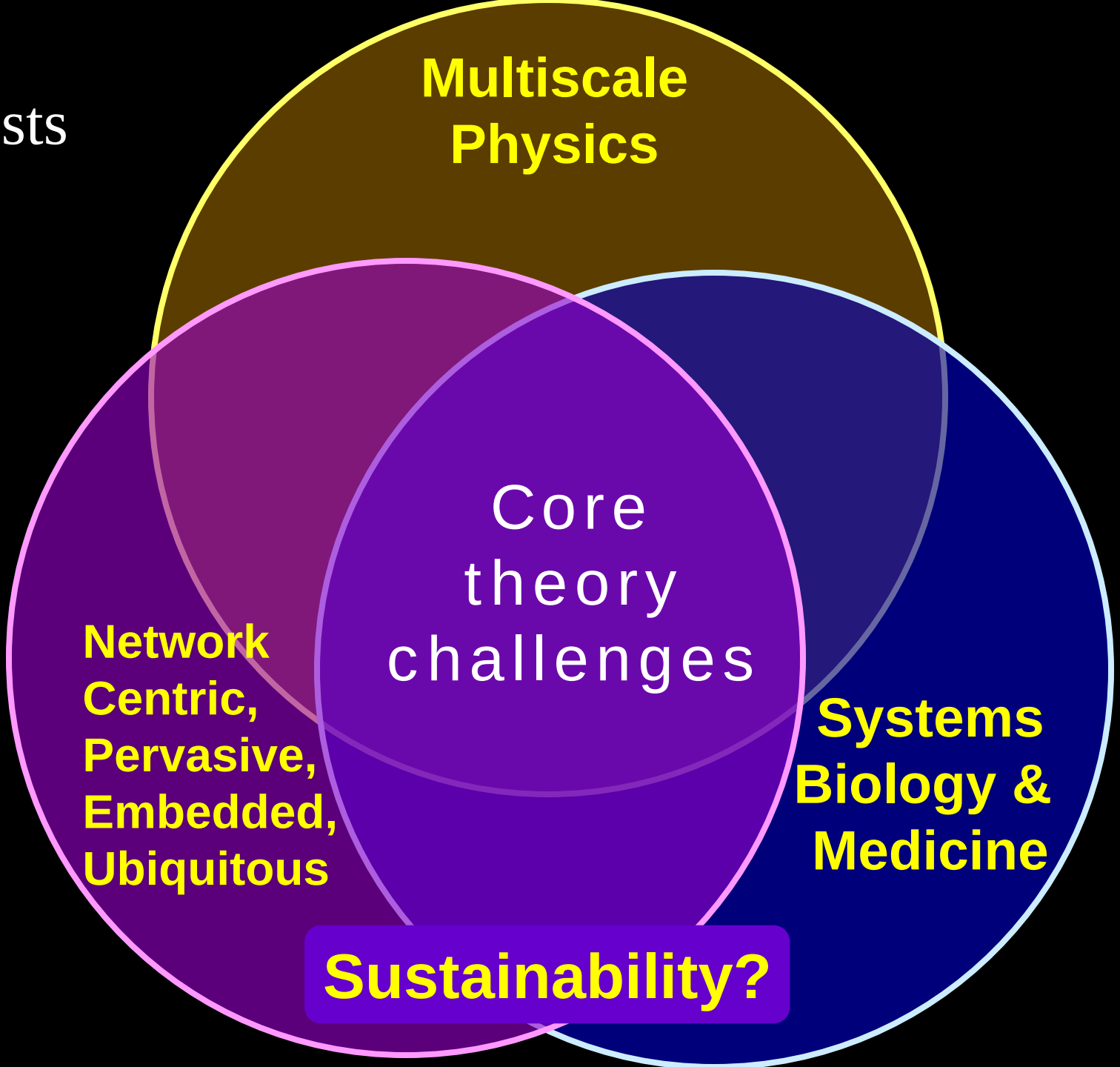
- NIH/NIGMS
- ARO/ICB
- DARPA
- Lee Center for Advanced Networking (Caltech)
- Boeing
- Pfizer
- Hiroaki Kitano (ERATO)
- Braun family

My interests



Essential ideas: Architecture

Robust
yet
fragile*

Question

* Carlson

Question: Human complexity

Robust

- ☺ Efficient, flexible metabolism
- ☺ Rich microbial symbionts
- ☺ Immune systems
- ☺ Regeneration & renewal
- Complex societies
- Advanced technologies

Yet Fragile

- ☹ Obesity and diabetes
- ☹ Parasites, infection
- ☹ Inflammation, Auto-Im.
- ☹ Cancer
- ☠ Epidemics, war, …
- Catastrophic failures

Mechanism?

Robust

- ☺ Efficient, flexible metabolism
  - ☺ Fat accumulation
  - ☺ Insulin resistance

Fluctuating energy

Yet Fragile

- ☹ Obesity and diabetes
  - ☹ Fat accumulation
  - ☹ Insulin resistance

Static energy

Implications/ Generalizations

Robust

- ☺ Efficient, flexible metabolism
- ☺ Rich microbial symbionts
- ☺ Immune systems
- ☺ Regeneration & renewal
- Complex societies
- Advanced technologies

Yet Fragile

- ☹ Obesity and diabetes
- ☹ Parasites, infection
- ☹ Inflammation, Auto-Im.
- ☹ Cancer
- ☠ Epidemics, war, …
- Catastrophic failures

- Fragility = Hijacking, side effects, unintended… of mechanisms evolved for robustness

- Easier to create robustness than to ***avoid*** fragility

- Math: New robust/fragile conservation laws

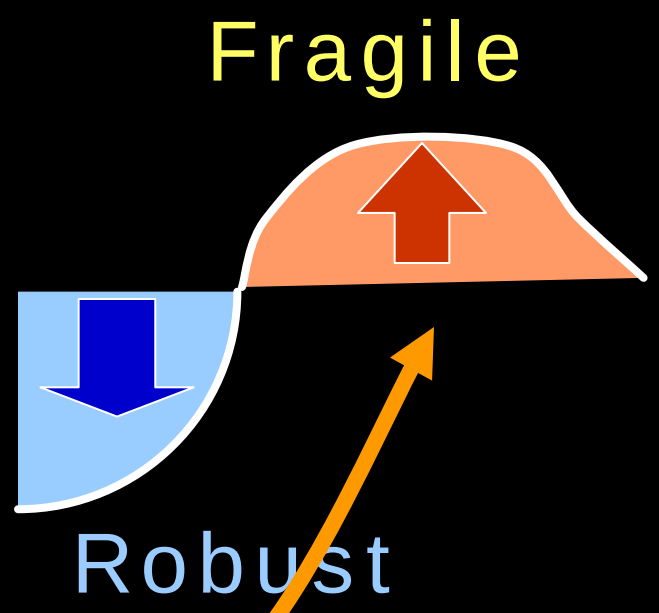
- Minimal functionality and demos are simple, easy
- Complexity is driven by control, robust/fragile

[a system] can have
[a property] ***robust*** for
[a set of perturbations]

Yet be ***fragile for***

[a different property]

Or [a different perturbation]



Robust yet fragile = fragile robustness

[a system] can have
[a property] ***robust*** for
[a set of perturbations]

Apply recursively

[a property]

[property] = ***robust*** for
[one set of perturbations]

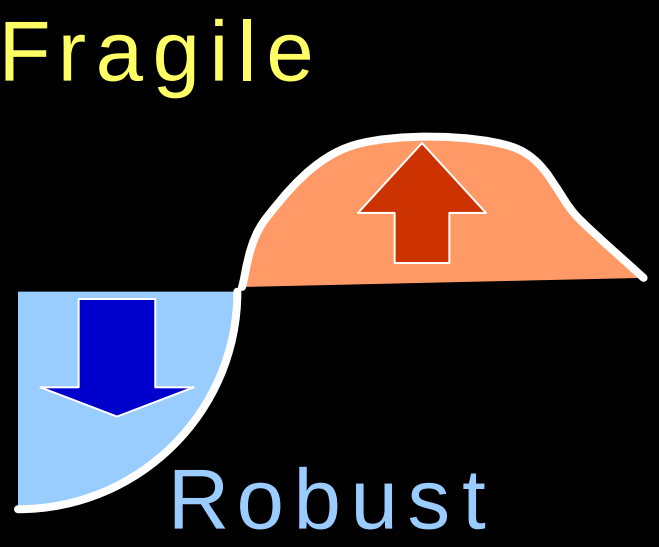
fragile for

[another property] or
[another set of perturbations]

[a perturbation]

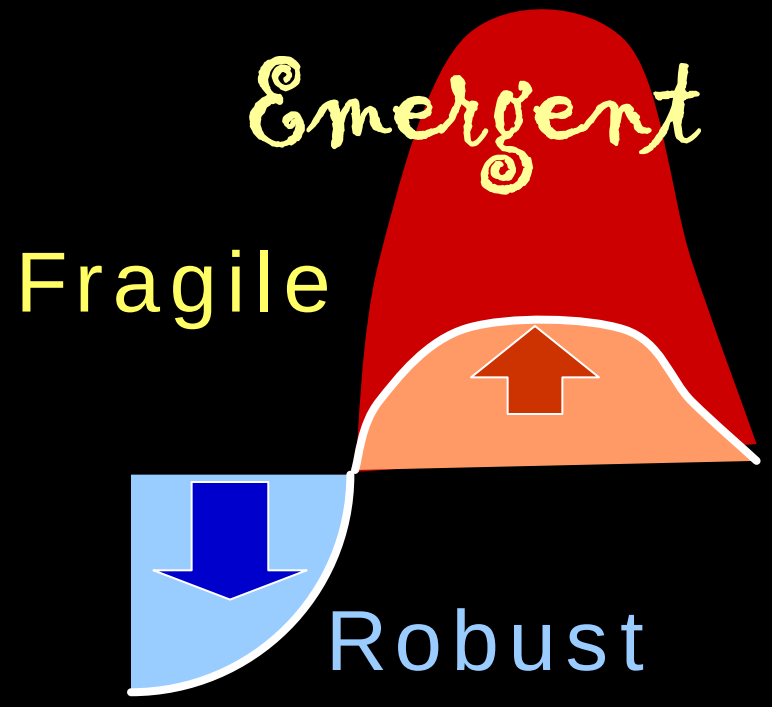
Robust yet fragile = fragile robustness

[a system] can have
[a property] ***robust*** for
[a set of perturbations]



- Some fragilities are inevitable in robust complex systems.

- But if robustness/fragility are ***conserved***, what does it mean for a ***system*** to be robust or fragile?



- Some fragilities are inevitable in robust complex systems.

- But if robustness/fragility are ***conserved***, what does it mean for a ***system*** to be robust or fragile?

- Robust ***systems*** systematically manage this tradeoff.
- Fragile ***systems*** waste robustness.

Definition: Resilience (www.wowwiki.com)

- **Resilience** is a character attribute that reduces the chance to receive critical strikes or spell critical strikes, reduces the effect of mana drain spells…
- Characters have no innate resilience. It can only be gained through external sources, e.g.
  - equipment,
  - elixirs,
  - enchantments,
  - gems, and
  - some spell effects

Definition: Resilience?

- Resilient systems effectively manage fragility tradeoffs?

- How does architecture facilitate resilience?

Robust yet fragile

Biology (and advanced tech) show extremes

- Robust Yet Fragile
- Simplicity and complexity
- Unity and diversity
- Evolvable and frozen

What makes this possible and/ or inevitable?

Architecture (= constraints)

Let’s dig deeper.

Why should we care here?

- Need automation/networking for sustainability
- For better or worse (or both)
- Security will become more critical
- ∃ fundamental but poorly understood tradeoffs

Architecture (= constraints)

Essential ideas: Architecture

Constraints that deconstrain*

Answer

* Gerhart and Kirschner

Essential ideas: Architecture

Constraints that deconstrain

Answer

Bad architecture:
Things are broken and you can’t fix it

Good architecture:
Things work and you don’t even notice

Hard limits.

No networks

Theoretical frameworks

Assume ***different*** architectures a priori.

- Thermodynamics (Carnot)
- Communications (Shannon)
- Control (Bode)
- Computation (Turing/Gödel)

New unifications are encouraging, but not yet accessible

Cyber

- Thermodynamics
- Communications
- Control
- Computation

Internet

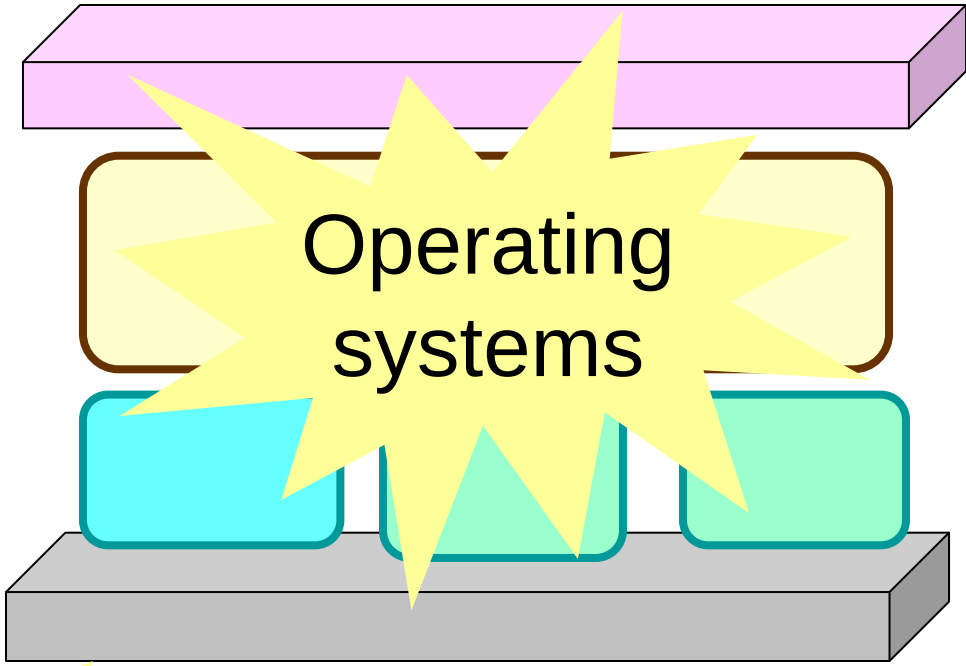
Physical

- Thermodynamics
- Communications
- Control
- Computation

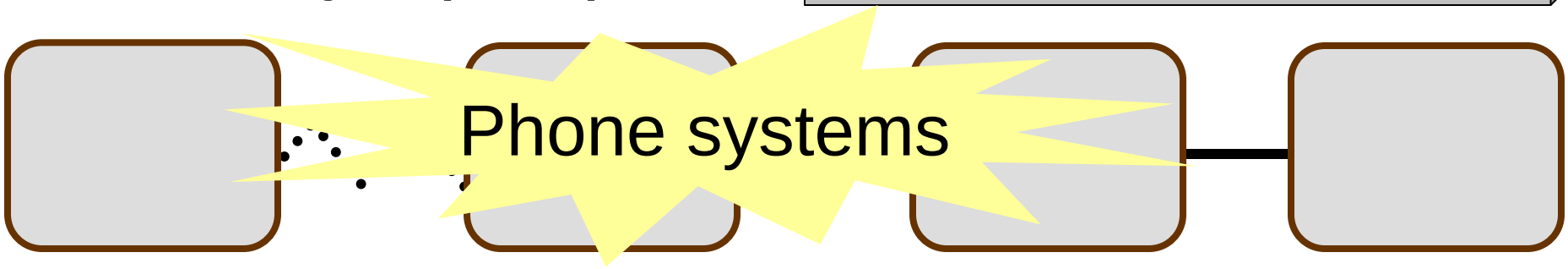
Bacteria

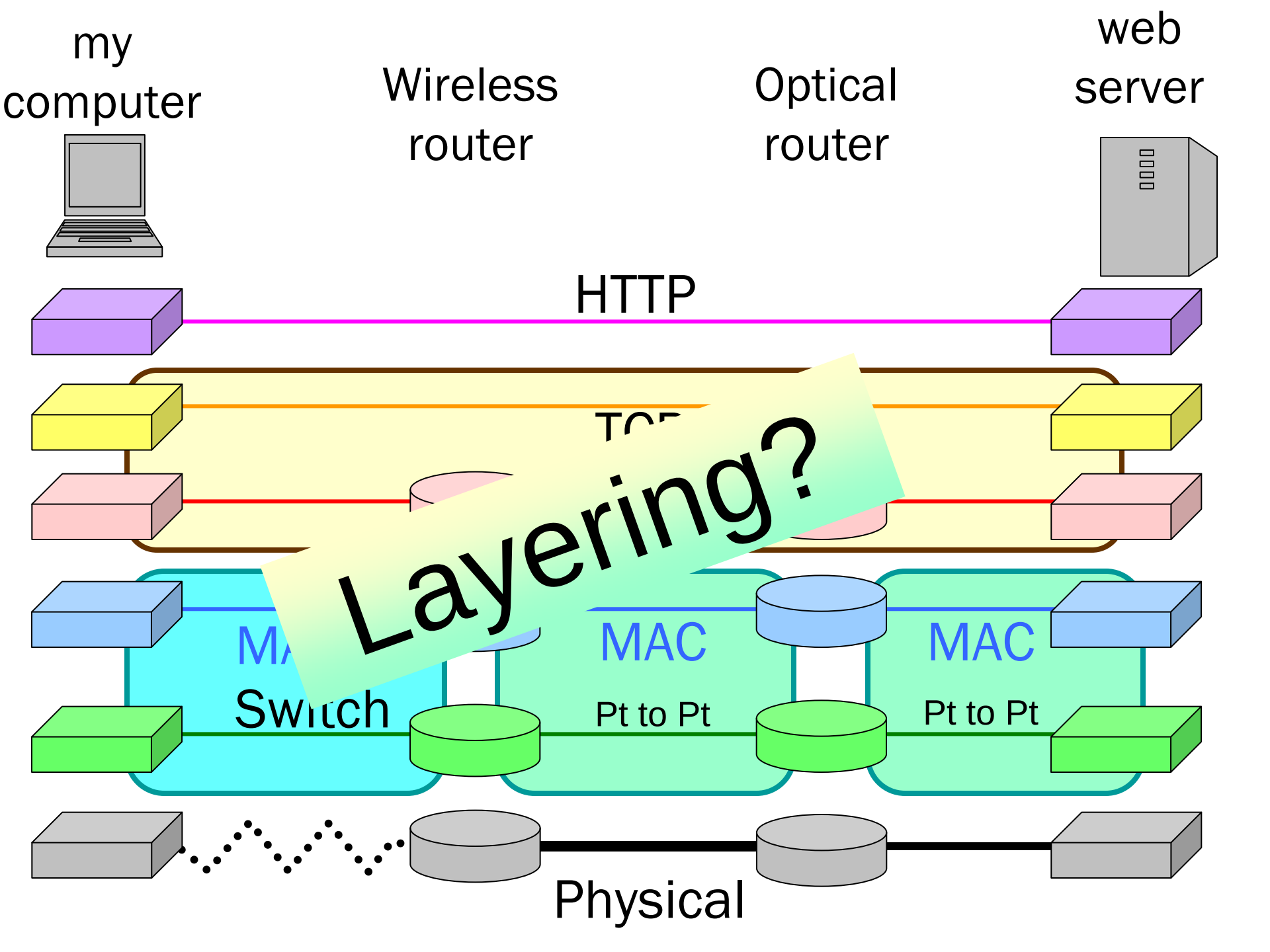
Ancient network architecture: “Bell-heads versus Net-heads”

Layers (Net)



Pathways (Bell)




my computer
Wireless router
Optical router
web server
HTTP
Layering?
MAC
Switch
MAC
Pt to Pt
MAC
Pt to Pt
Physical

Application

Diverse

Highly conserved core control processes

Operating system

Layered

Hardware

Diverse

Application

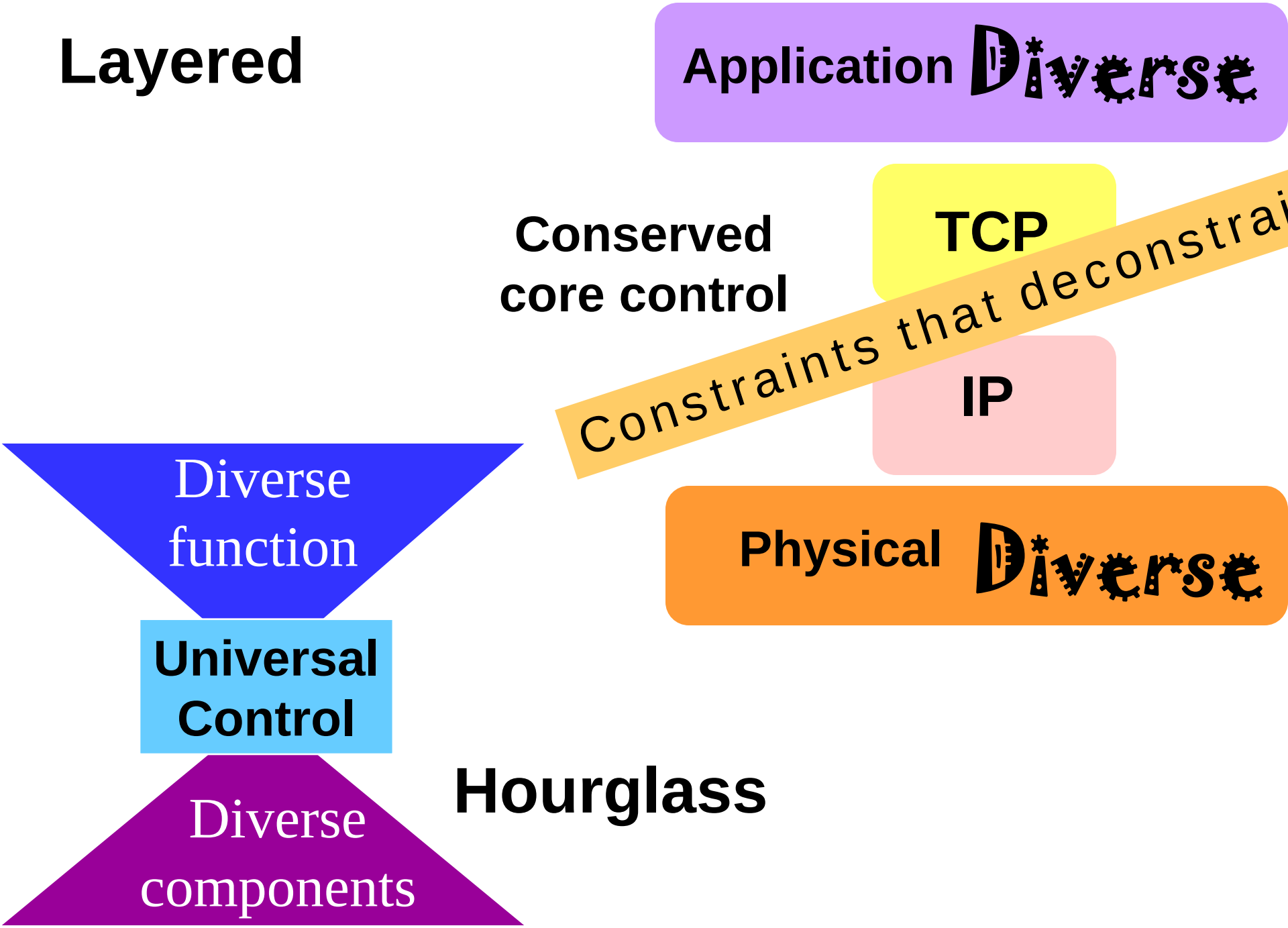
Diverse

Hidden to most users and technologies

Physical

Diverse

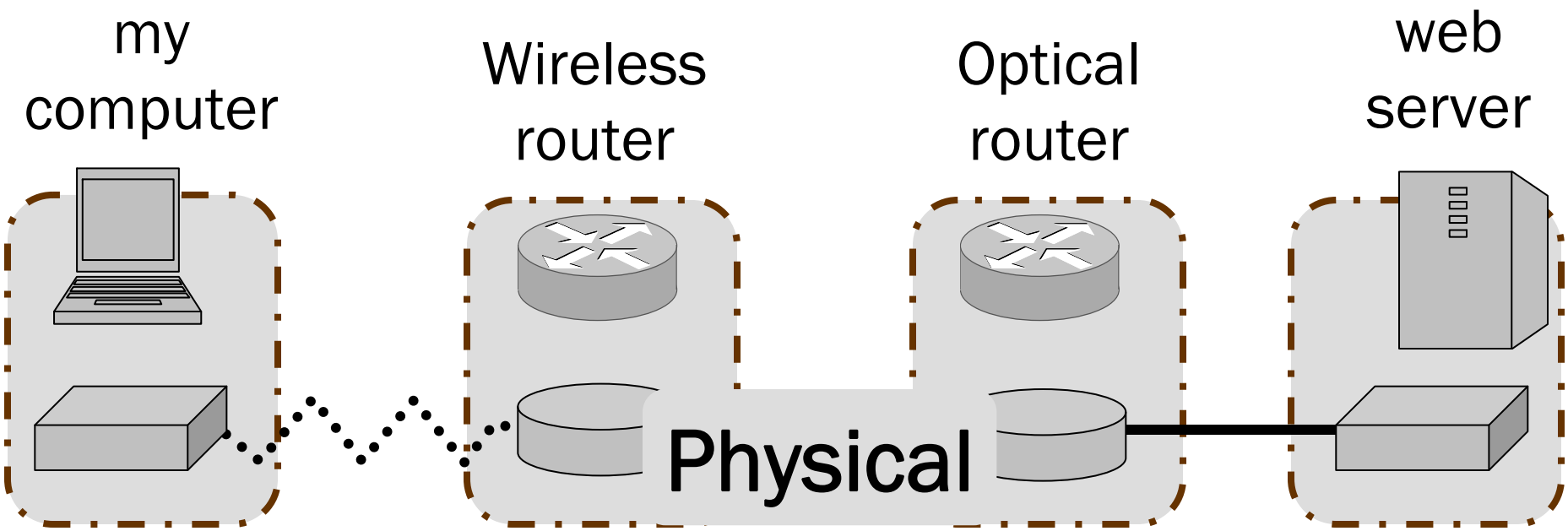
Layered

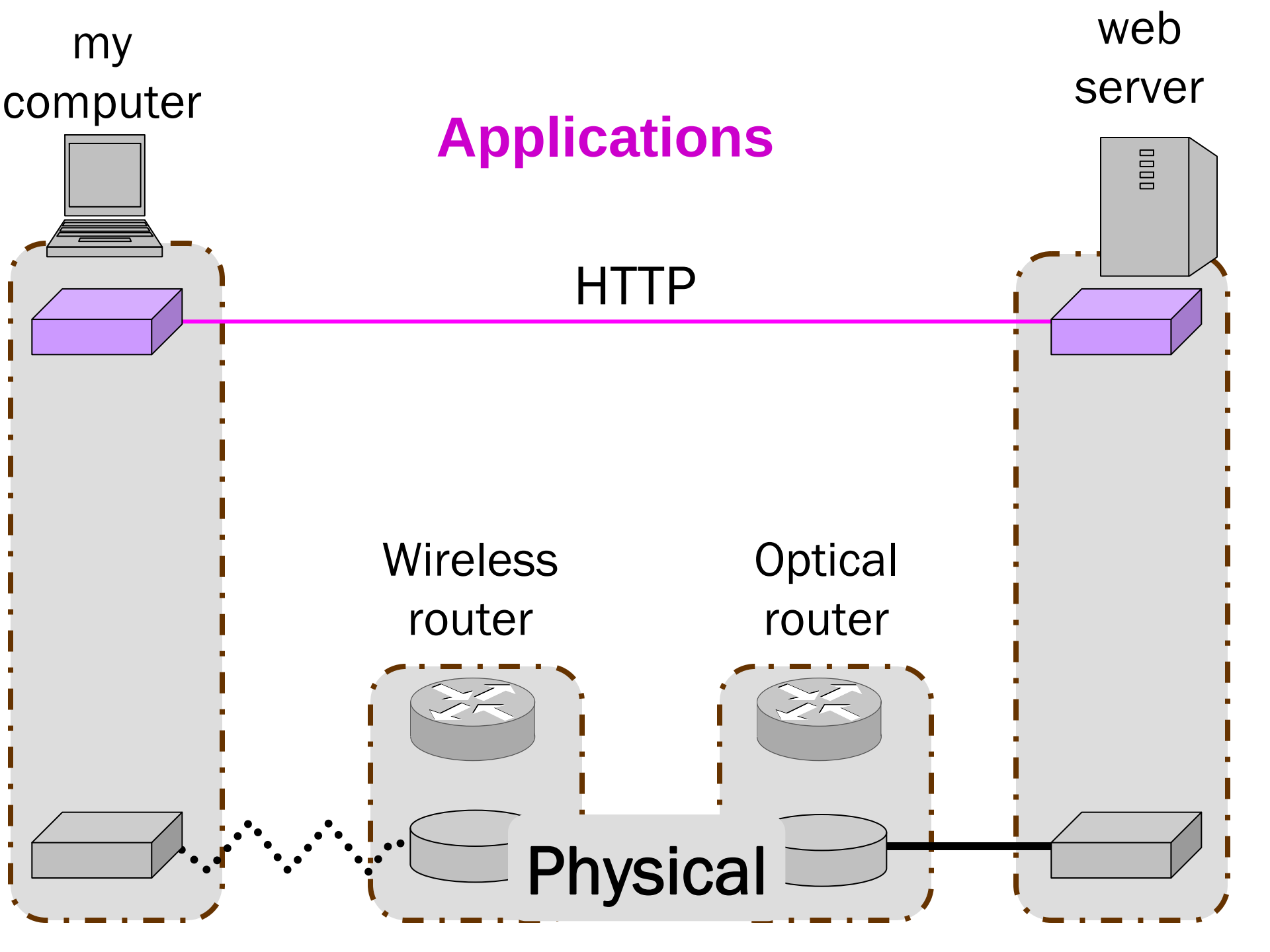

Application Diverse
Conserved
core control
TCP
Constraints that deconstrai
IP
Physical Diverse
Diverse
function
Universal
Control
Diverse
components
Hourglass

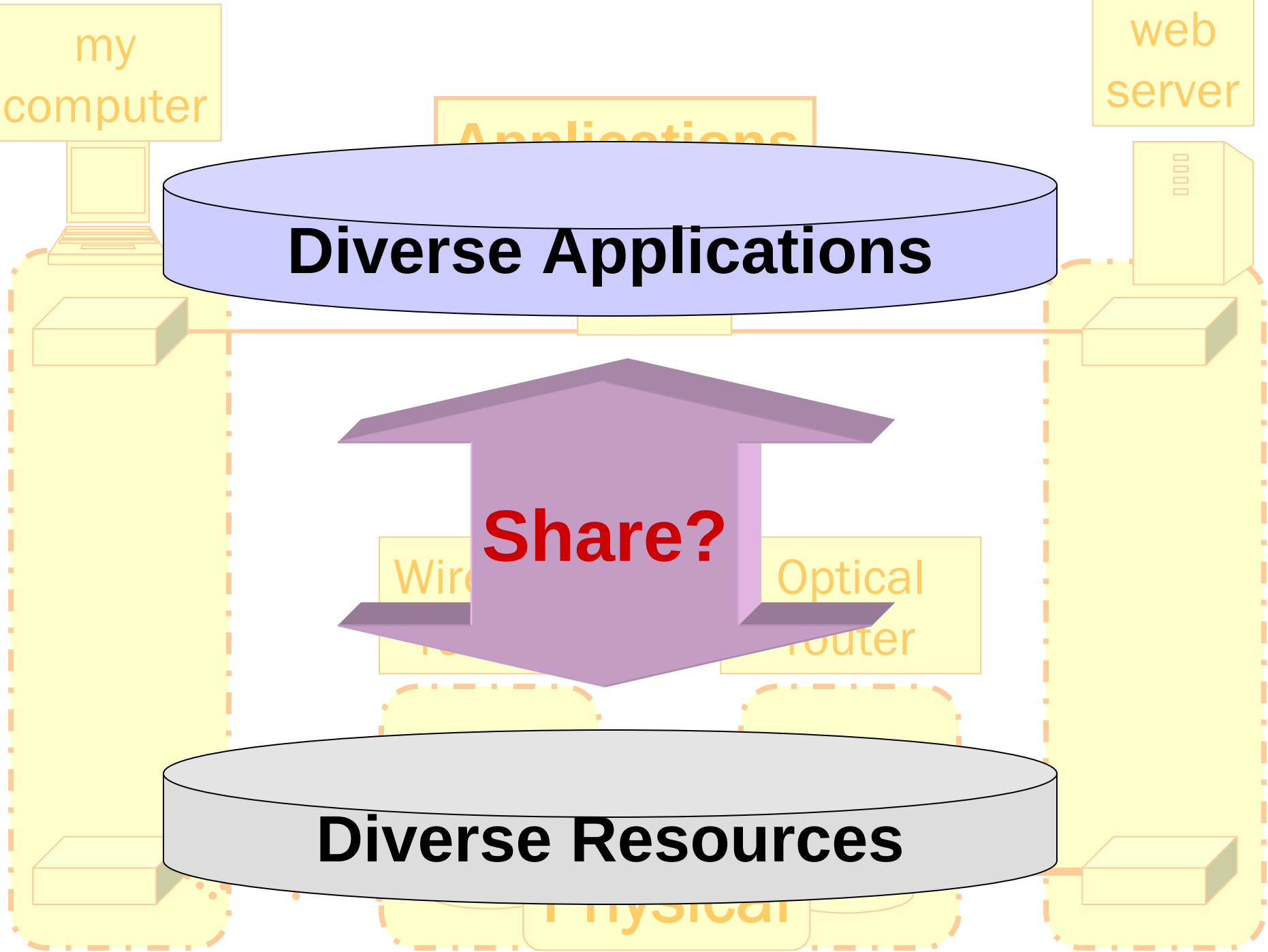
Applications

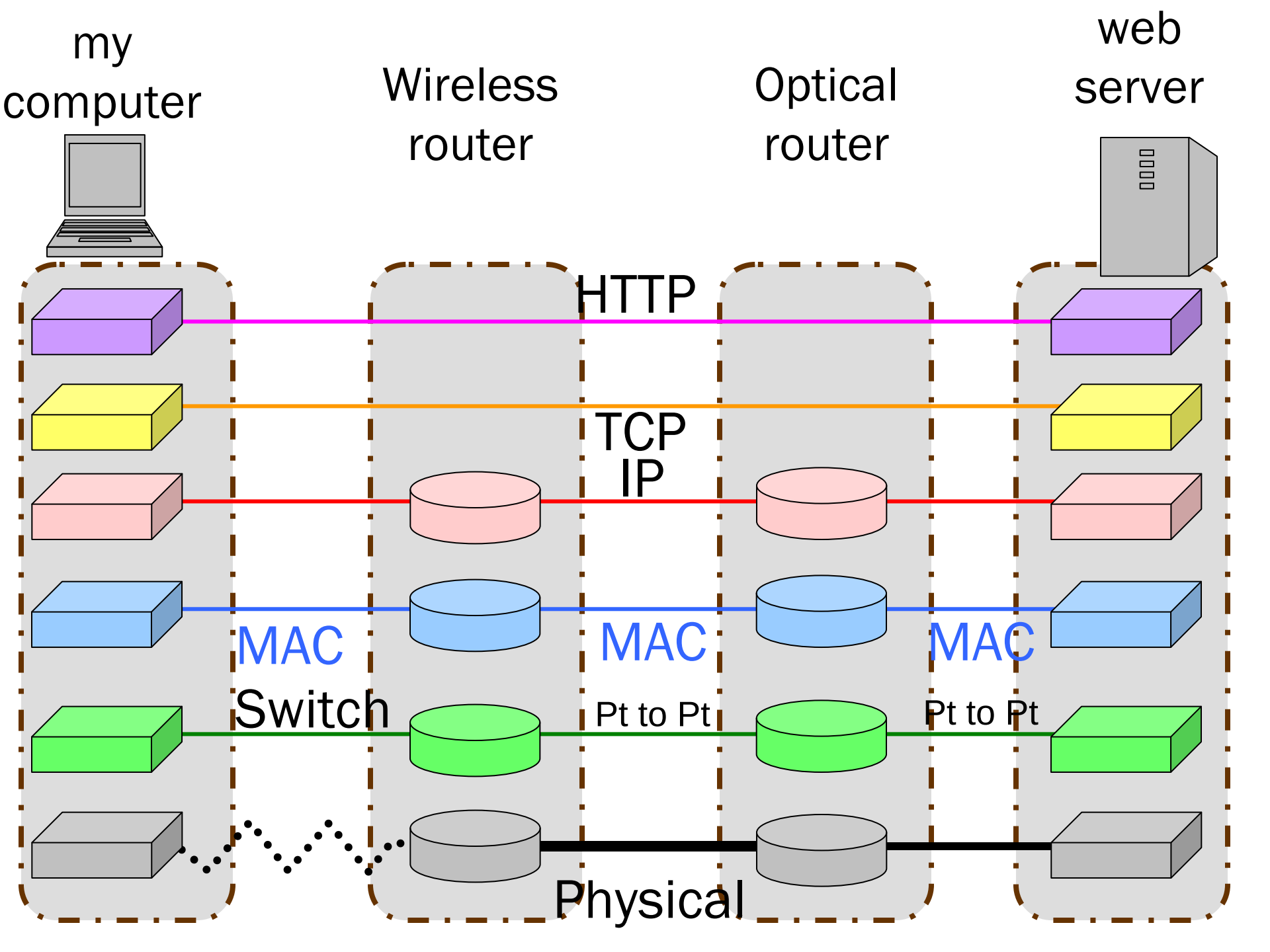
Browsing the web

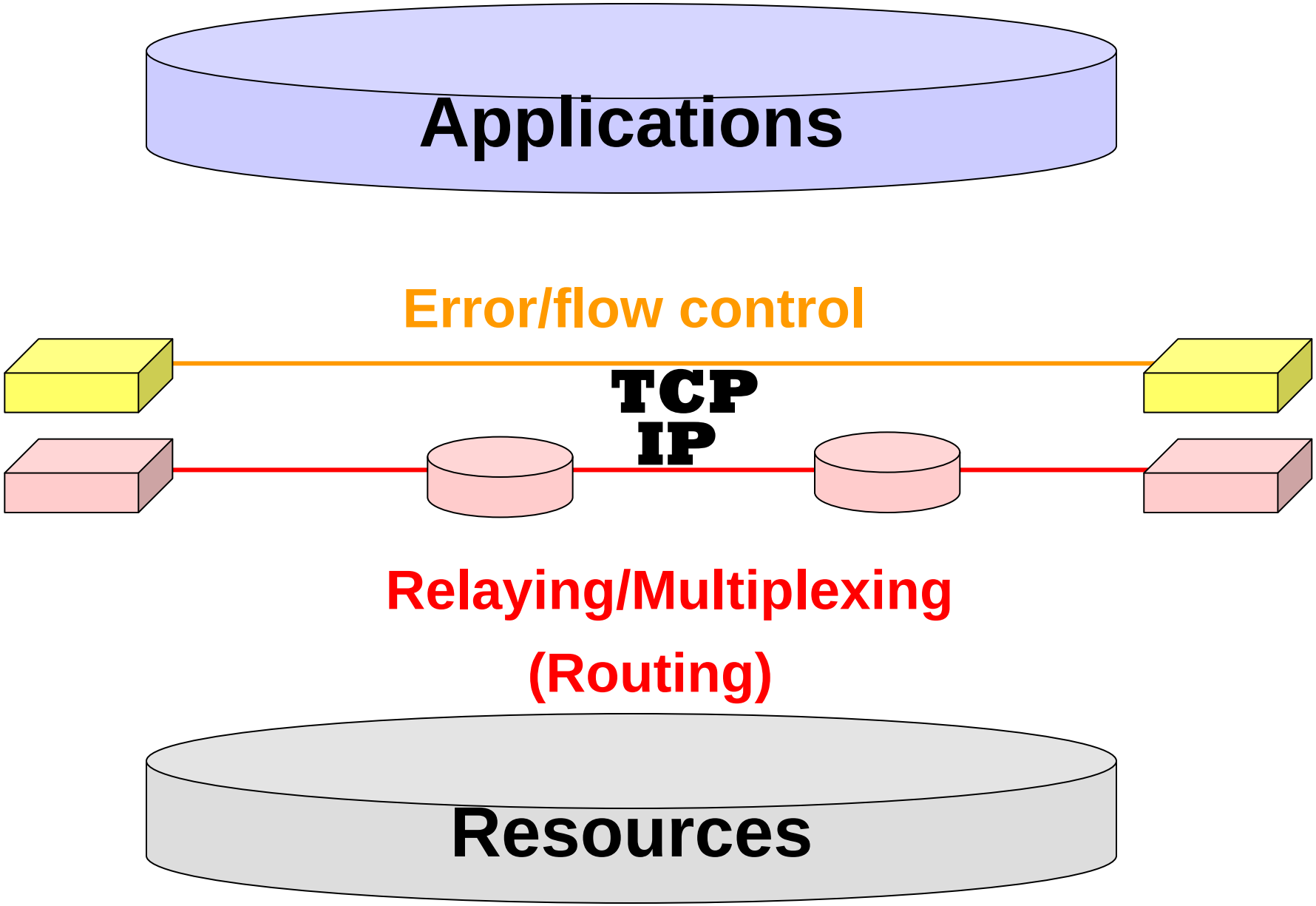
The physical pathway

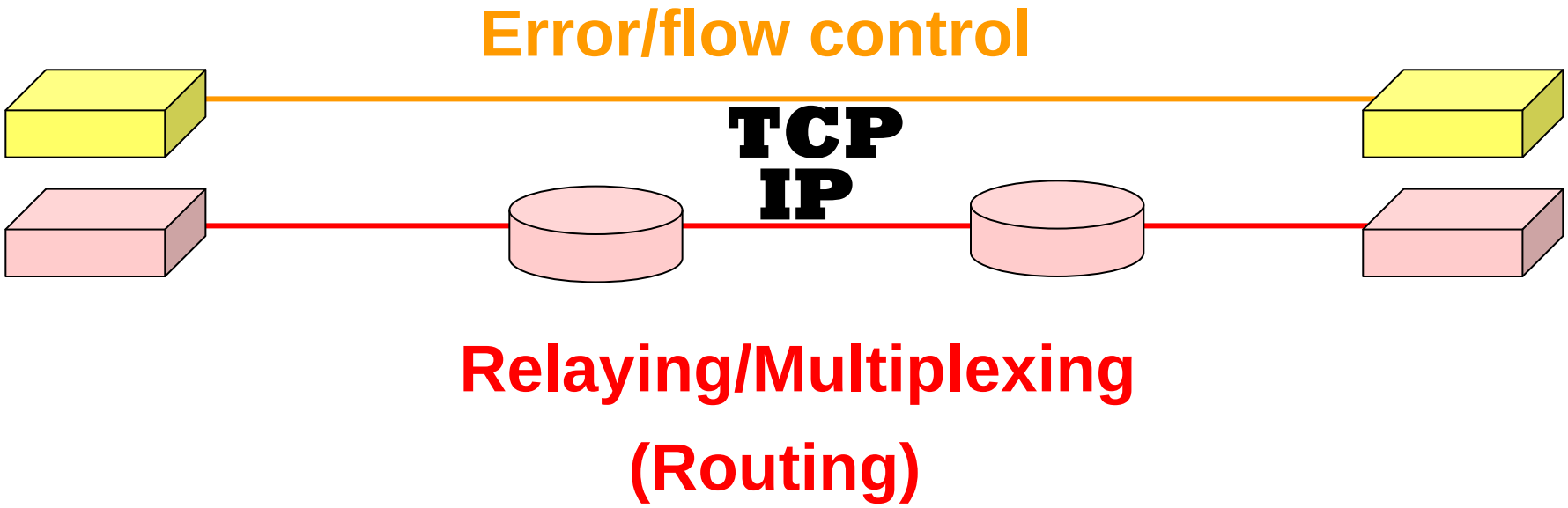


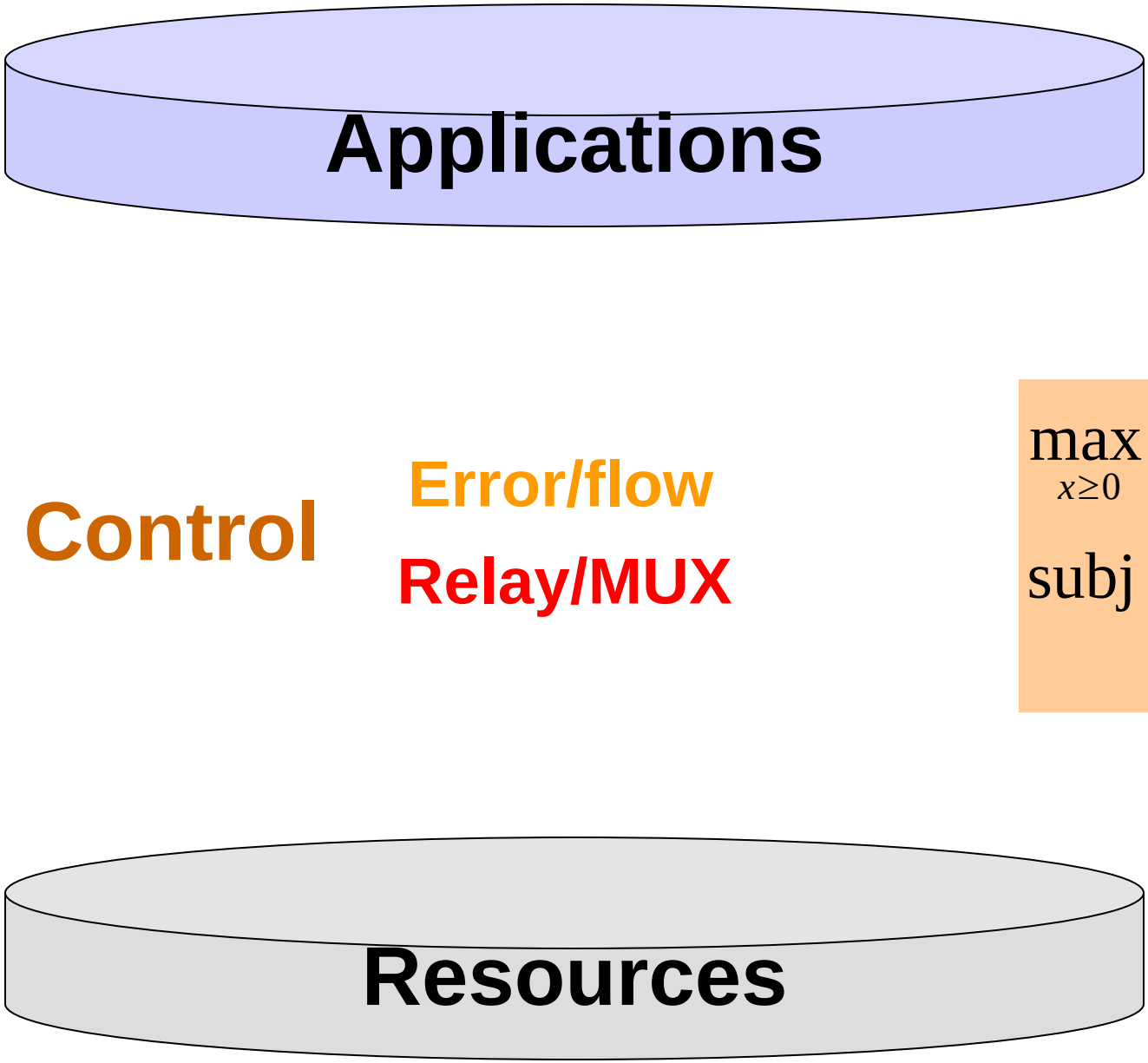

my computer
web server
Applications
HTTP
Wireless router
Optical router
Physical


my computer
web server
Diverse Applications
Share?
Optical
Diverse Resources


my computer
Wireless router
Optical router
web server
HTTP
TCP
IP
MAC
MAC
MAC
Switch
Pt to Pt
Pt to Pt
Physical


Applications
Error/flow control
TCP
IP
Relaying/Multiplexing
(Routing)
Resources

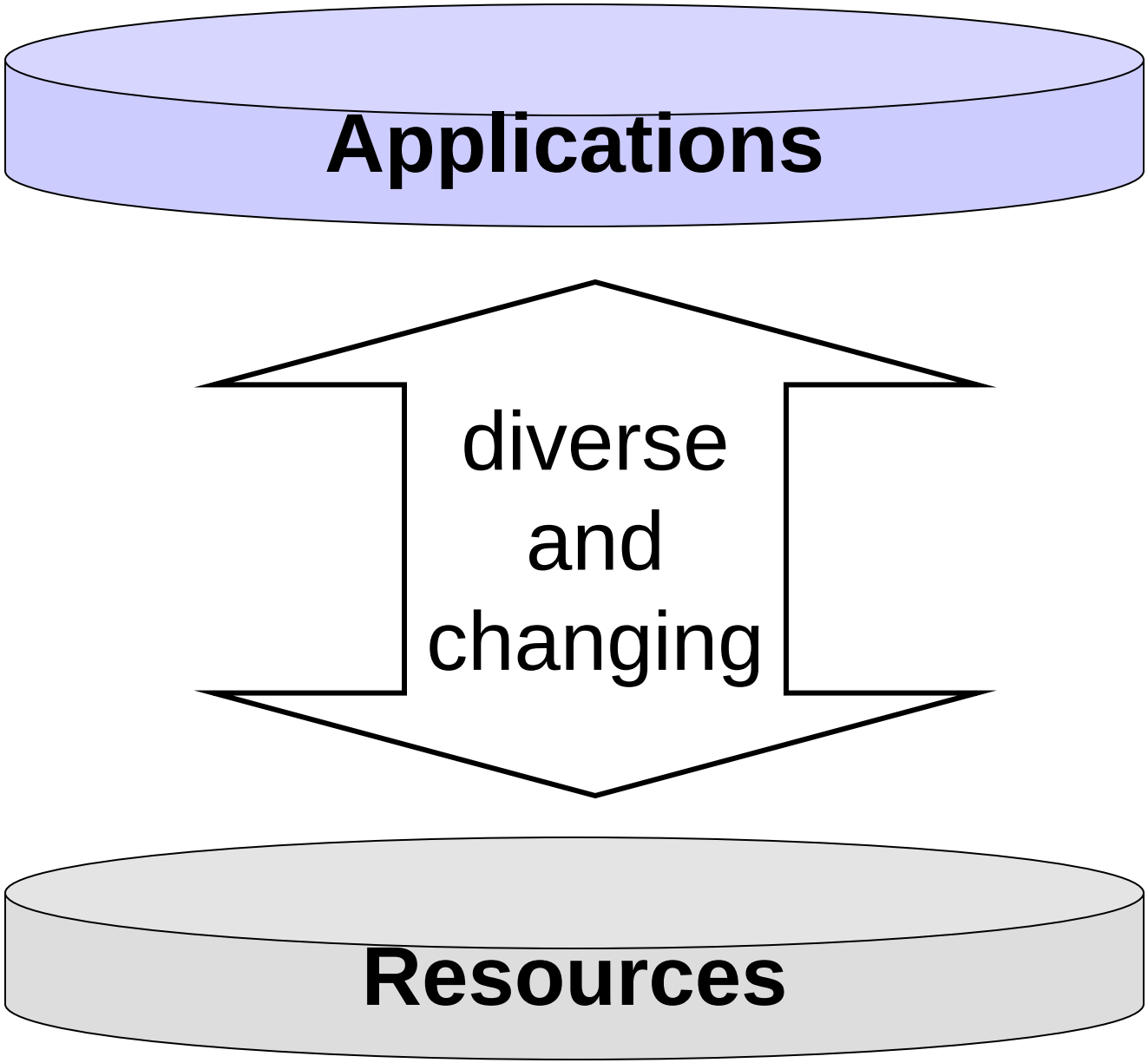

Error/flow control
TCP
IP
Relaying/Multiplexing
(Routing)



$$\max_{x \geq 0} \quad \sum_i U_i(x_i)$$

$$\text{subj to} \quad Rx \leq c(p)$$

$$x \in X$$


Applications
diverse
and
changing
Resources

Fixed and universal

Control

Error/flow

Relay/MUX

$$\begin{aligned} \max_{x \geq 0} \quad & \sum_i U_i(x_i) \\ \text{subj to} \quad & Rx \leq c(p) \\ & x \in X \end{aligned}$$

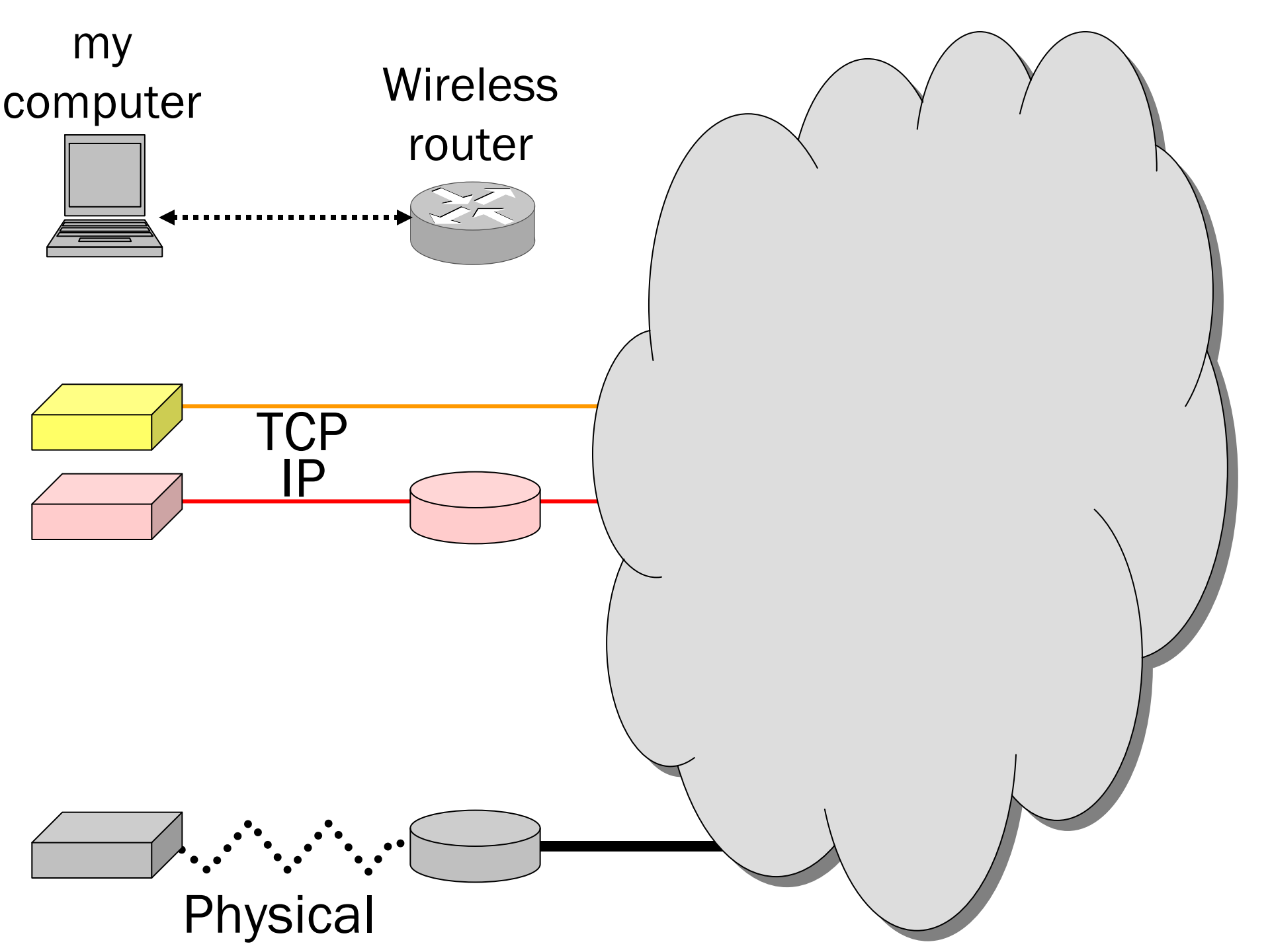
Applications Deconstrained

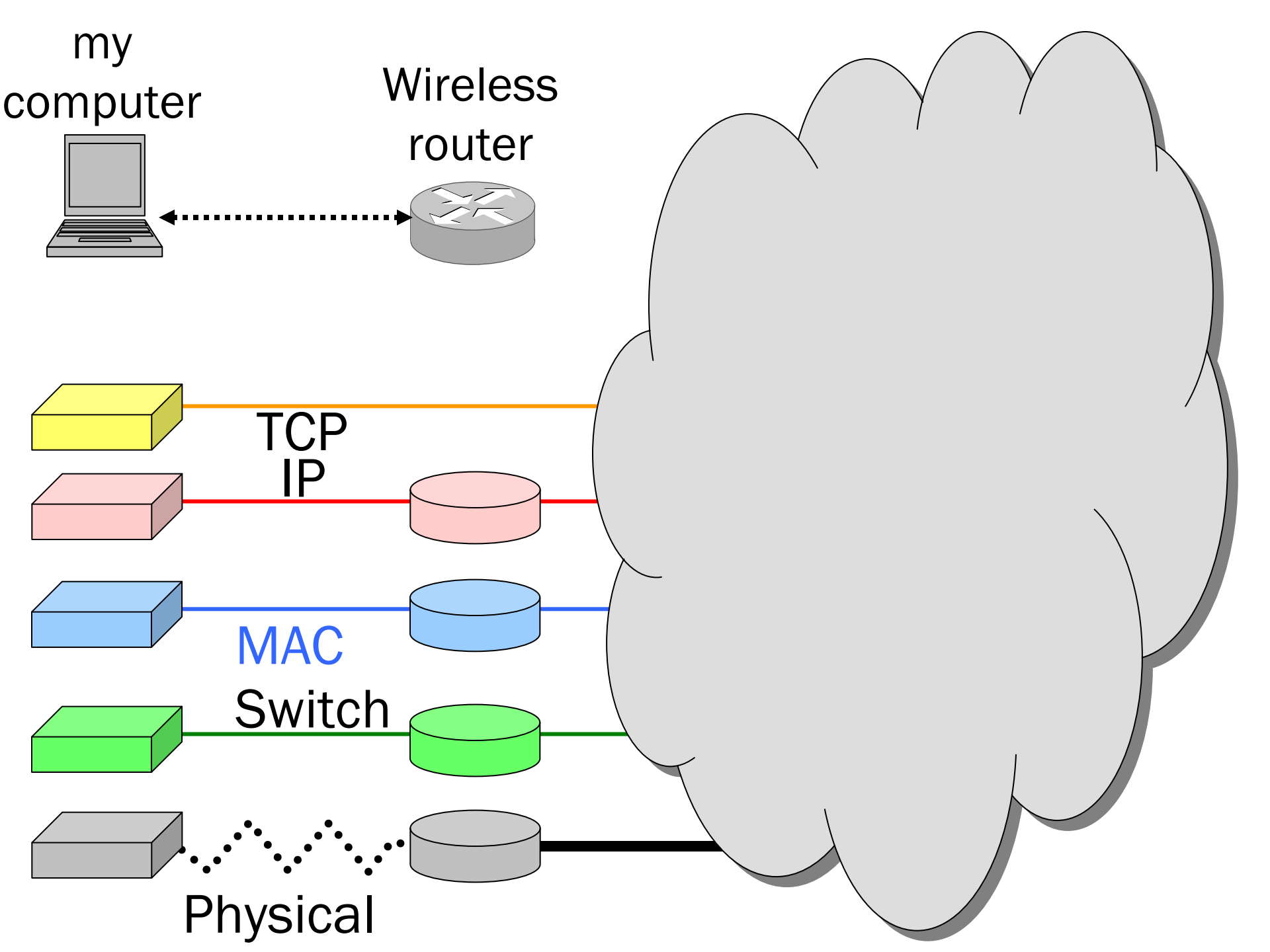
Constraints that deconstrain

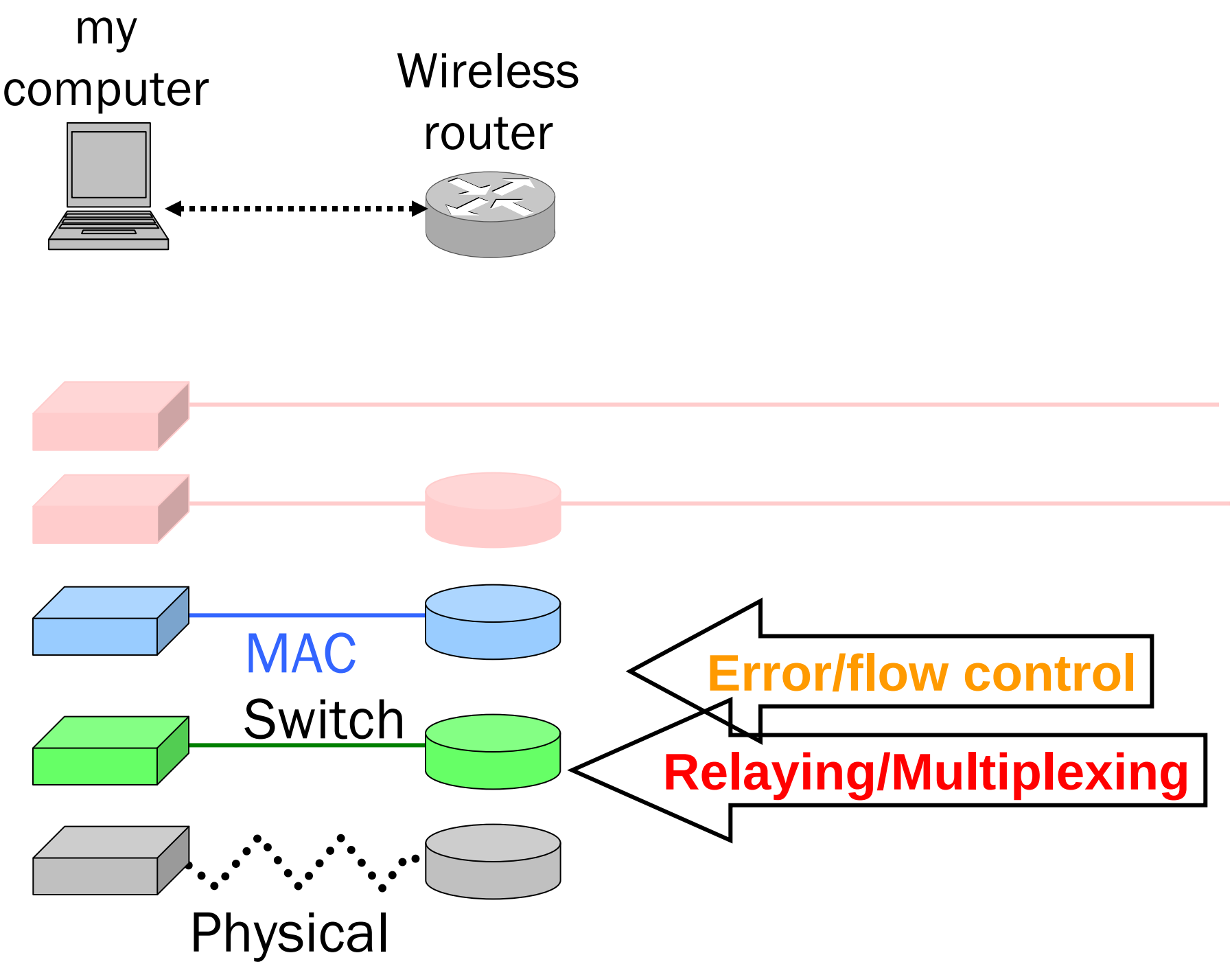
$$\max_{x \geq 0} \quad \sum_i U_i(x_i)$$
$$\text{subj to} \quad Rx \leq c(p)$$
$$x \in X$$

Resources Deconstrained

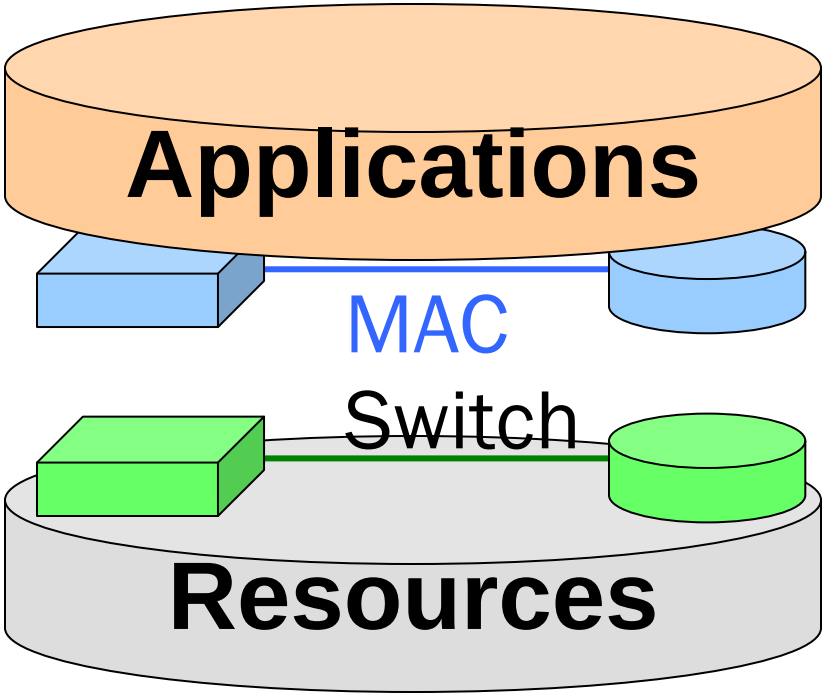
Gerhart and Kirschner


my
computer
Wireless
router
TCP
IP
Physical


my computer
Wireless router
TCP
IP
MAC
Switch
Physical


my computer
Wireless router
MAC
Switch
Physical
Error/flow control
Relaying/Multiplexing

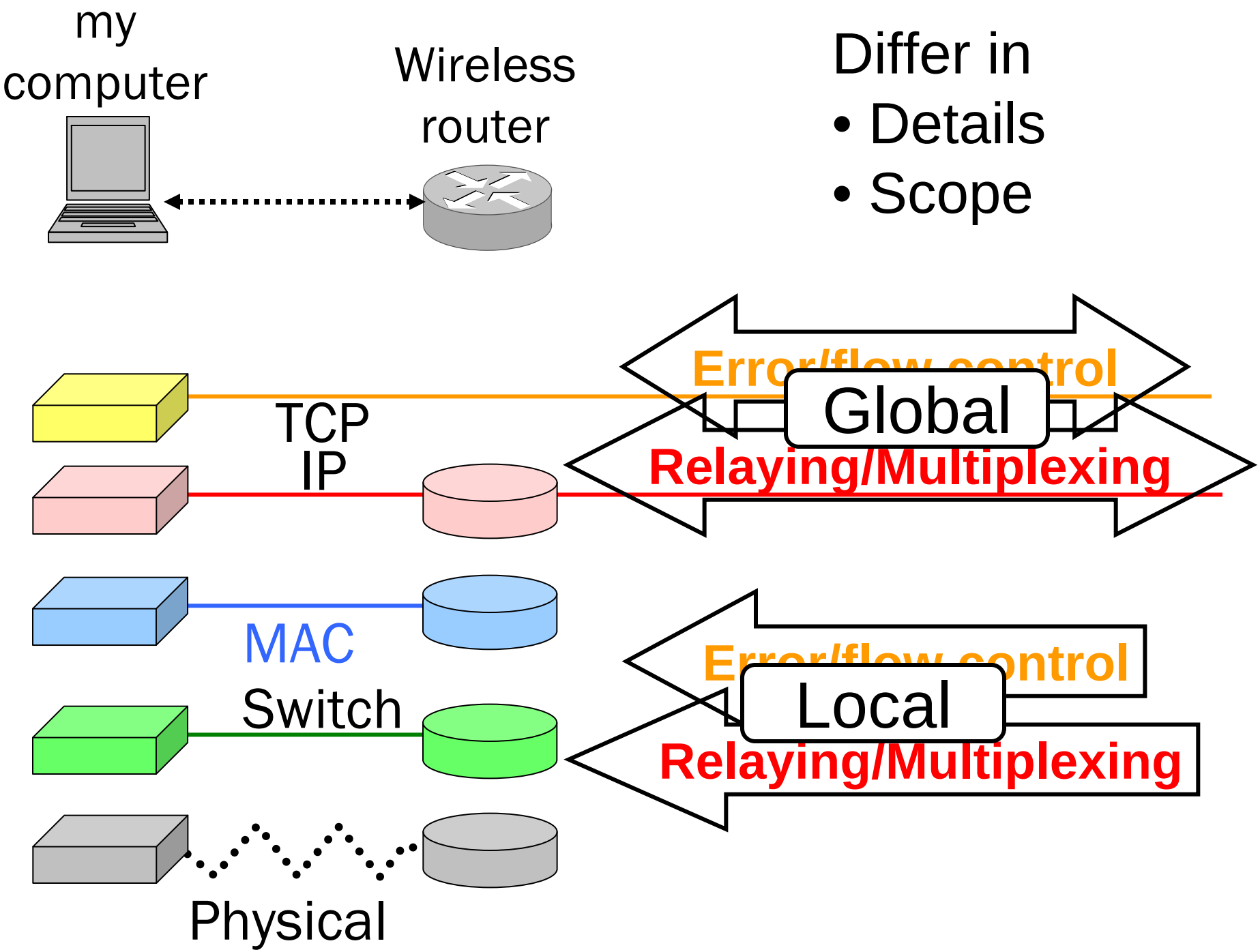
Wireless
router

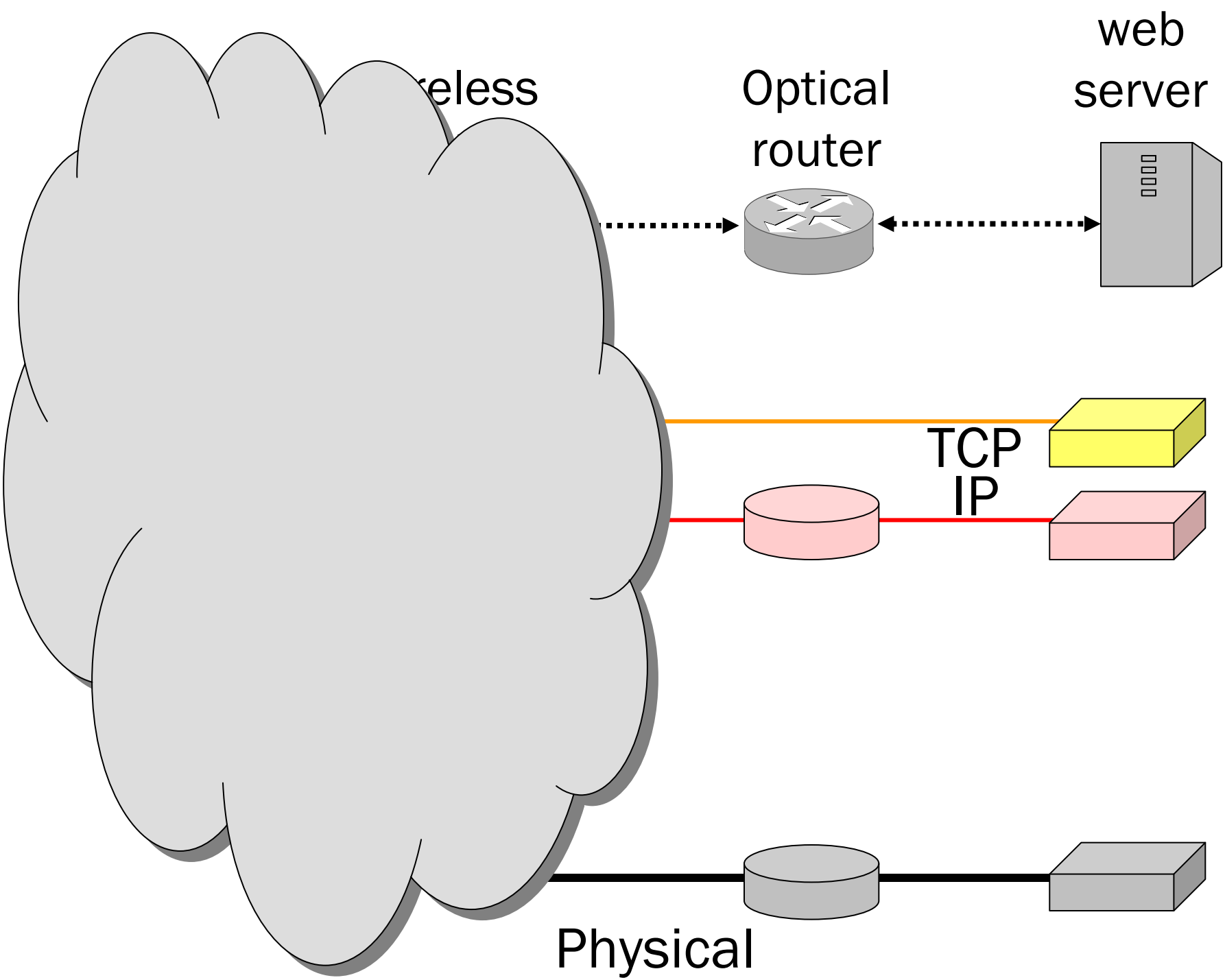


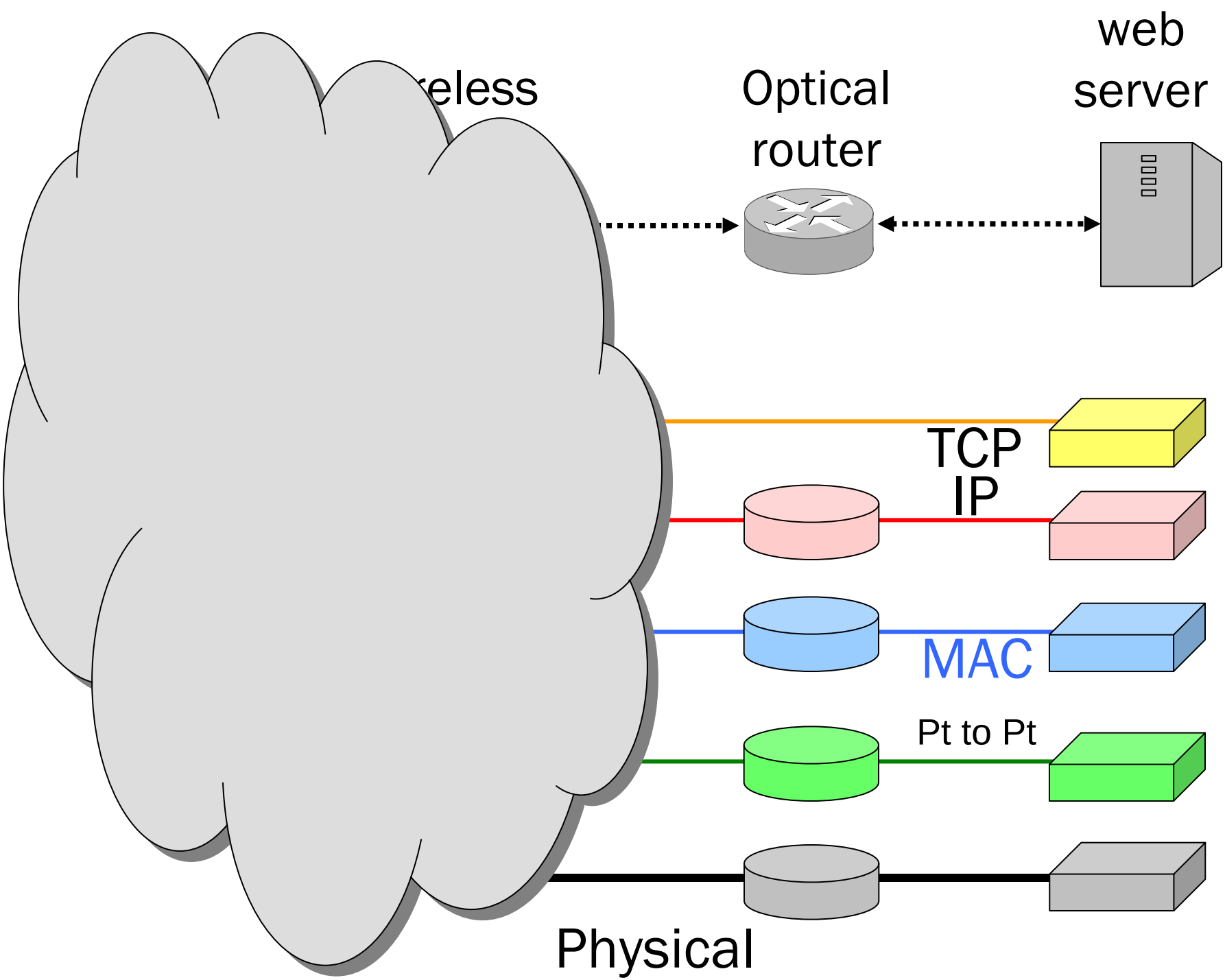
Error/flow control

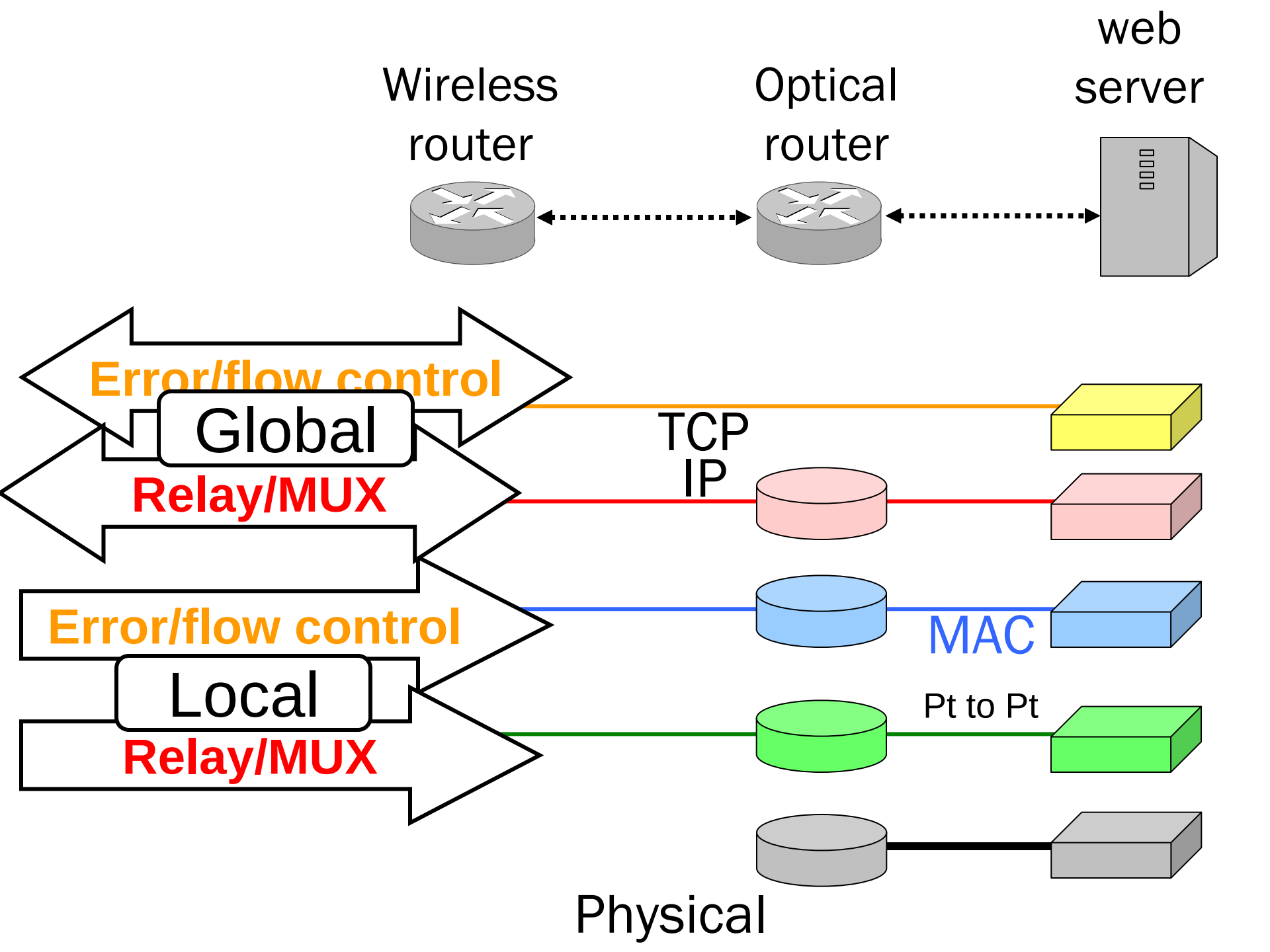
Local

Relaying/Multiplexing


my computer
Wireless router
Differ in
• Details
• Scope
Error/flow control
Global
Relaying/Multiplexing
TCP
IP
MAC
Switch
Error/flow control
Local
Relaying/Multiplexing
Physical


reless
Optical
router
web
server
TCP
IP
Physical


web
server
Optical
router
TCP
IP
MAC
Pt to Pt
Physical


Wireless router
Optical router
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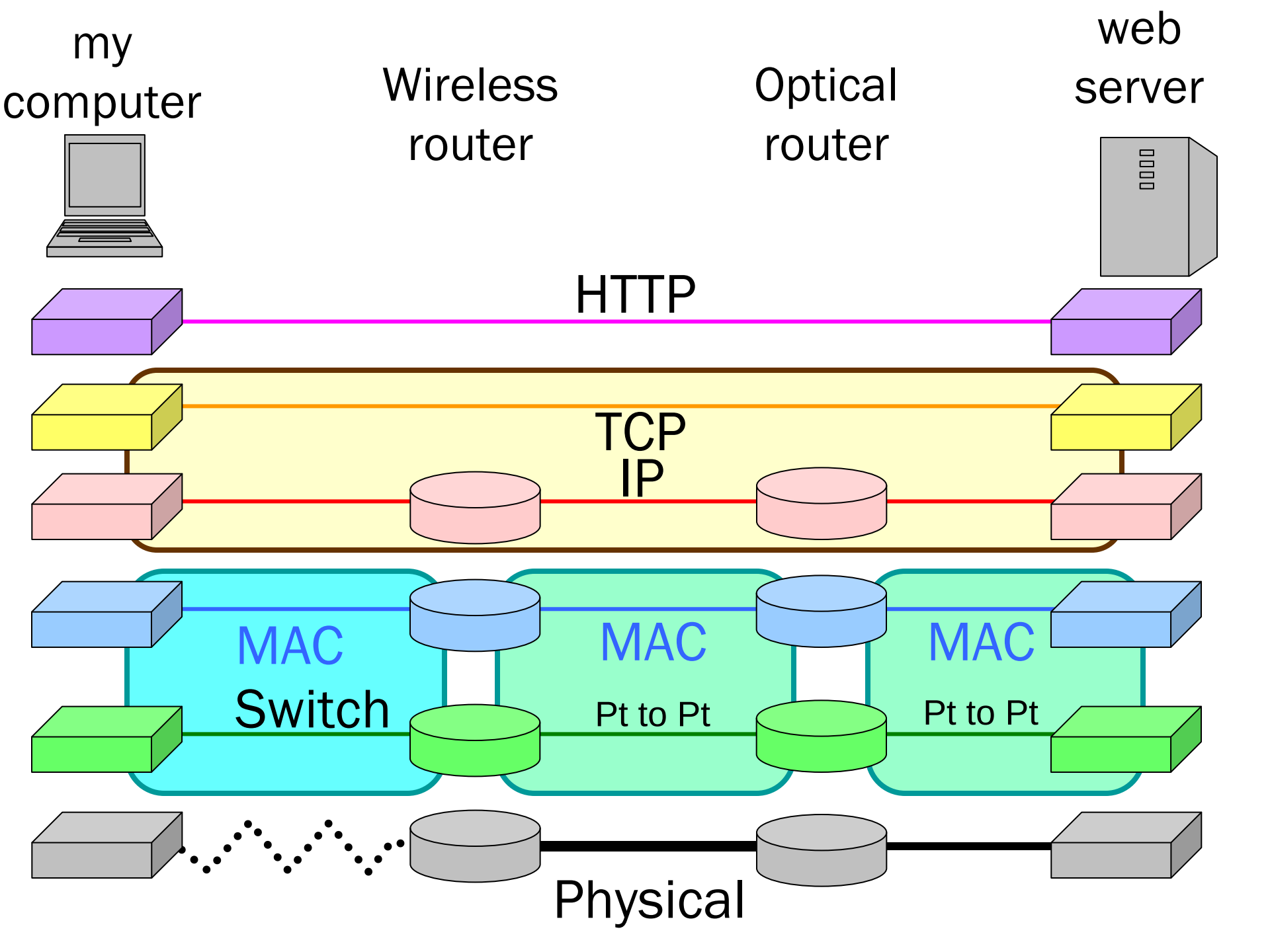
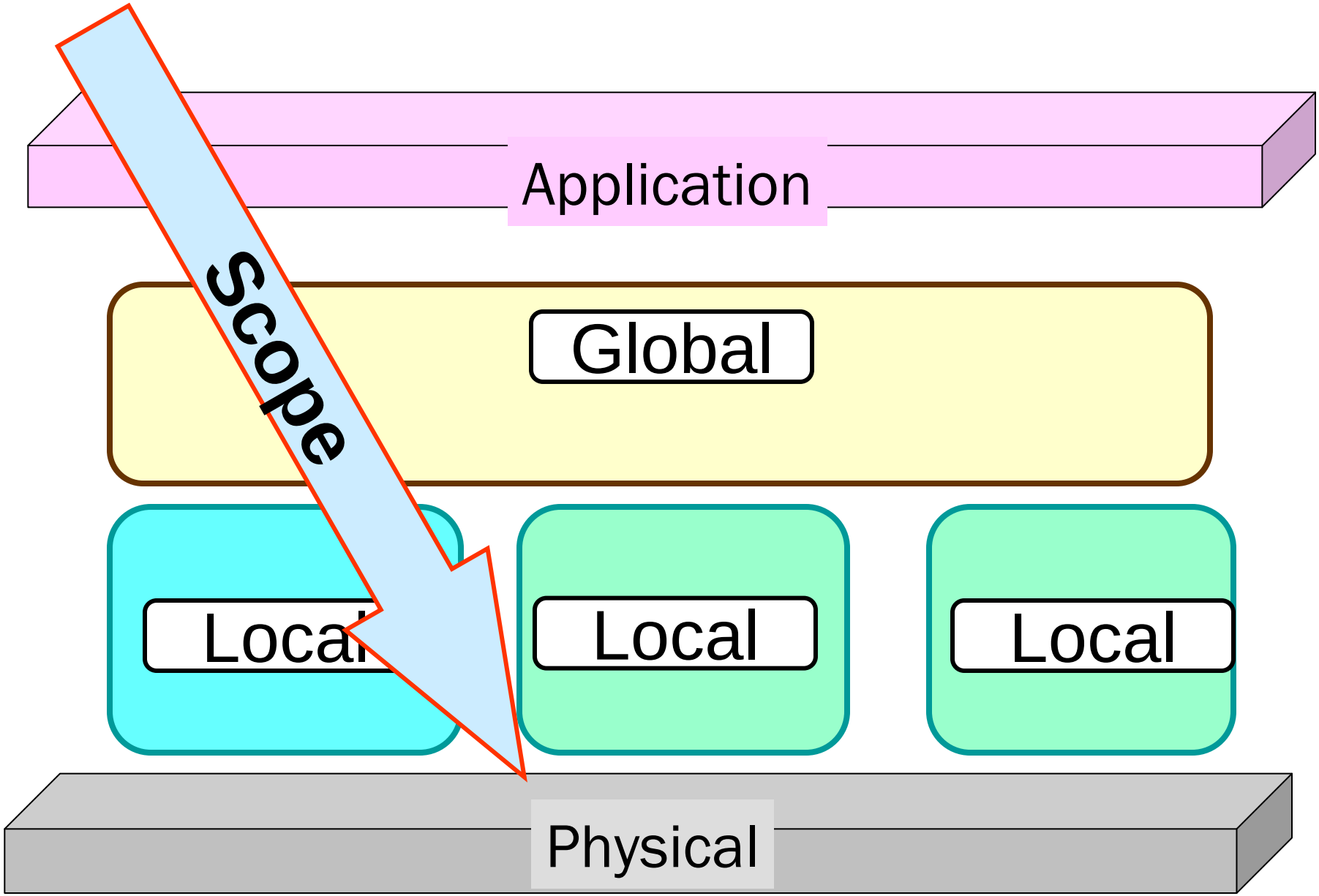
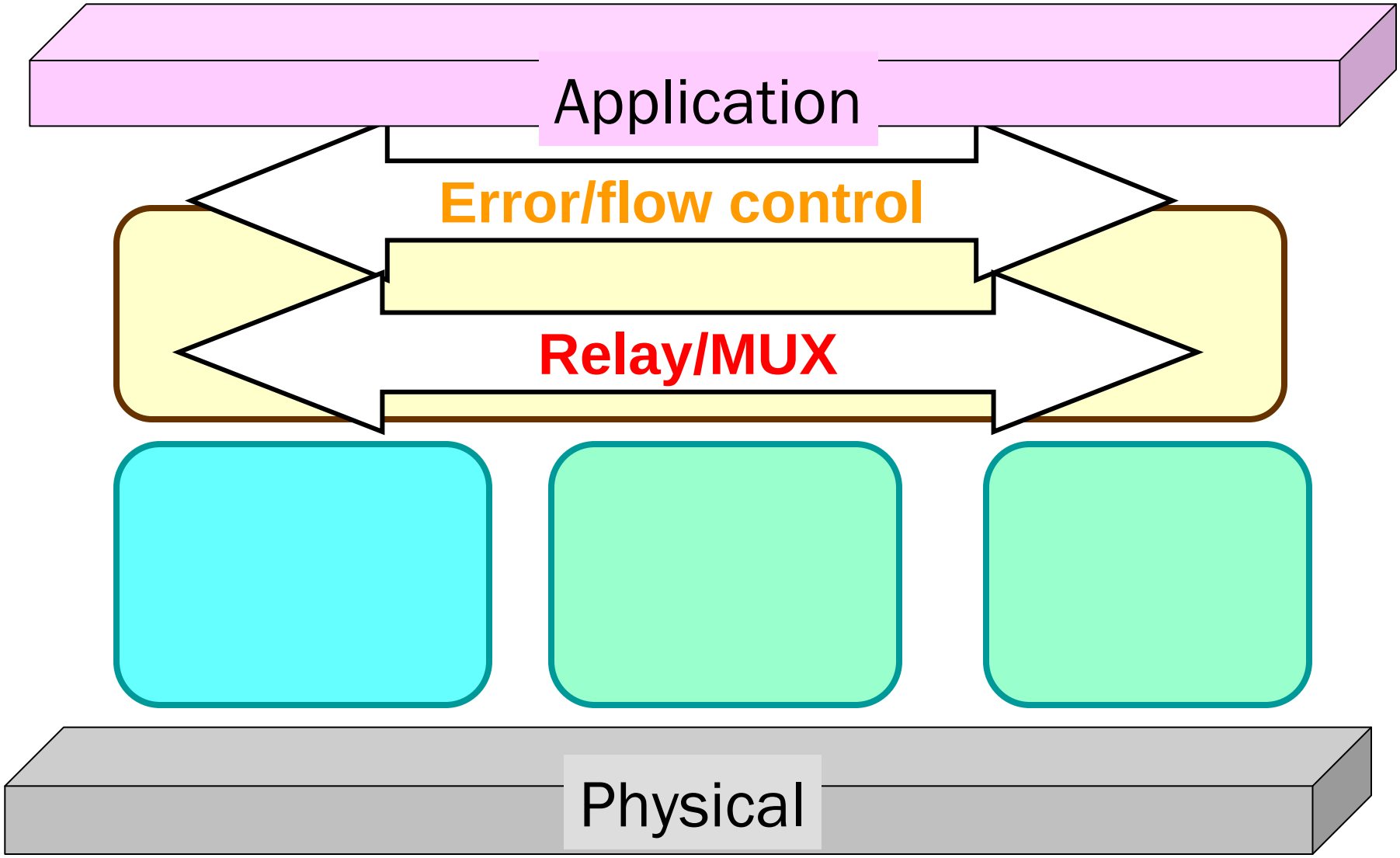
Error/flow control
Global
Relay/MUX
TCP
IP
Error/flow control
Local
Relay/MUX
MAC
Pt to Pt
Physical


my computer
Wireless router
Optical router
web server
HTTP
TCP
IP
MAC
Switch
MAC
Pt to Pt
MAC
Pt to Pt
Physical

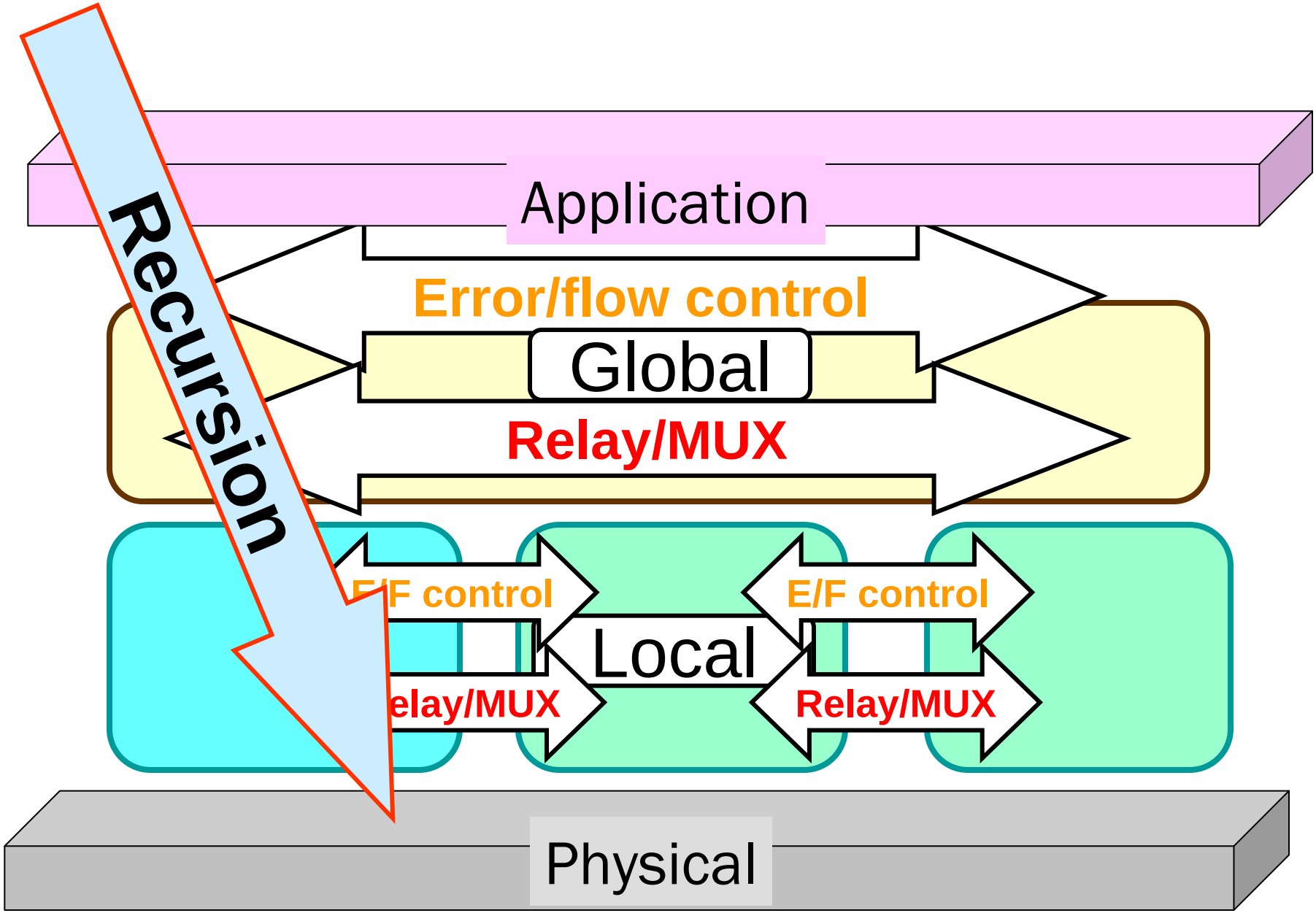
Recursive control structure



Recursive control structure



Recursive control structure



Constraints that deconstrain

Applications Deconstrained

$$\min_{\mathbf{x}} \left\{ \int \left(\left\| R\tilde{\mathbf{x}} - \mathbf{c} \right\|^2 + \left\| R\mathbf{x} - \mathbf{c} \right\|^2 \right) dt \right\}$$

$$\left| \; \tilde{\mathbf{x}} = \arg\max_{\mathbf{v}} L\left(\mathbf{v}, \mathbf{p}\right), \quad \dot{\mathbf{p}} = R\mathbf{x} - \mathbf{c} \right.$$

$$\Rightarrow x_s = \arg\max_{v} L_s\left(v, \mathbf{p}\right)$$

Resources Deconstrained

Generalizations

- Optimization
- Optimal control
- Robust control
- Game theory
- Network coding

Fragilities
are legion

Applications Deconstrained

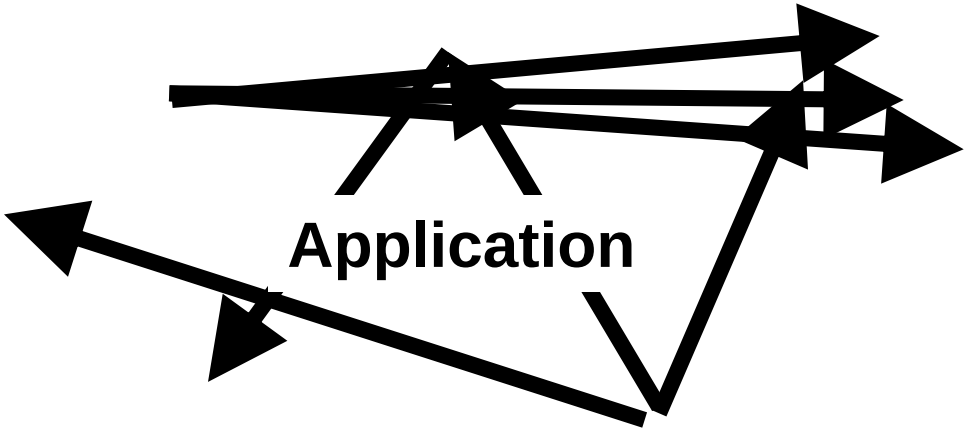
Constraints that deconstrain

Fragility?

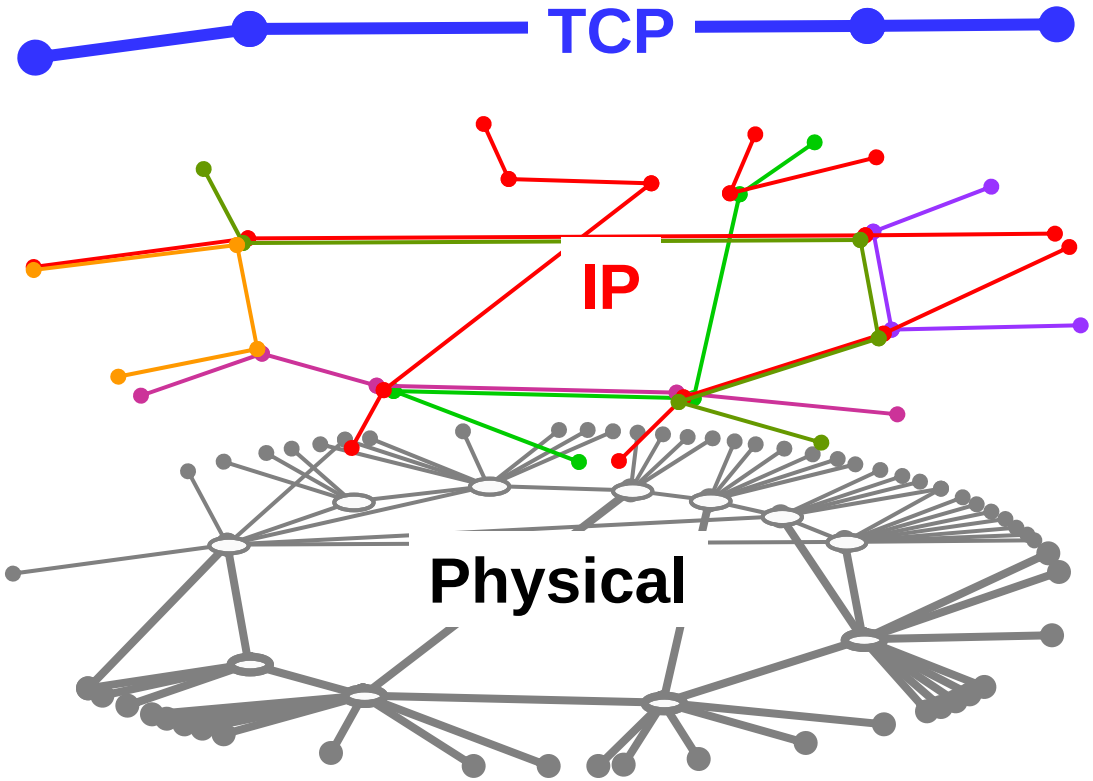
Resources Deconstrained

All are forms
of “hijacking””

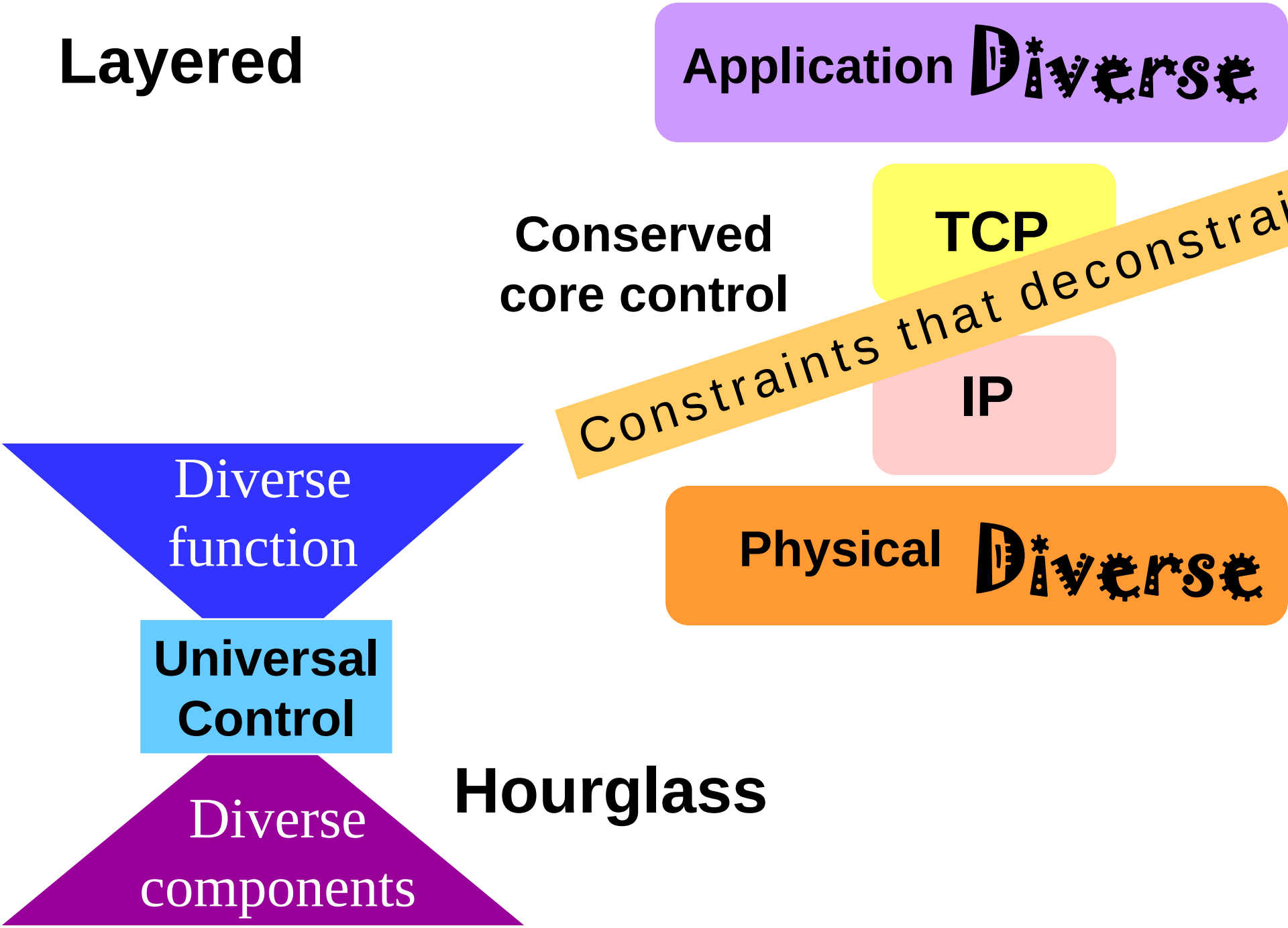
What is the graph of the Internet?



Wrong question.



Layered


Application Diverse
Conserved
core control
TCP
Constraints that deconstrai
IP
Physical Diverse
Diverse
function
Universal
Control
Diverse
components
Hourglass

Cyber-physical networks?

- Water
- Waste
- Food
- Power
- Transportation
- Healthcare
- Finance

All examples of bad architectures:

- Unsustainable
- Hard to fix

Constraints:

- Burning fossil fuels
- Individual vehicles
- Lots of plastic
- Standing armies
- Monocultures
- etc etc

Biology versus the Internet

Similarities

- Evolvable architecture
- Robust yet fragile
- Layering, modularity
- Hourglass with bowties
- Dynamics
- Feedback
- Distributed/decentralized

- ***Not*** scale-free, edge-of-chaos, self-organized criticality, etc

Differences

- Metabolism
- Materials and energy
- Autocatalytic feedback
- Feedback complexity
- Development and regeneration
- ~~>3B~~ years of evolution

>4B

Biology versus the Internet

Similarities

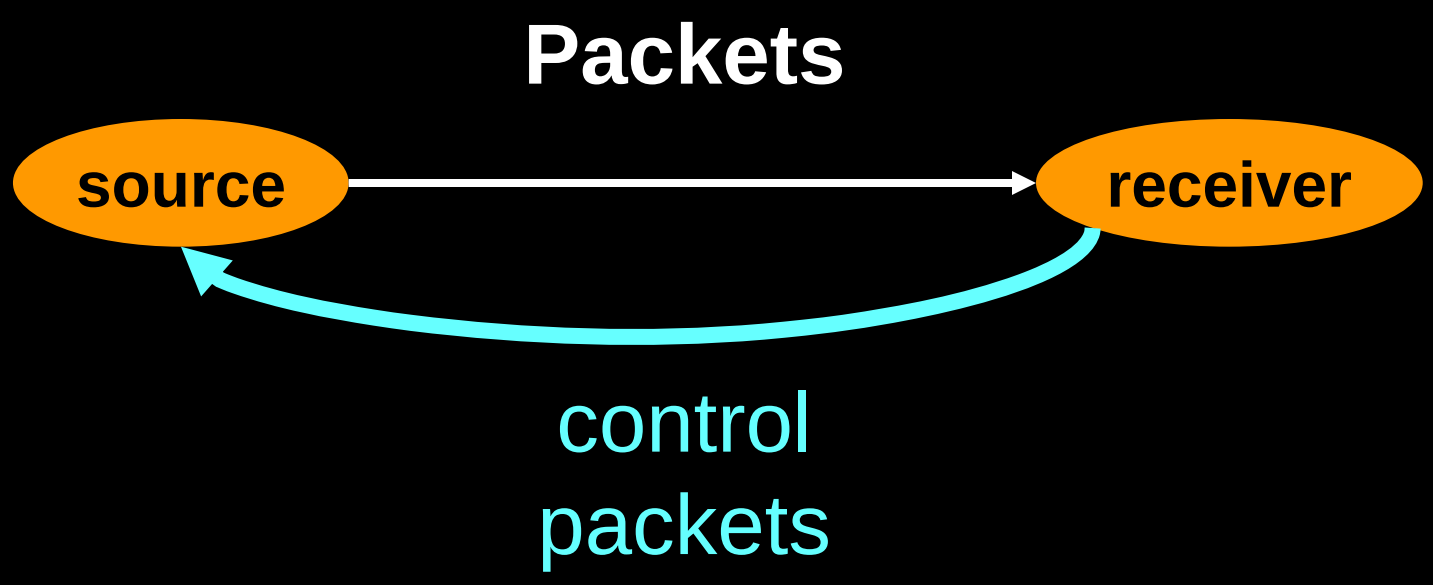
- Evolvable architecture
- Robust yet fragile
- **Layering, modularity**
- Hourglass with bowties
- Dynamics
- Feedback
- Distributed/decentralized

- ***Not*** scale-free, edge-of-chaos, self-organized criticality, etc

Differences

- Metabolism
- Materials and energy
- **Autocatalytic feedback**
- Feedback complexity
- Development and regeneration
- >3B years of evolution

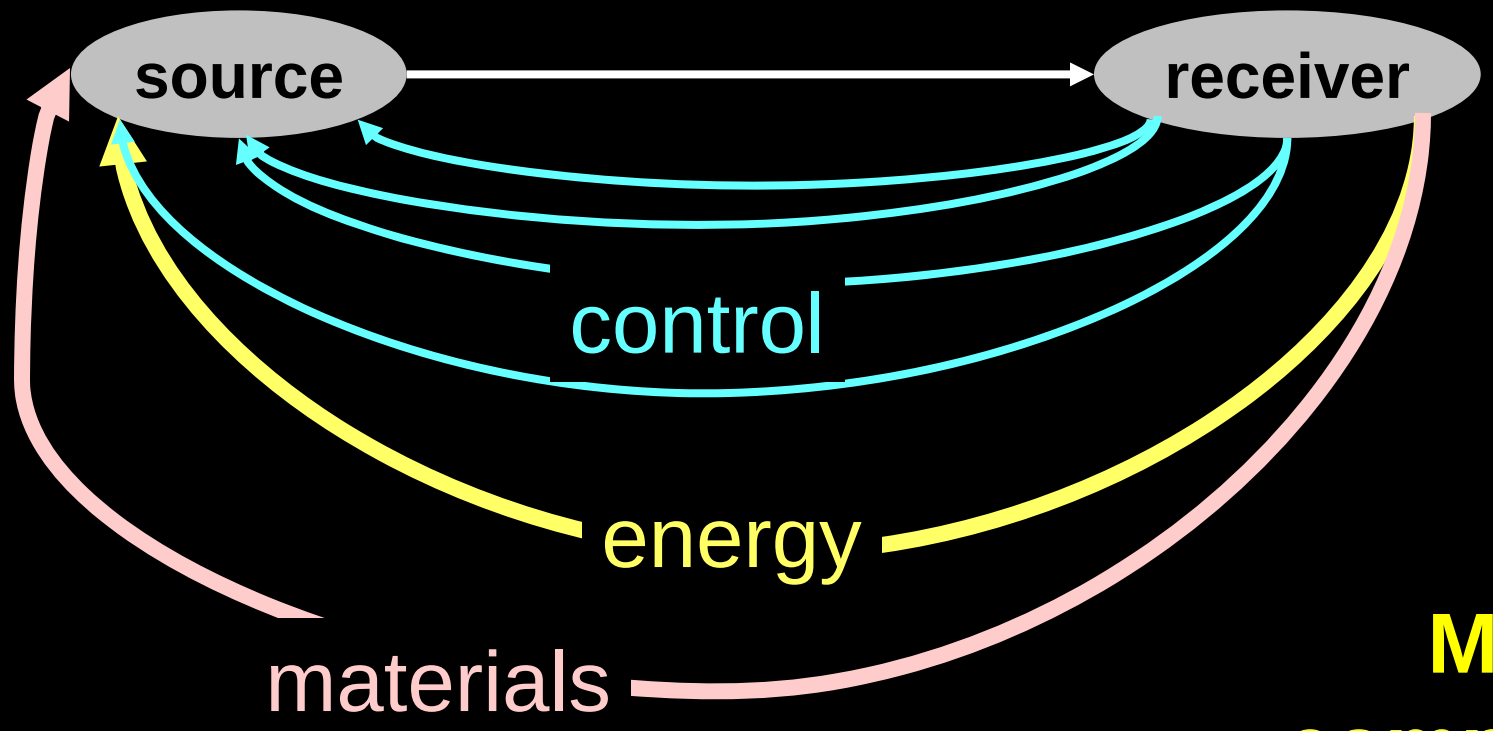
Control of the Internet



signaling
gene expression
metabolism
lineage

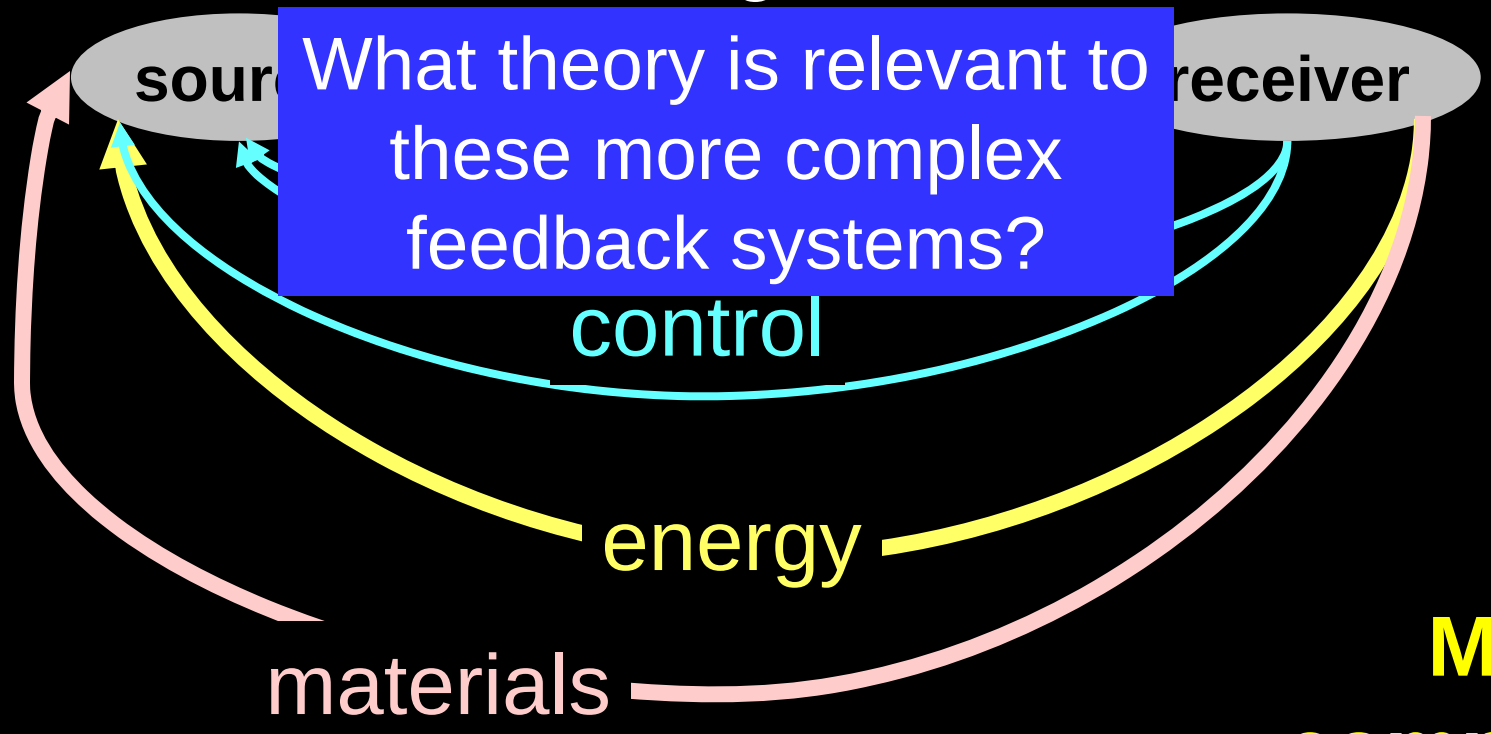
Biological pathways

signaling
gene expression
metabolism
lineage



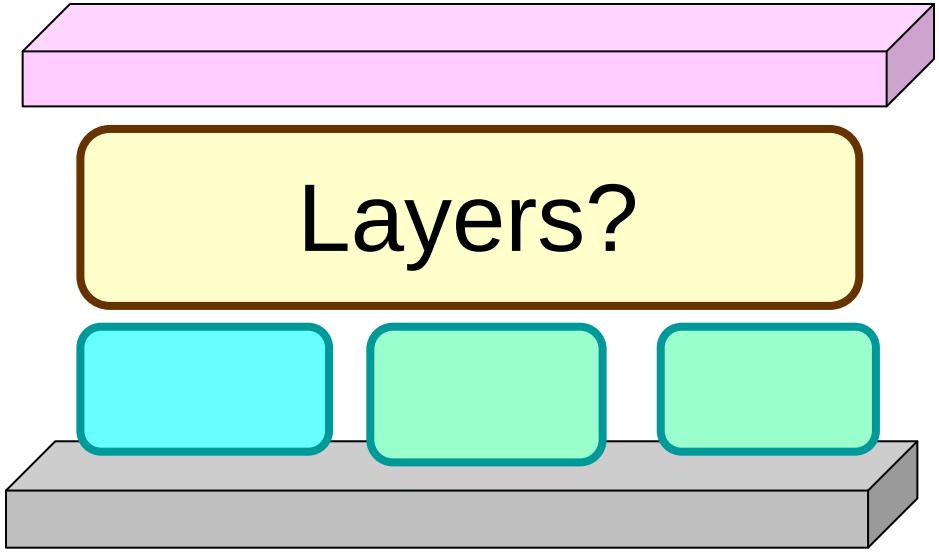
More complex feedback

signaling
gene expression
metabolism
lineage



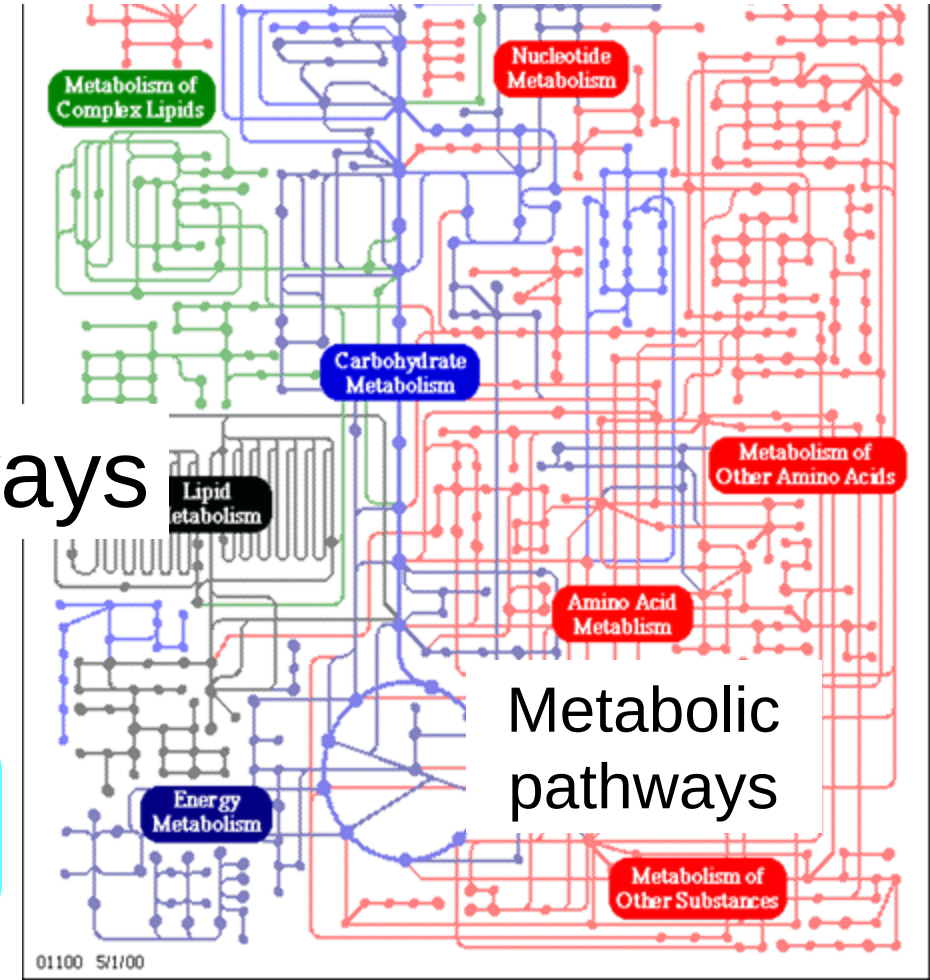
What theory is relevant to these more complex feedback systems?

More complex feedback



Network architecture?

Pathways

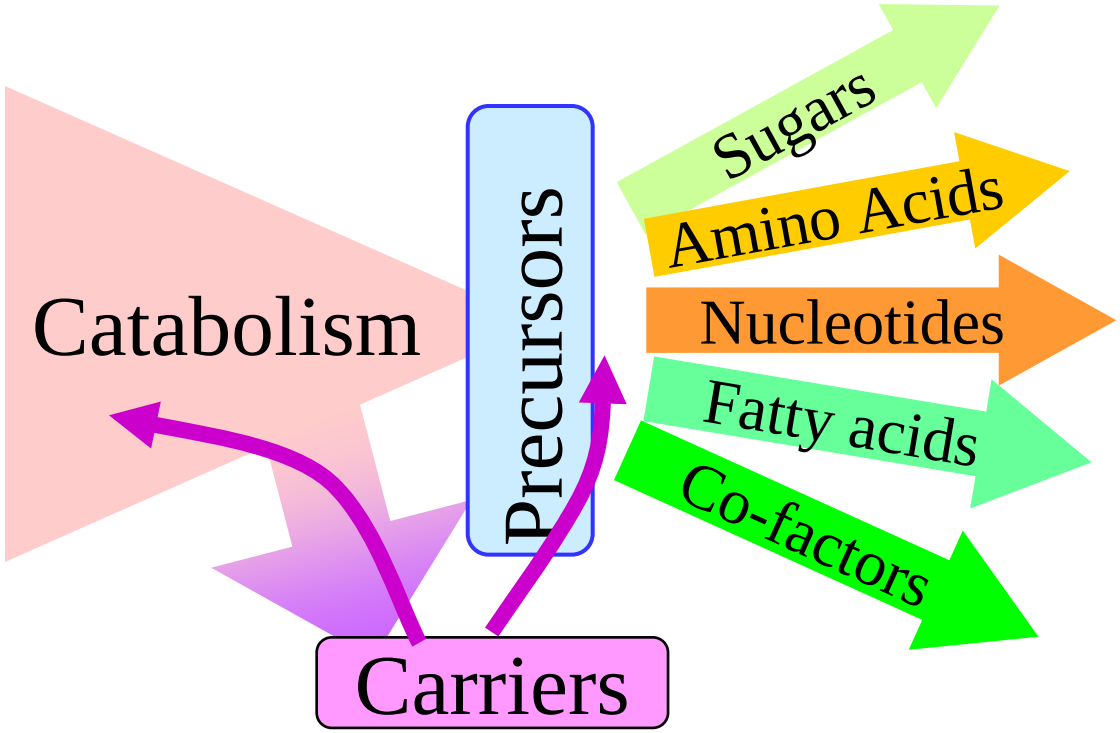


Metabolic pathways

"Central dogma"

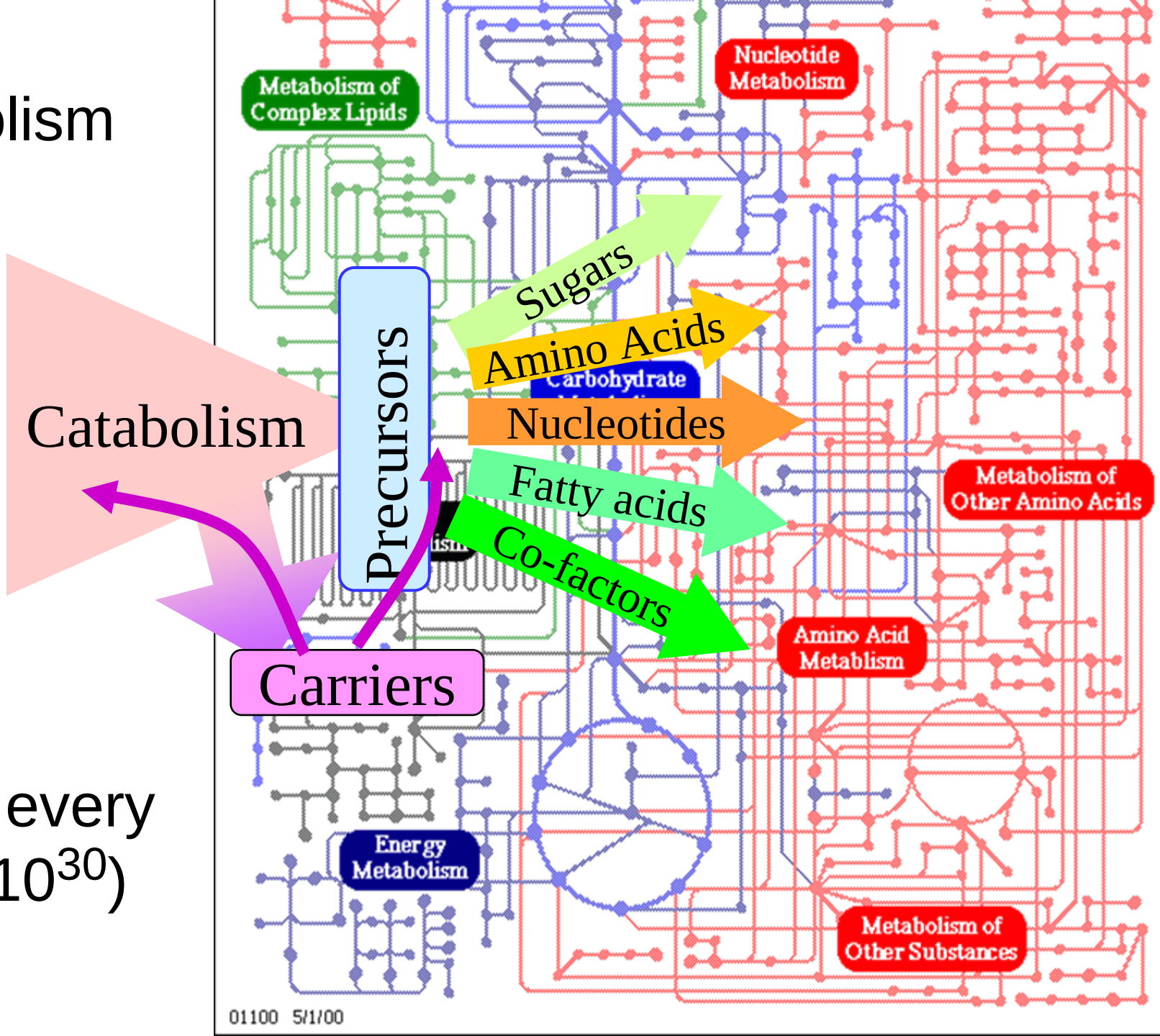
DNA → RNA → Protein

Metabolism



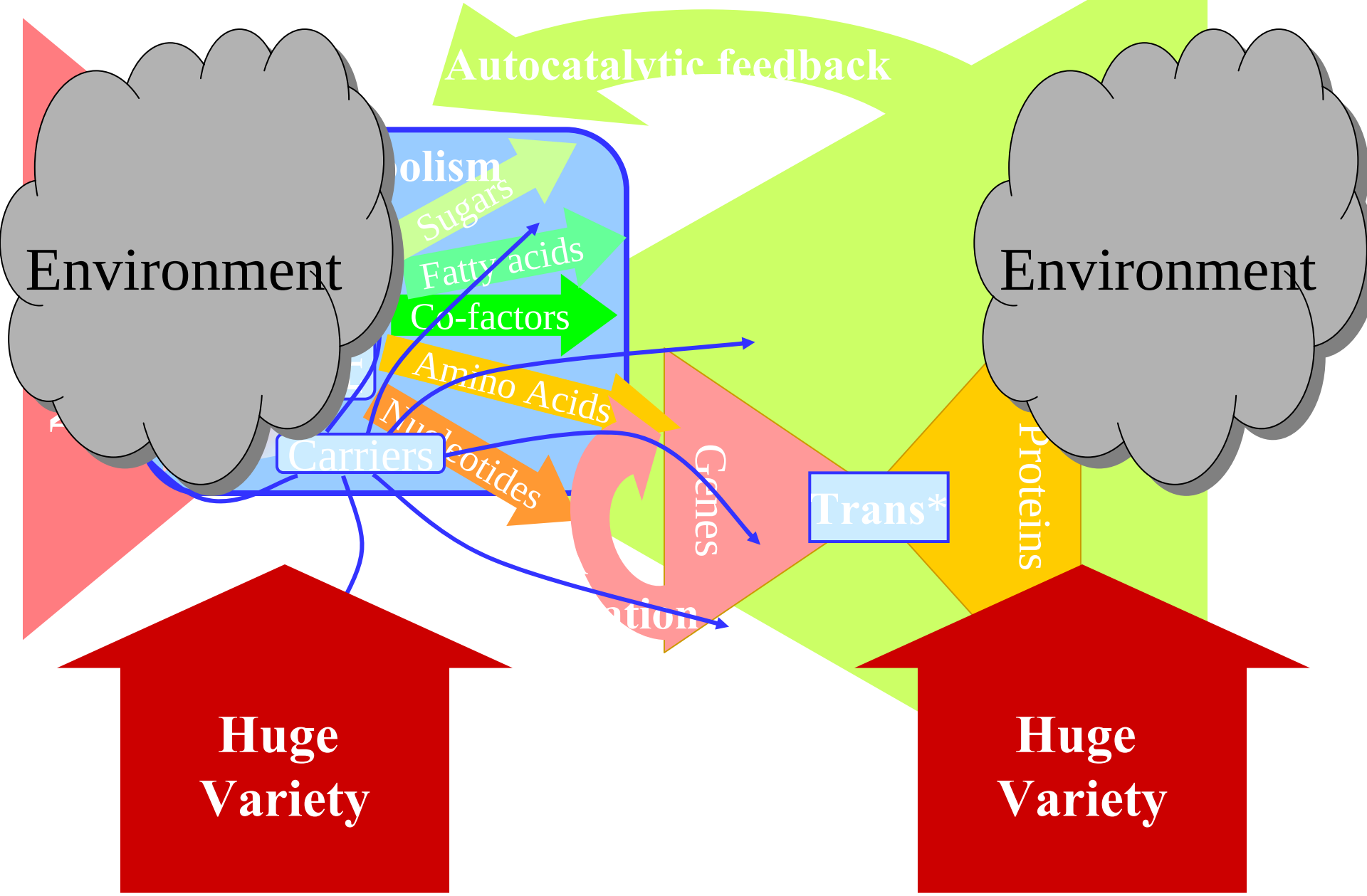
energy
materials

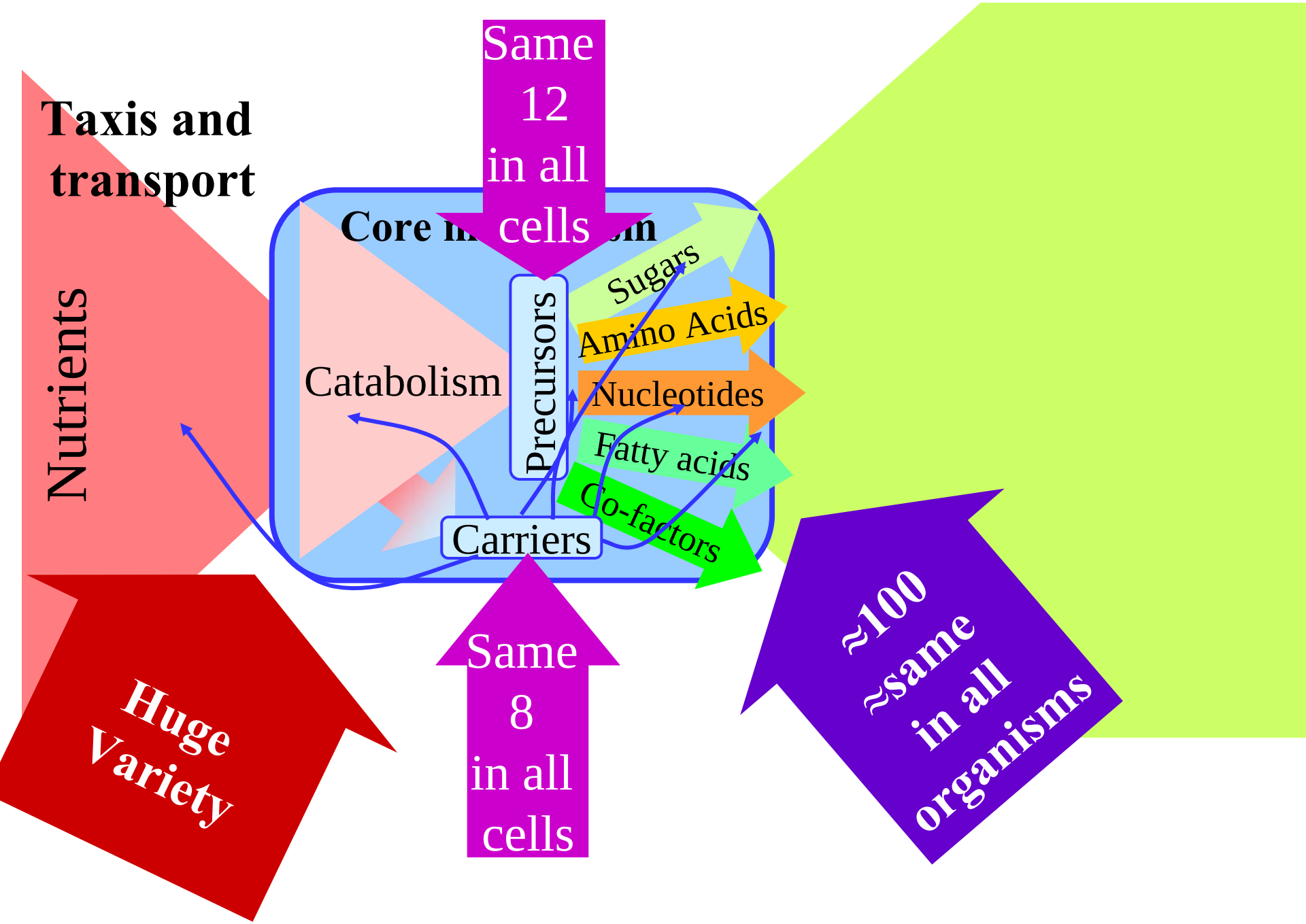
Core metabolism

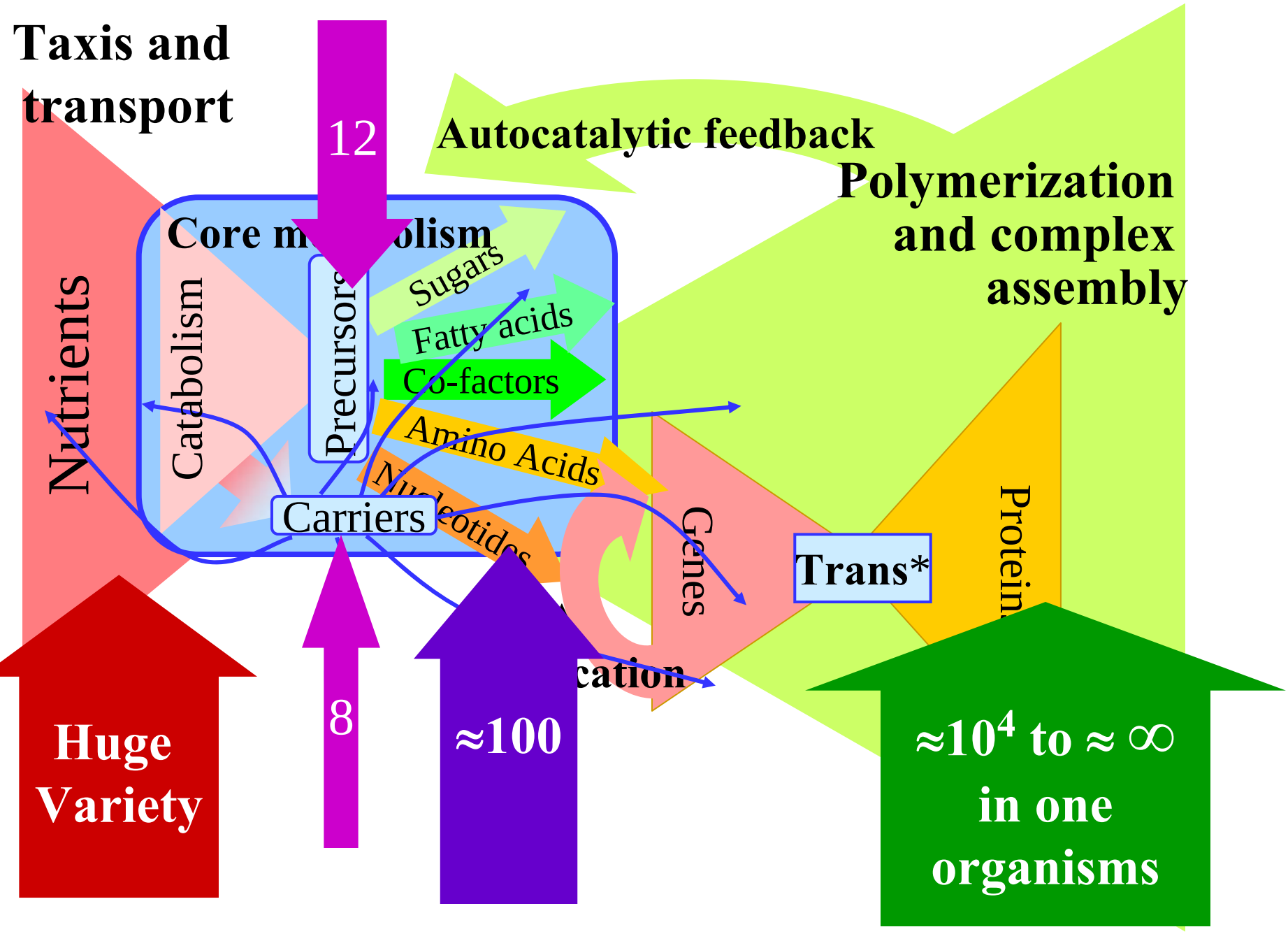


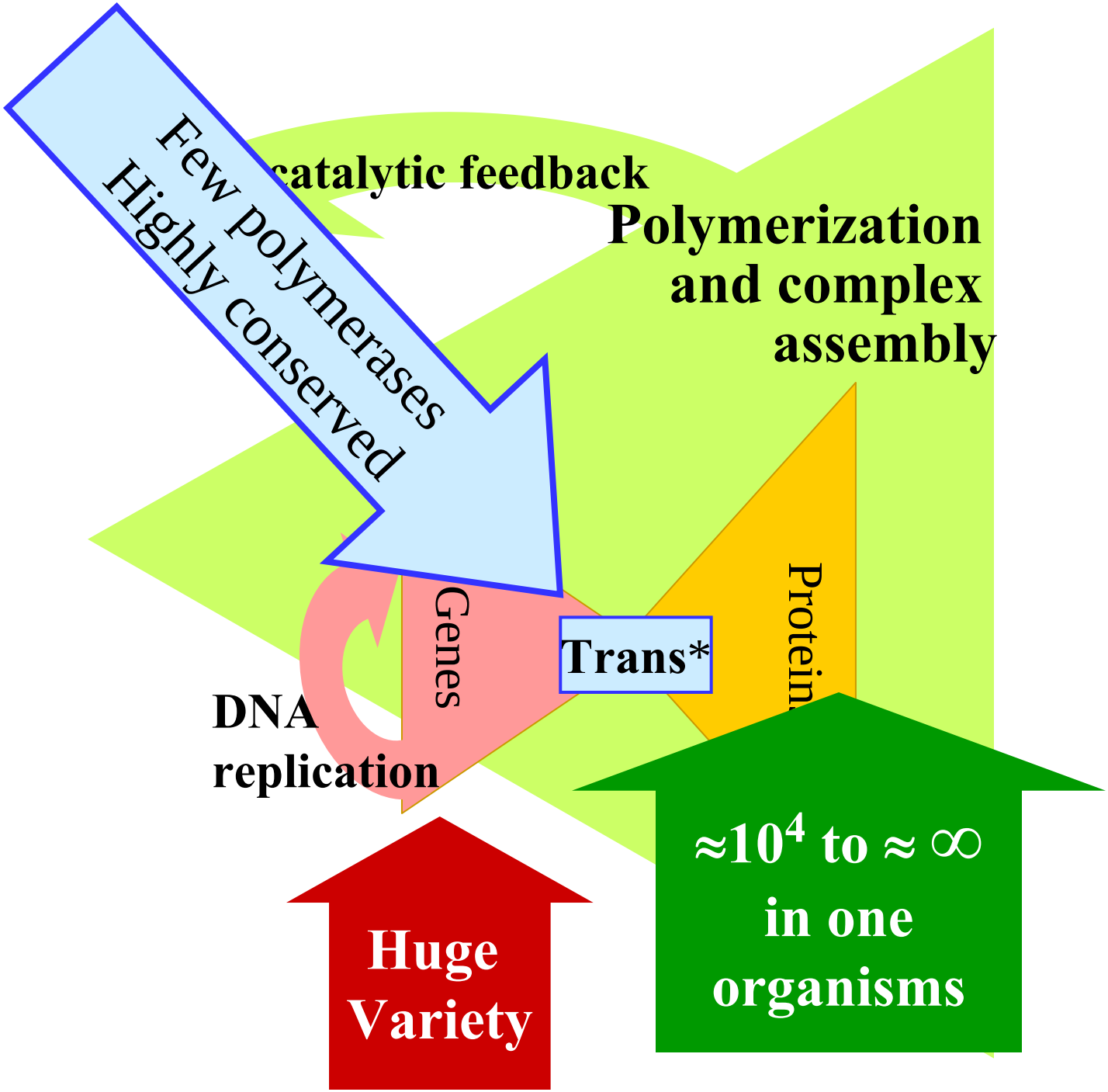
Inside every cell ($\approx 10^{30}$)

Bacterial cell

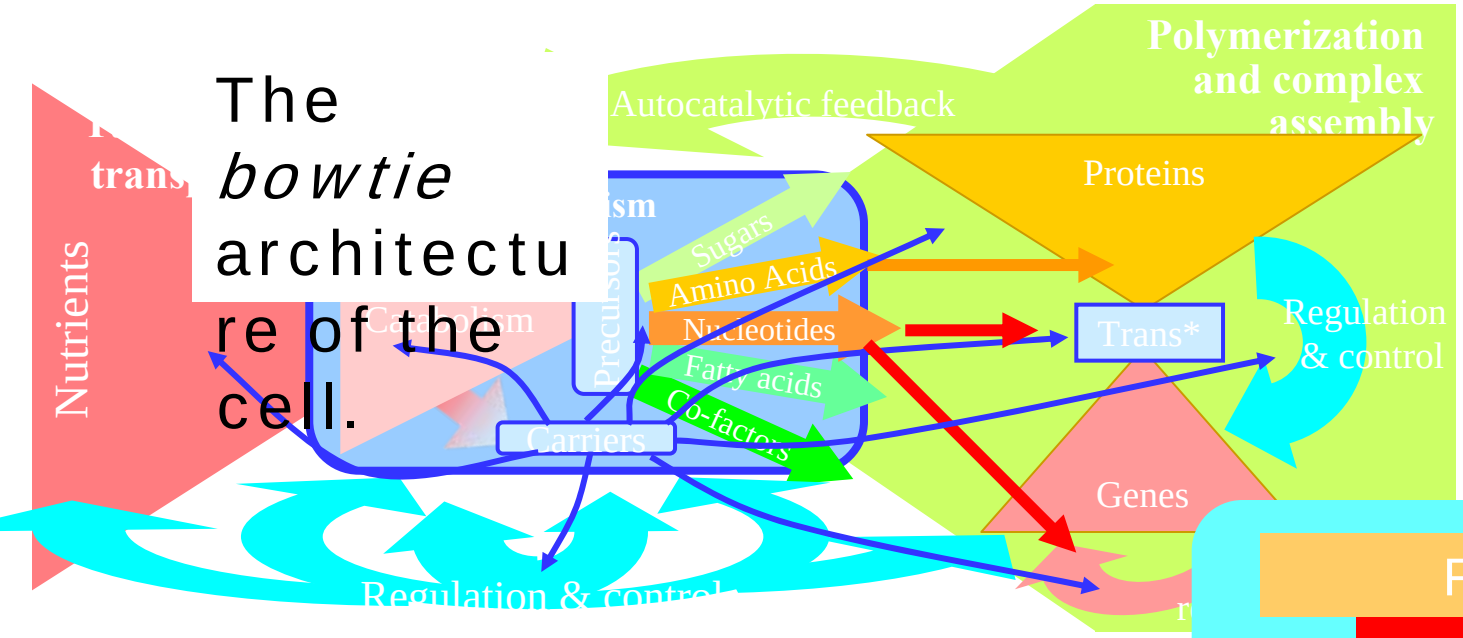



Taxis and transport
Nutrients
Same 12 in all cells
Core metabolism
Catabolism
Precursors
Sugars
Amino Acids
Nucleotides
Fatty acids
Co-factors
Carriers
Huge Variety
Same 8 in all cells
≈100 ≈same in all organisms


Taxis and transport
12
Autocatalytic feedback
Polymerization and complex assembly
Core m olism
Nutrients
Catabolism
Precursors
Sugars
Fatty acids
Co-factors
Amino Acids
Carriers
Genes
Trans*
Protein
cation
Huge Variety
8
≈100
≈10^4 to ≈ ∞ in one organisms

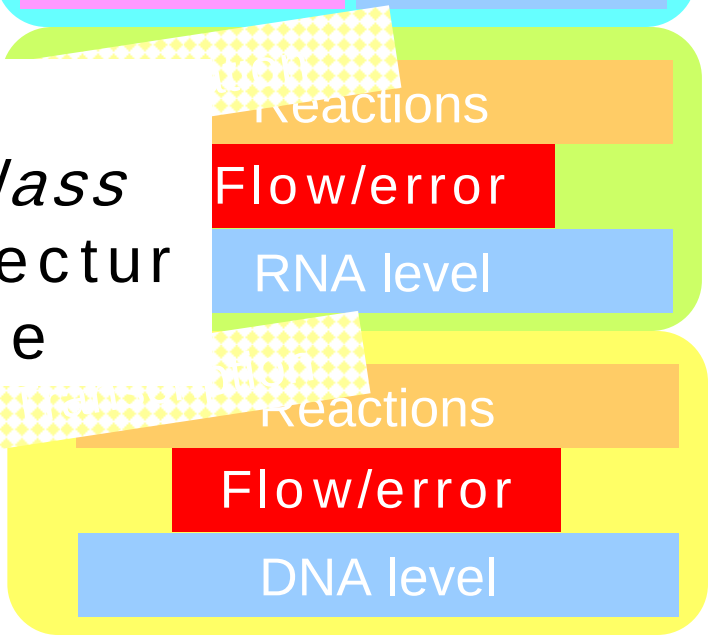

Few polymerases
Highly conserved
catalytic feedback
Polymerization
and complex
assembly
Genes
Trans*
Proteins
DNA
replication
Huge
Variety
≈10^4 to ≈ ∞
in one
organisms

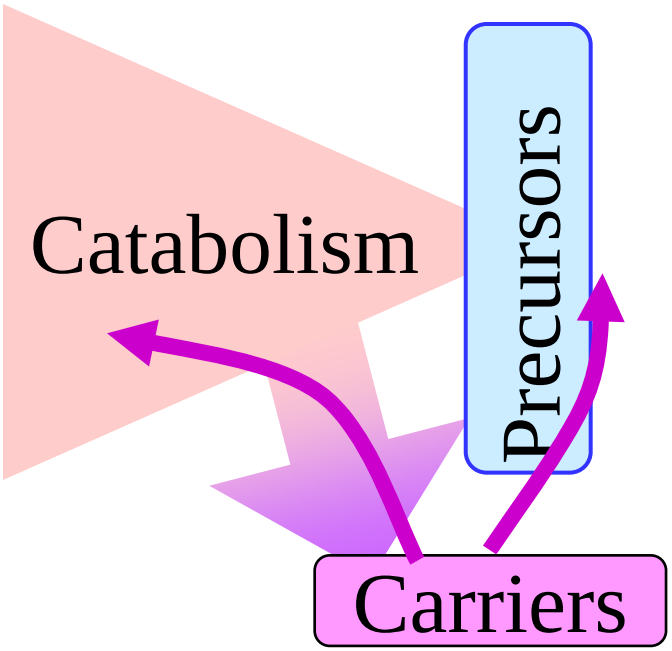
The *bowtie* architecture of the cell.

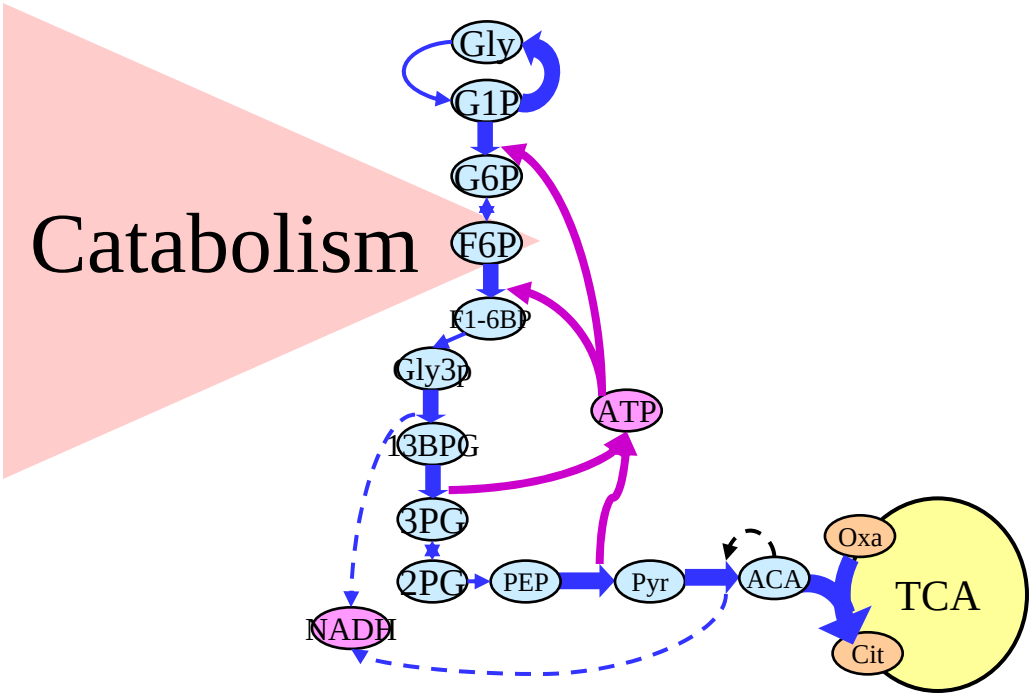


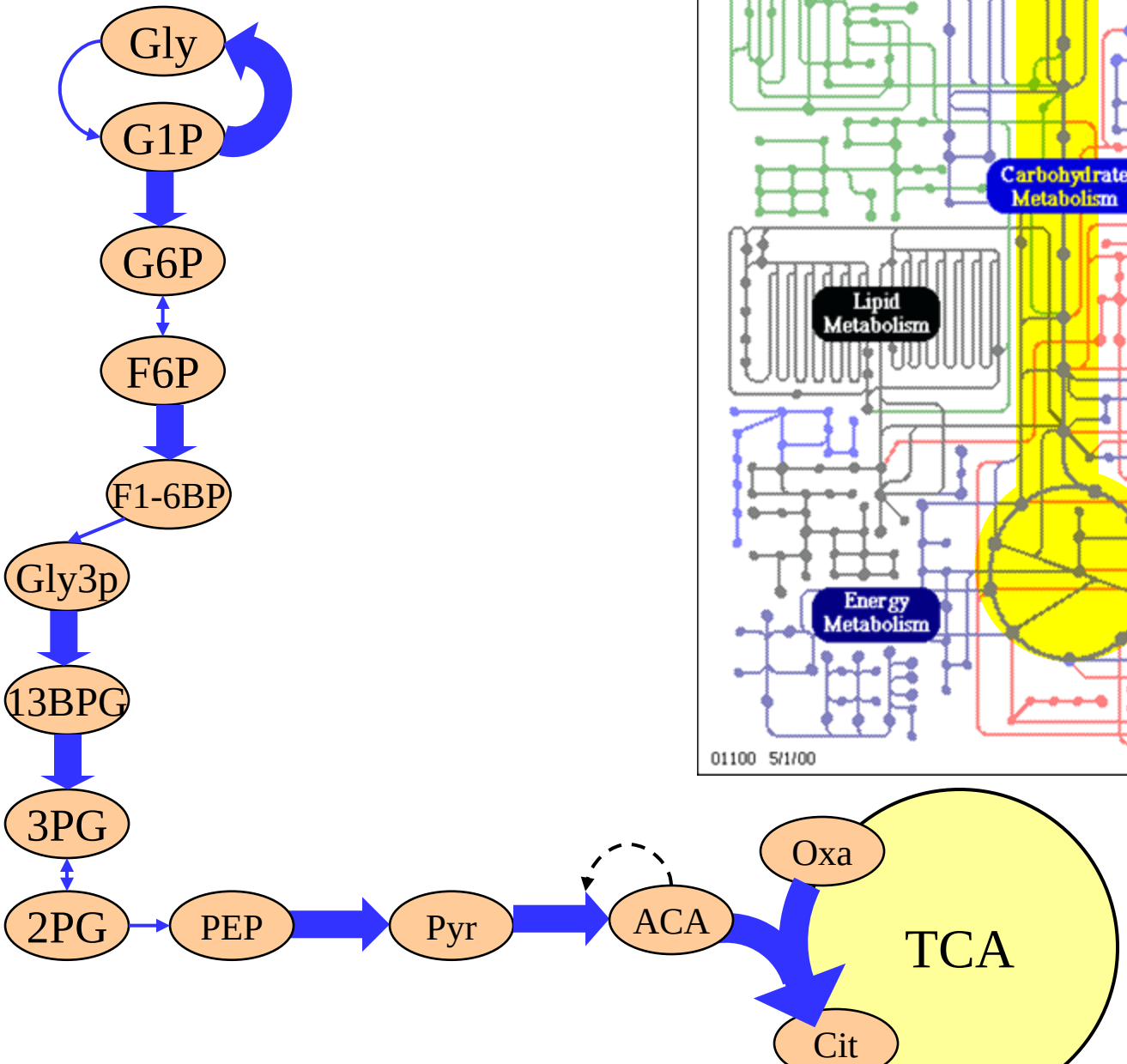
Need a more coherent cartoon to visualize how these fit together.

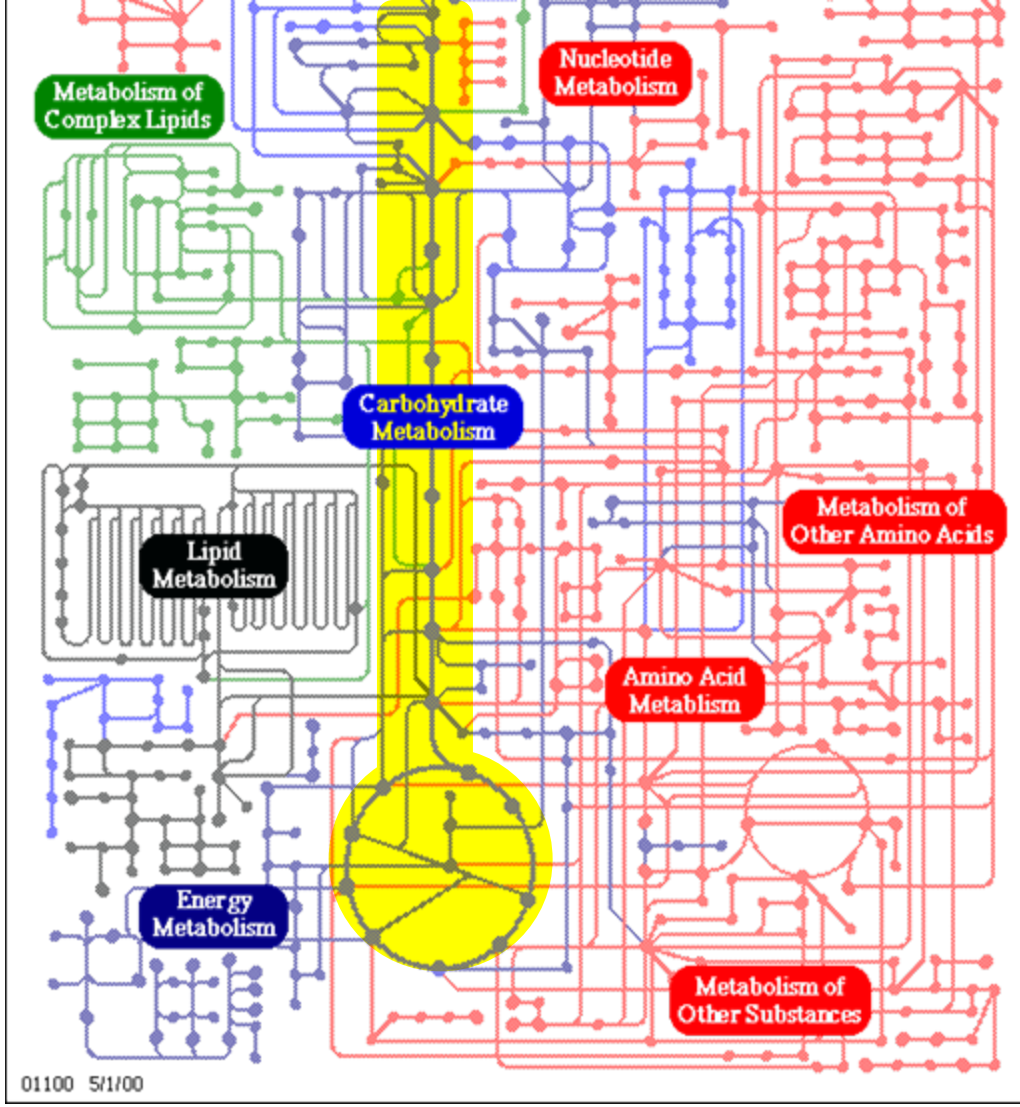
The *hourglass* architecture of the cell.

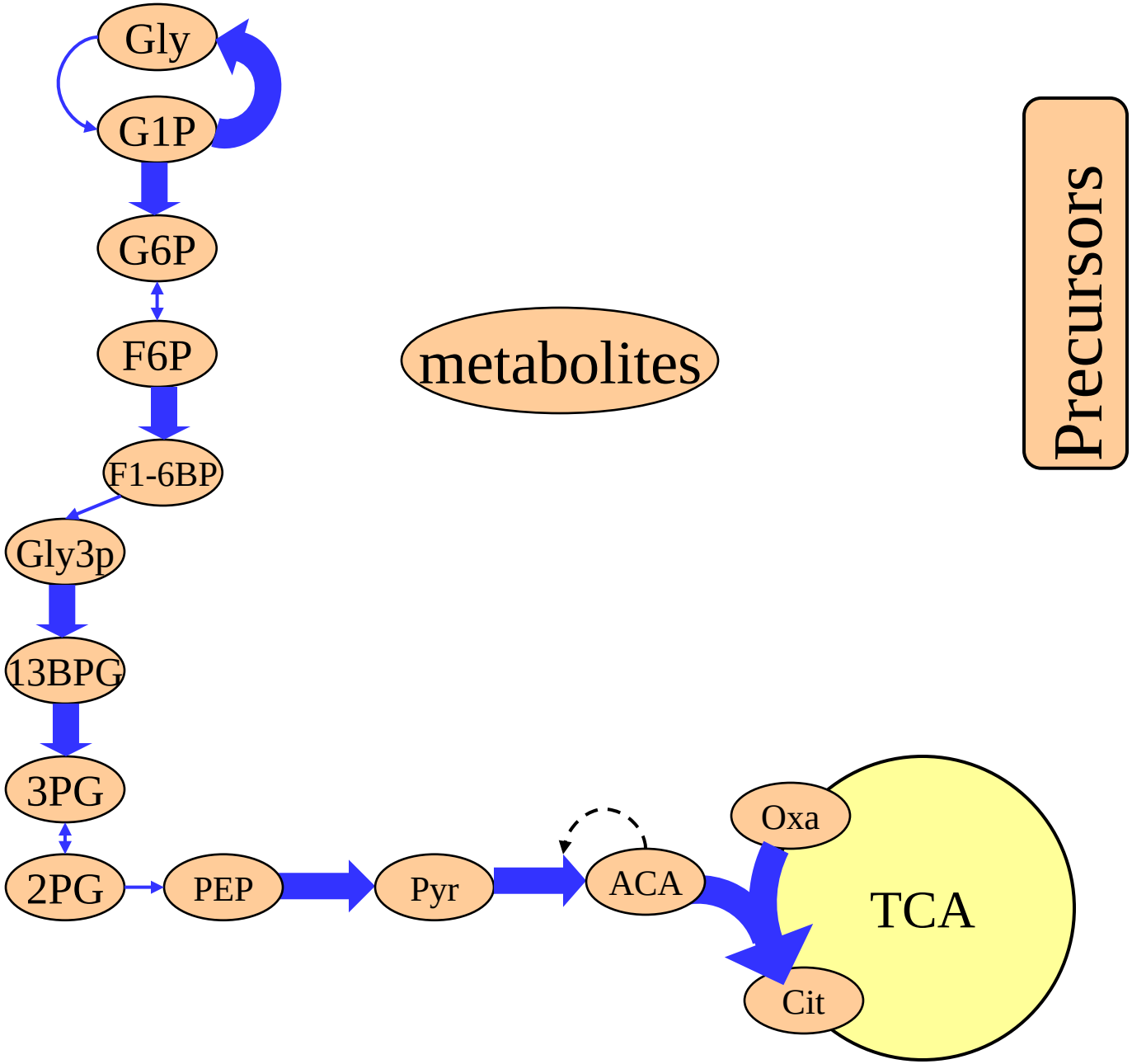



Catabolism
Precursors
Carriers

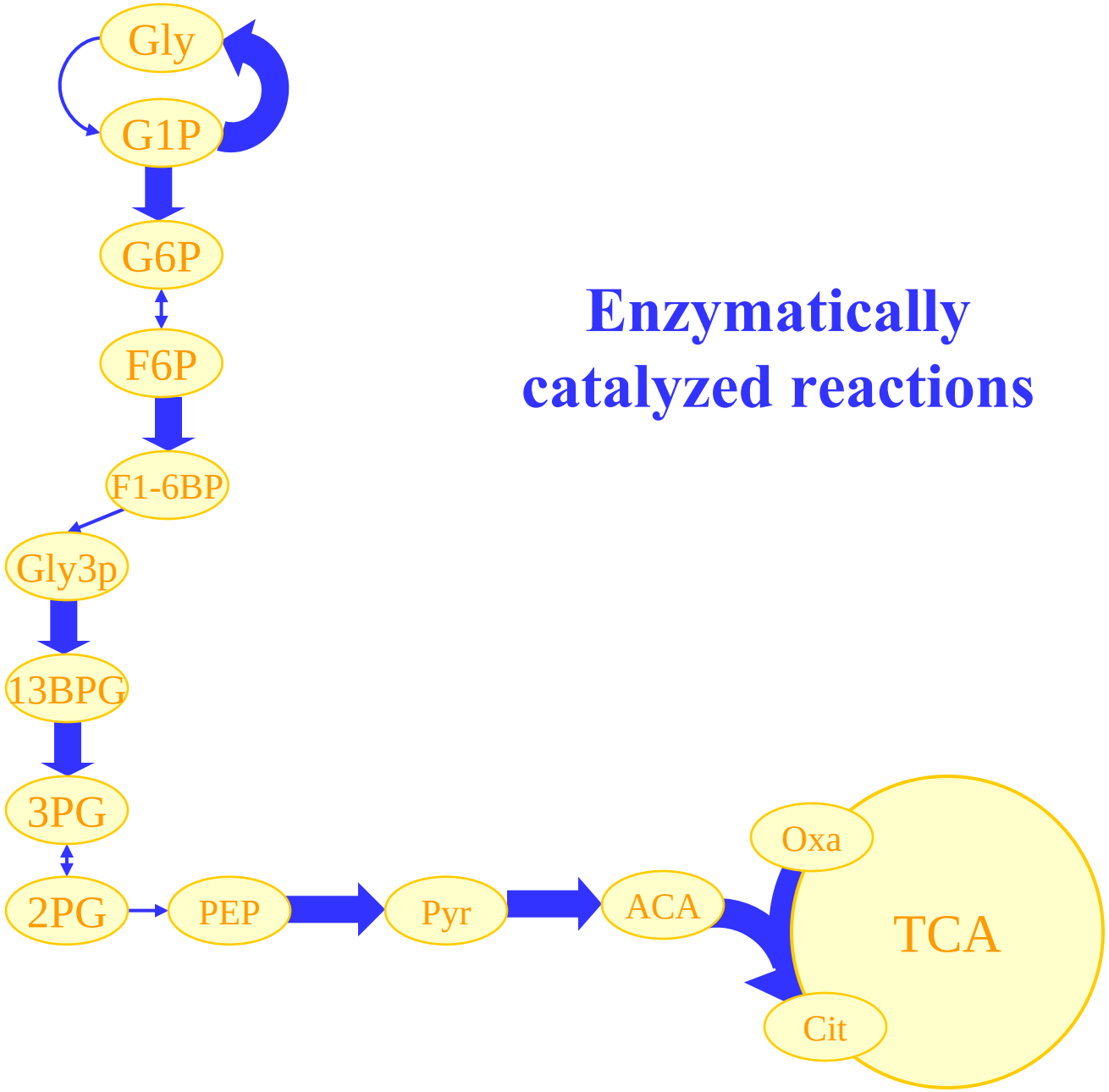

Catabolism
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
Cit
TCA

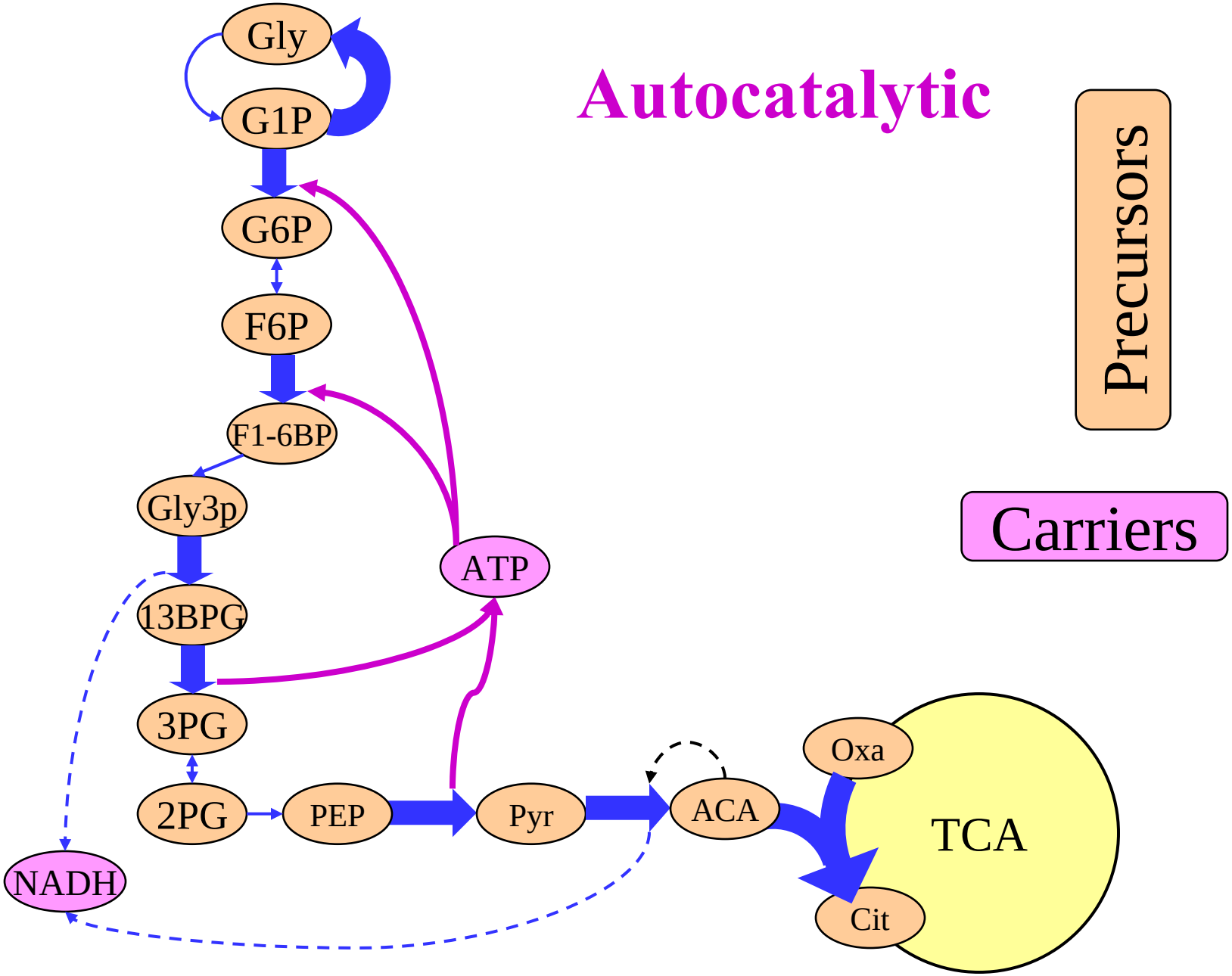

Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit

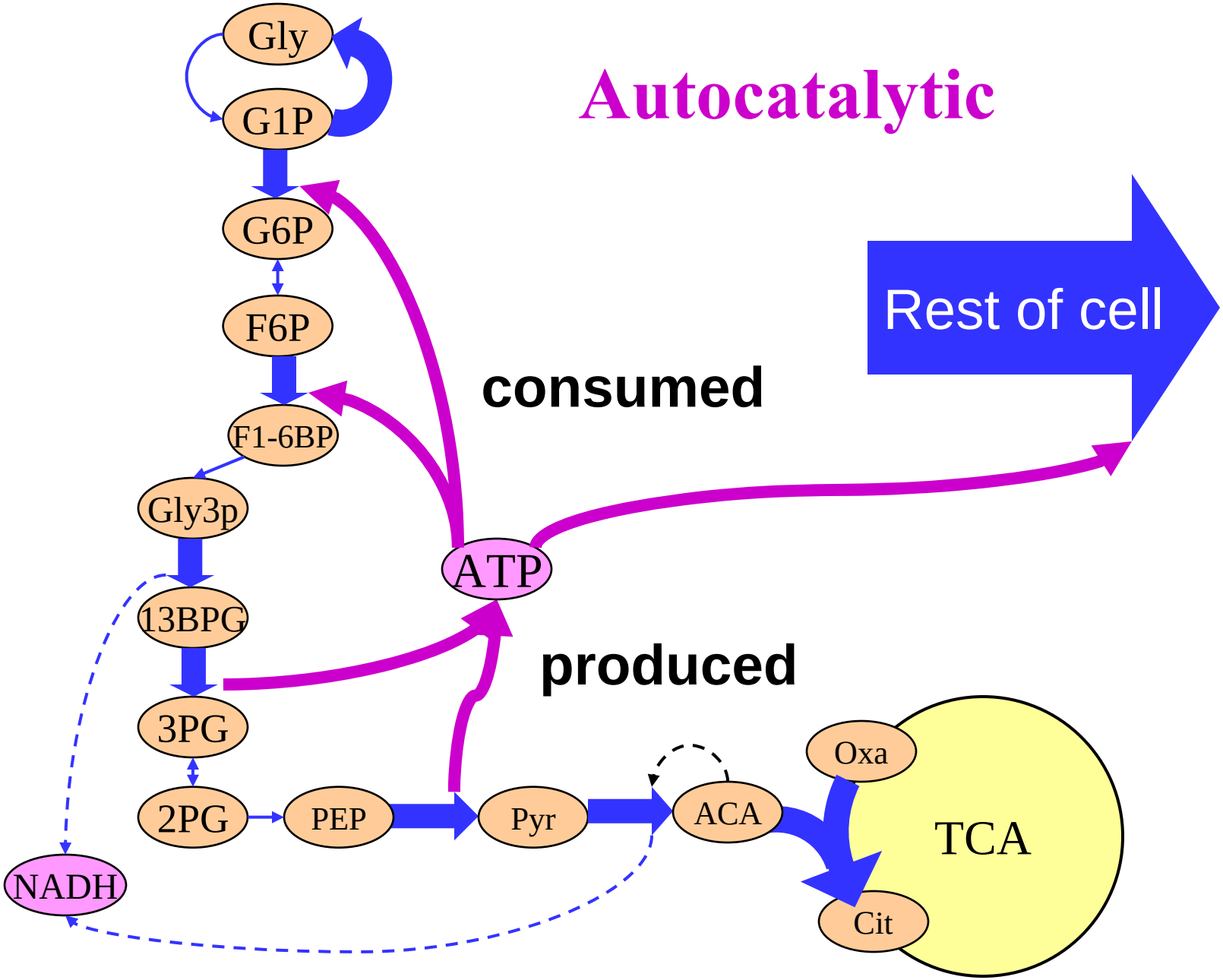

Metabolism of Complex Lipids
Nucleotide Metabolism
Carbohydrate Metabolism
Lipid Metabolism
Metabolism of Other Amino Acids
Amino Acid Metablism
Energy Metabolism
Metabolism of Other Substances
01100 5/1/00

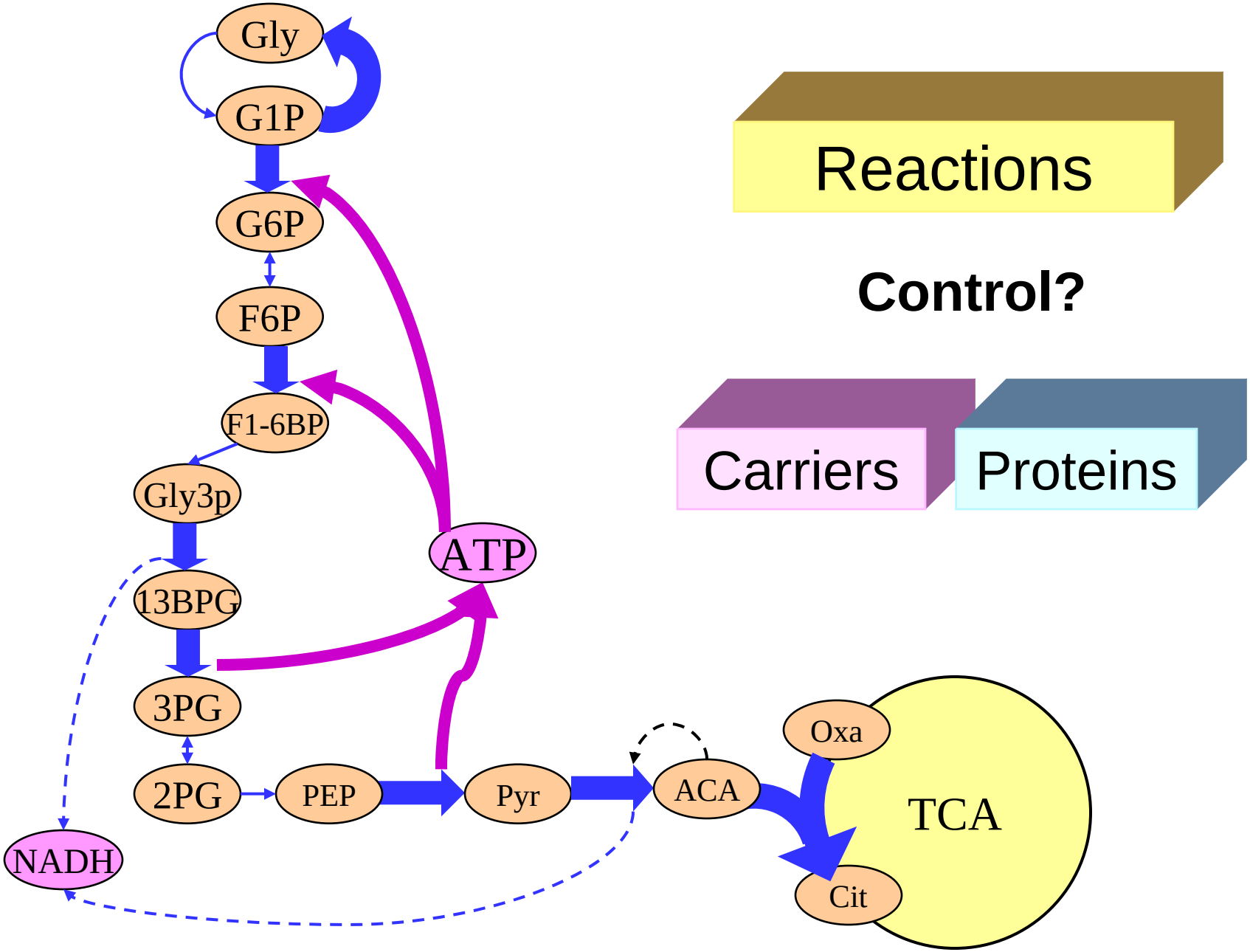

Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
Cit
TCA
metabolites
Precursors

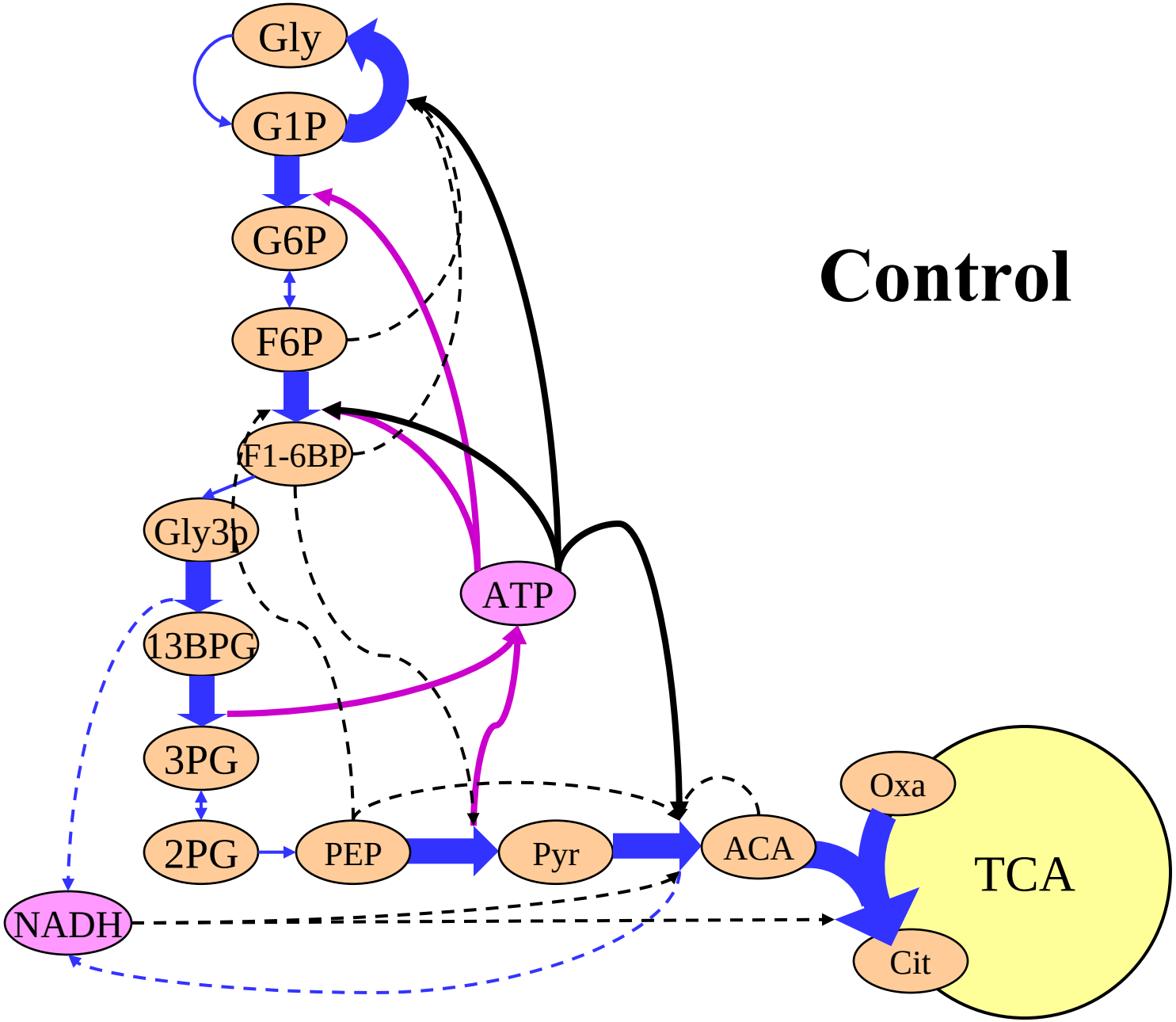
Enzymatically catalyzed reactions

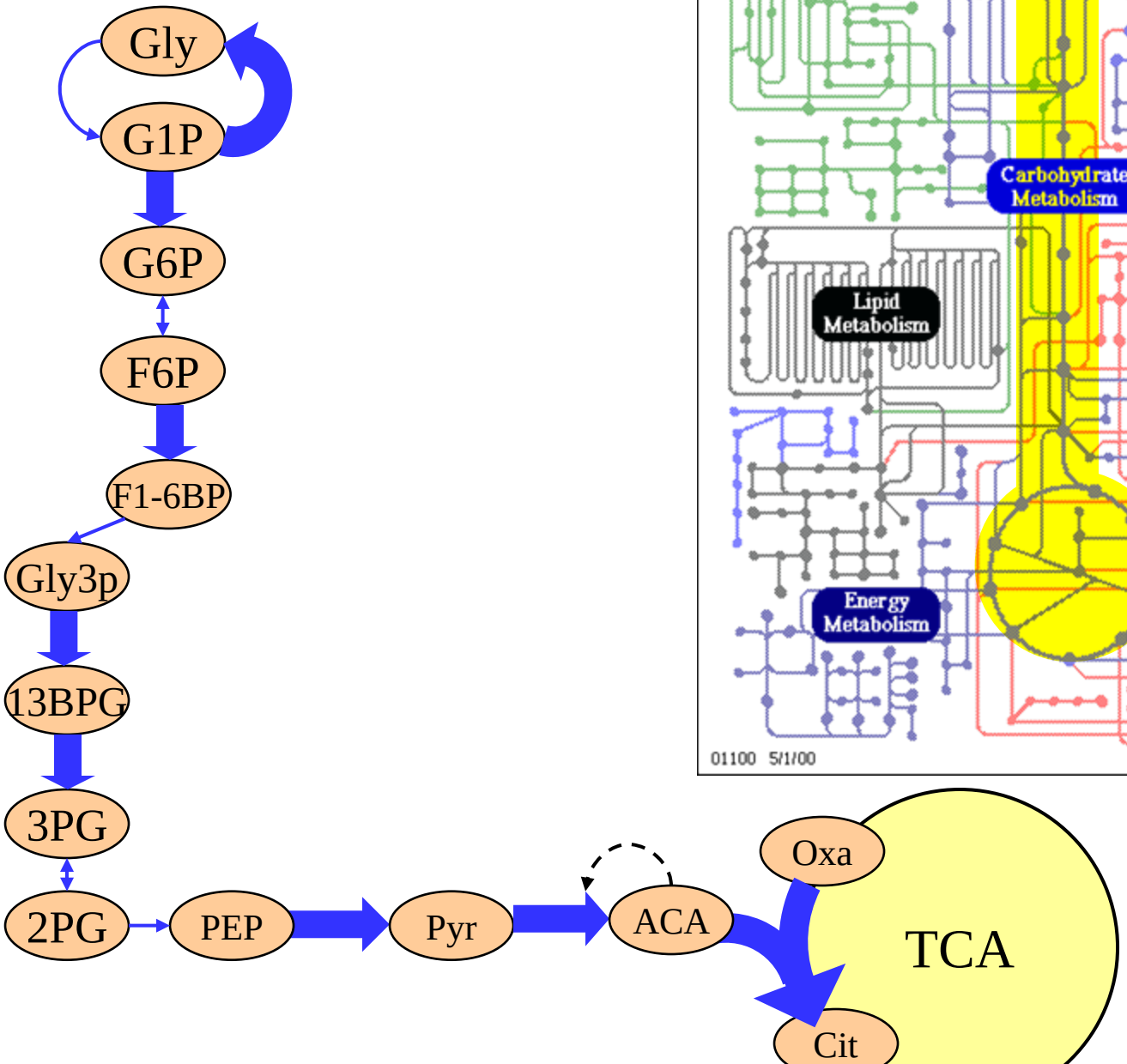


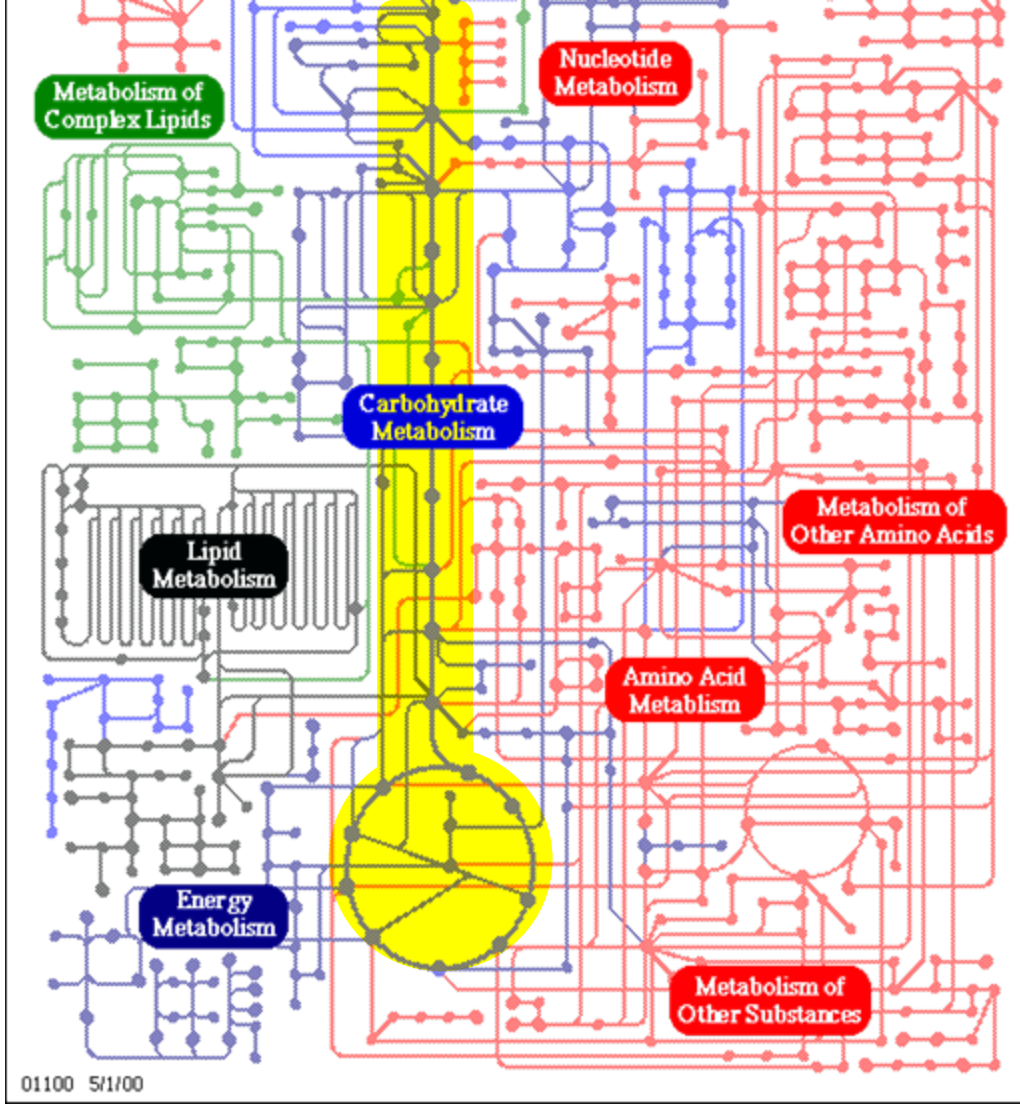

Autocatalytic
Precursors
Carriers
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
Cit
TCA


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

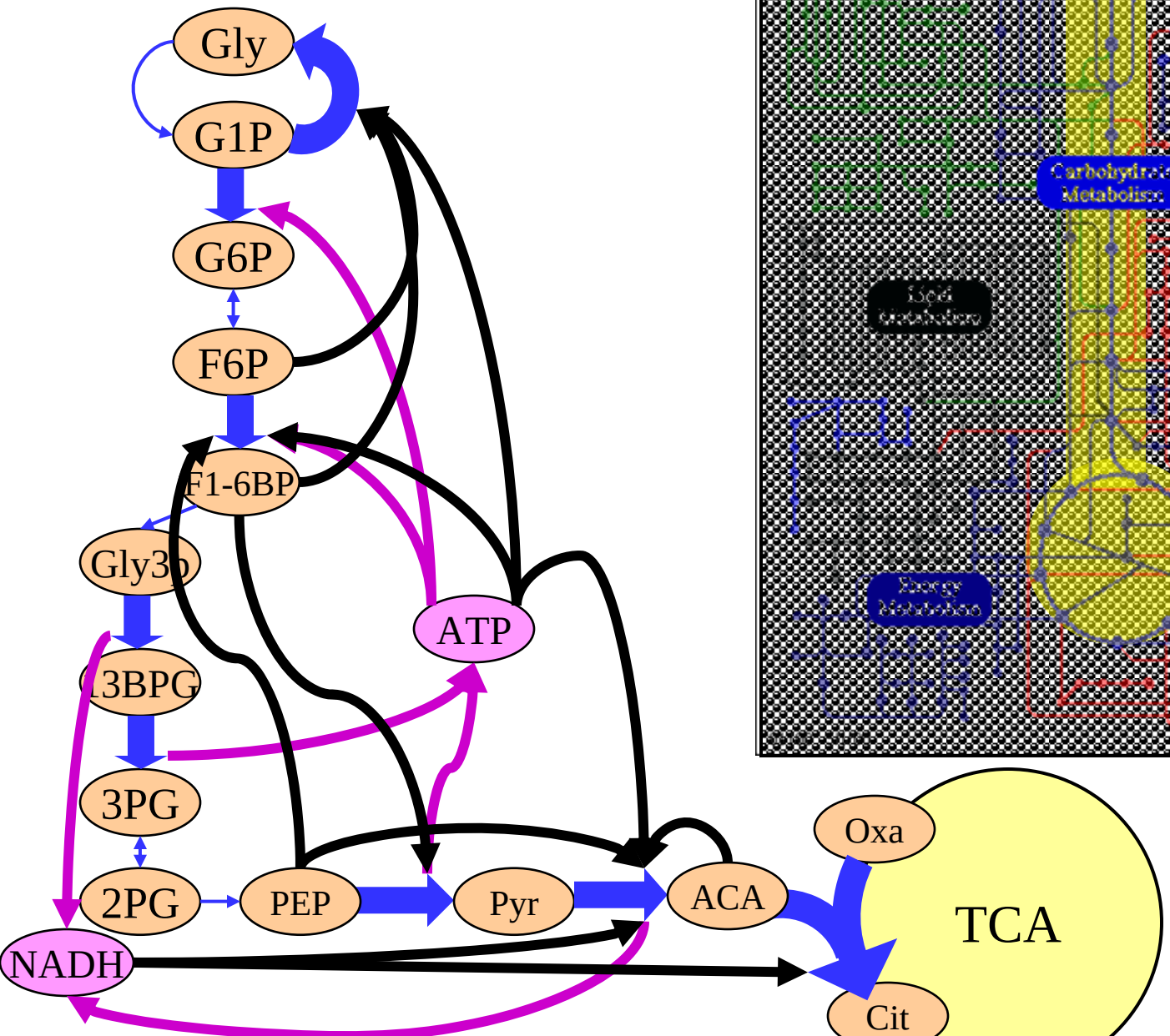

Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit
NADH
ATP
Reactions
Control?
Carriers
Proteins

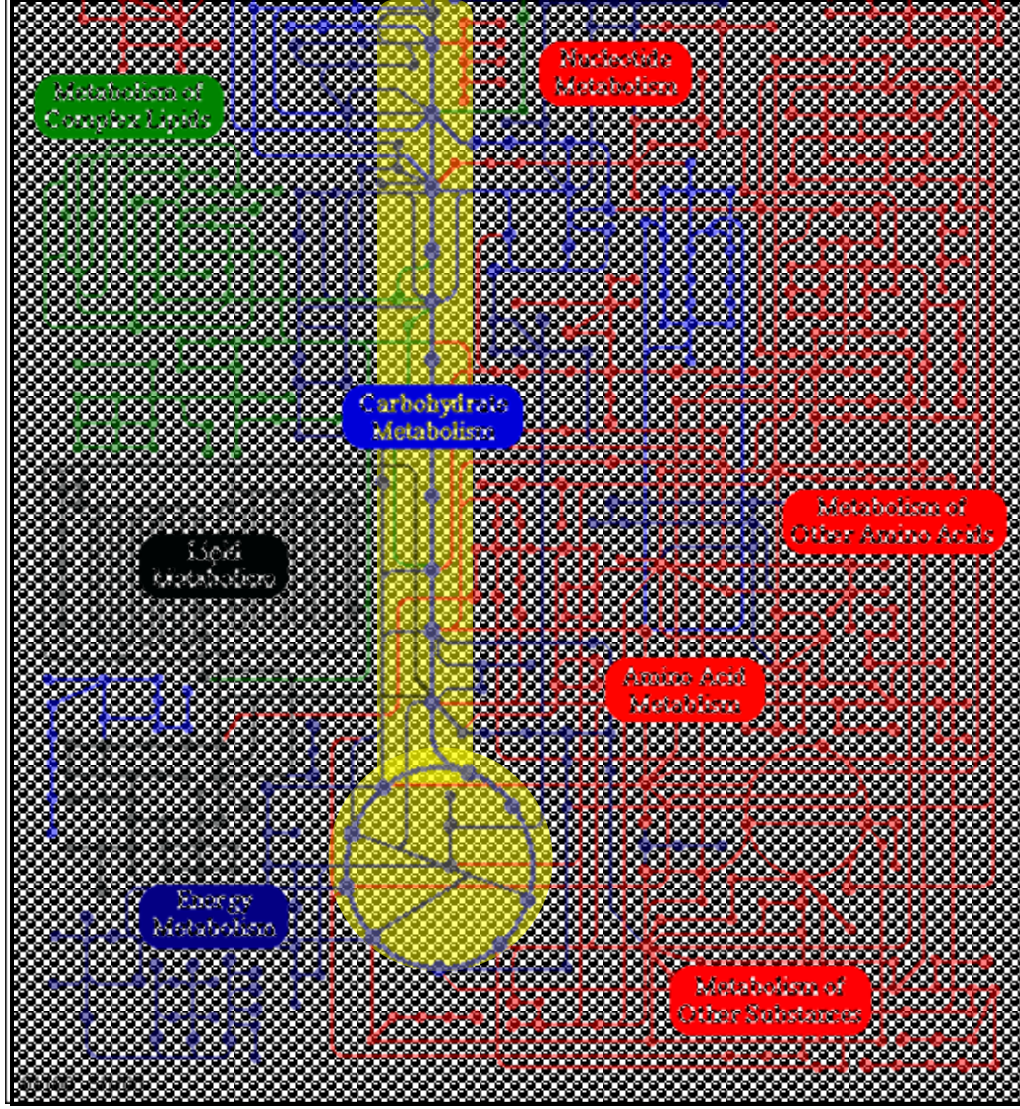

Control
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
Cit
TCA

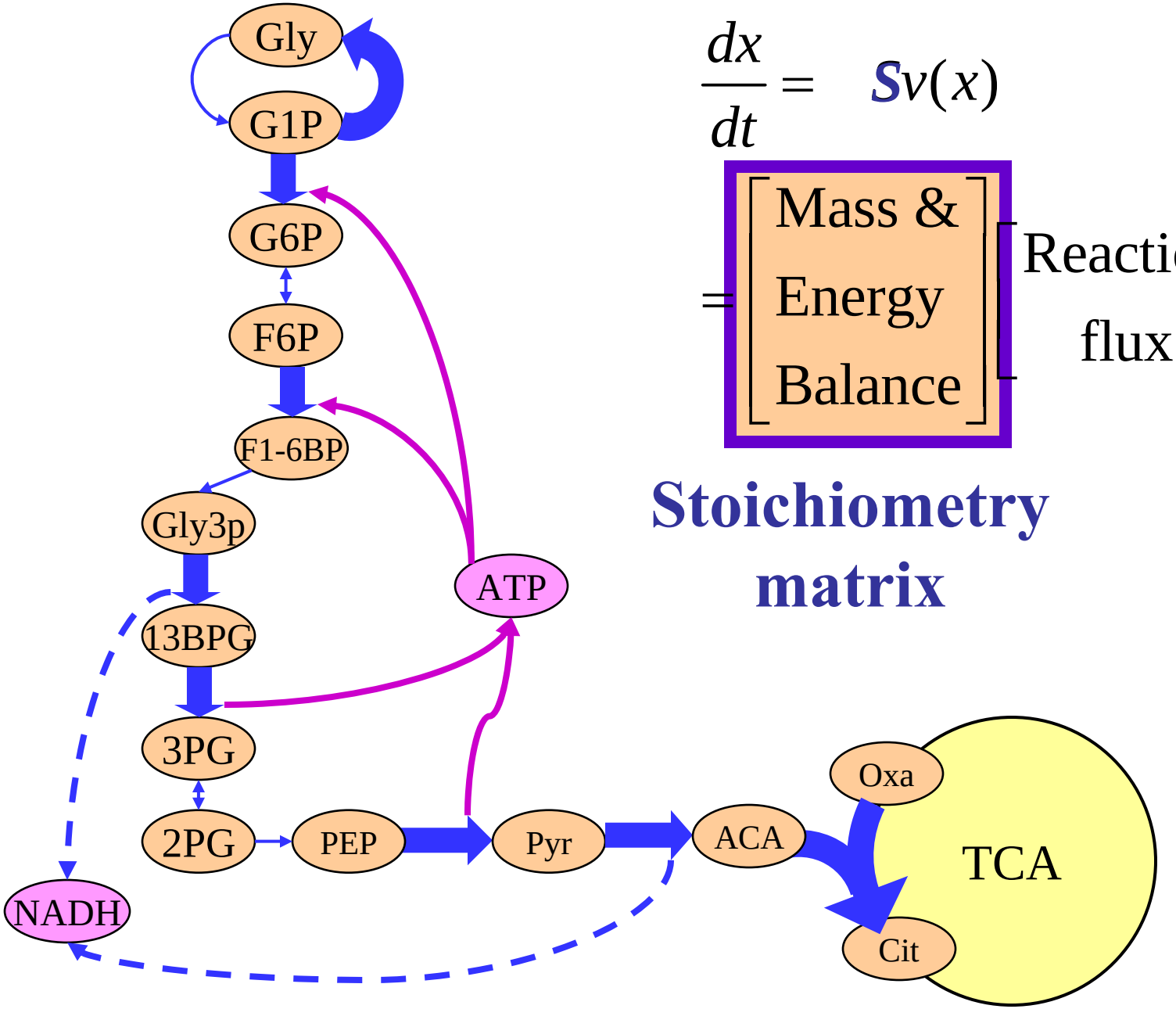

Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit


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

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



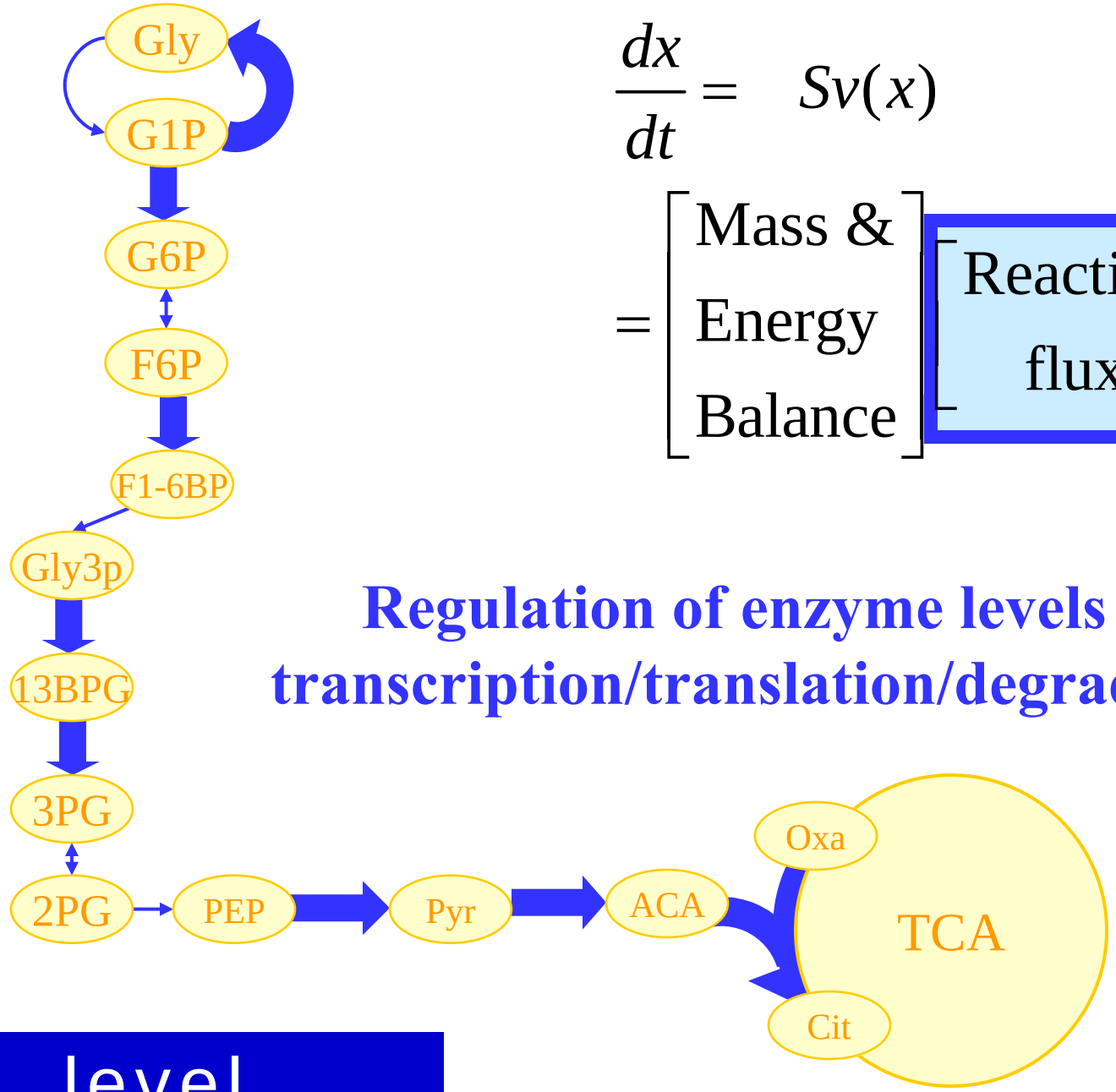




$$\frac{dx}{dt} = \boldsymbol{S}v(x)$$

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

Stoichiometry matrix

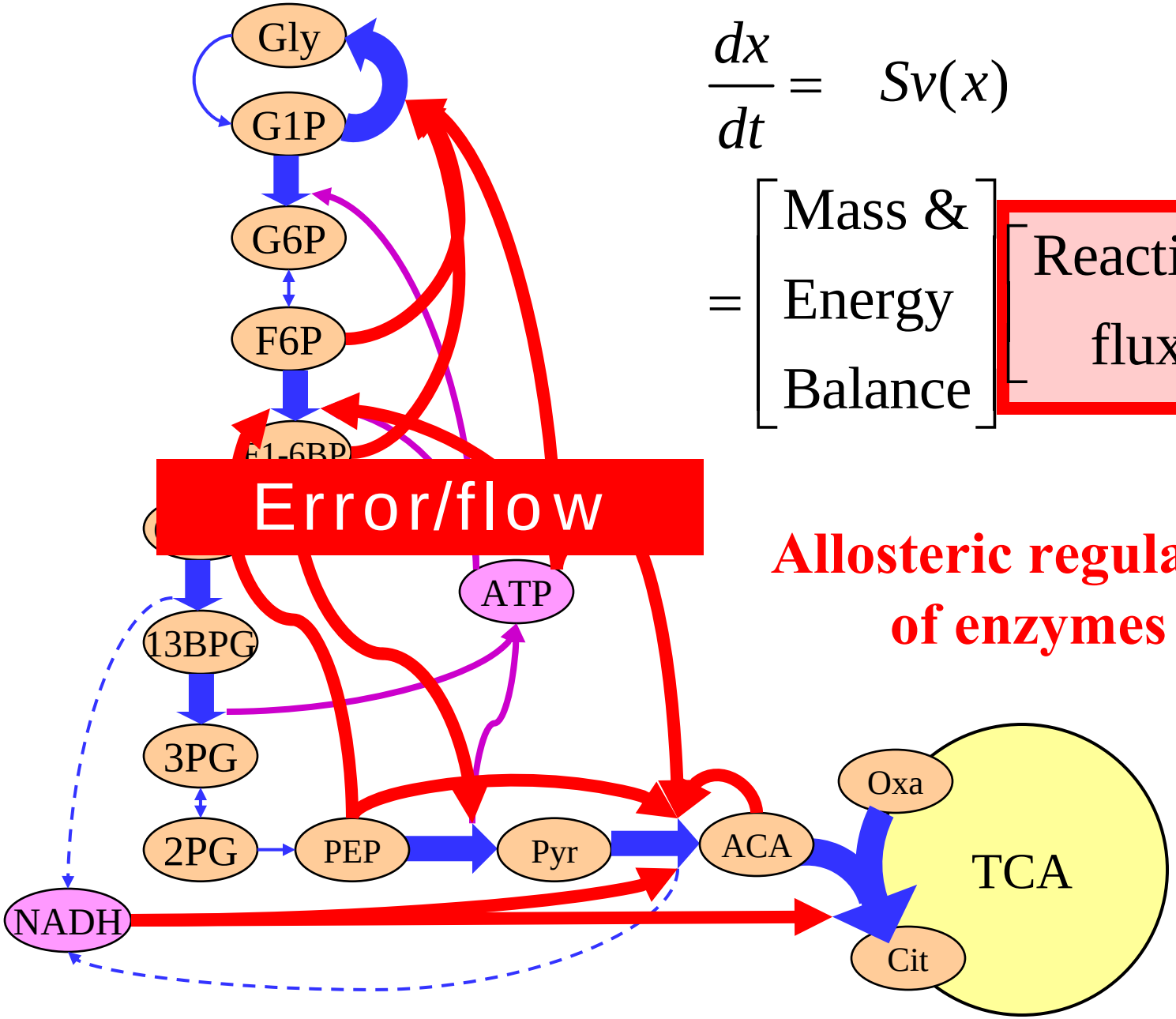


$$\frac{dx}{dt} = Sv(x)$$

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

Regulation of enzyme levels by transcription/translation/degradation

level

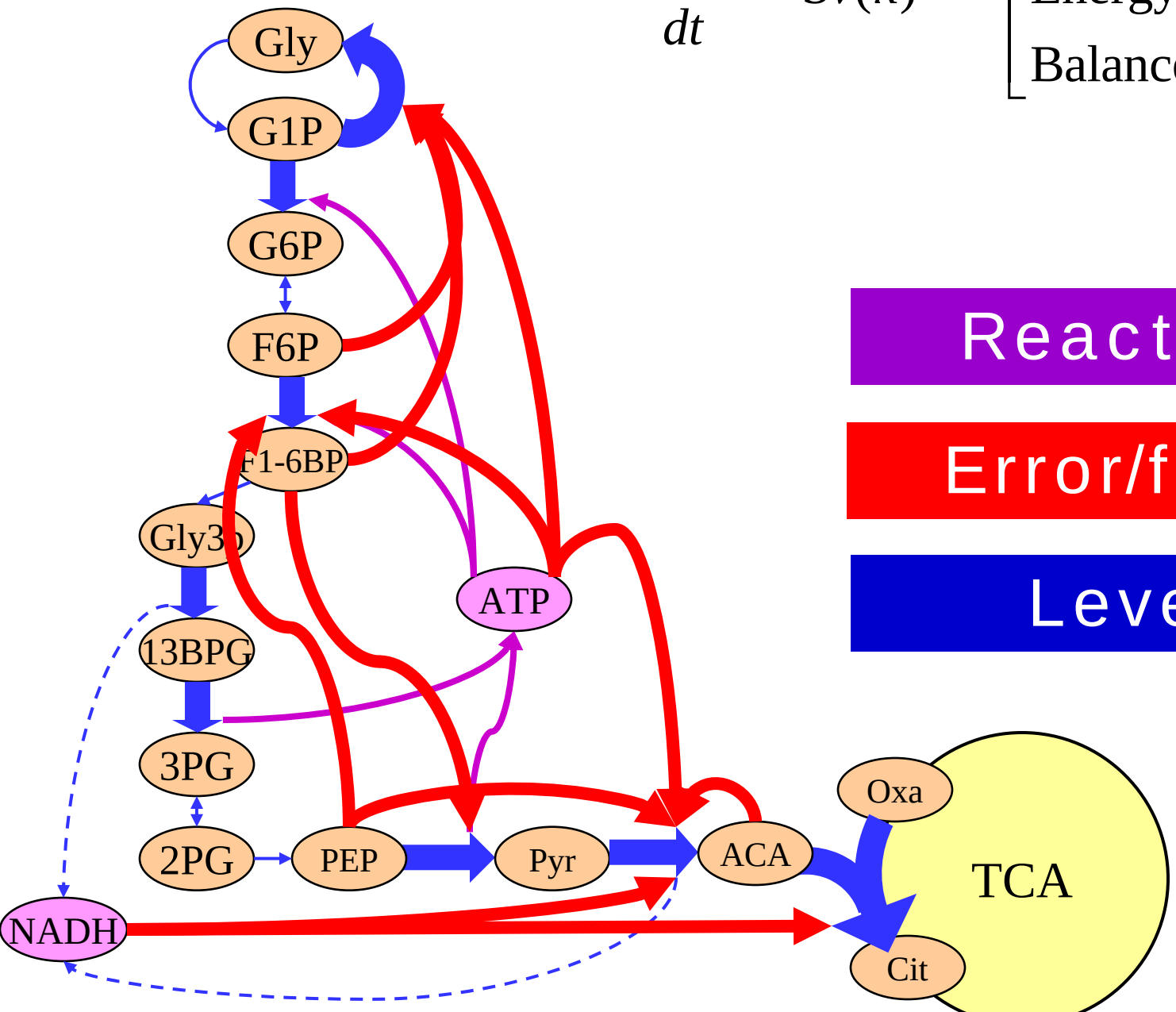


$$\frac{dx}{dt} = Sv(x)$$

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

Allosteric regulation of enzymes

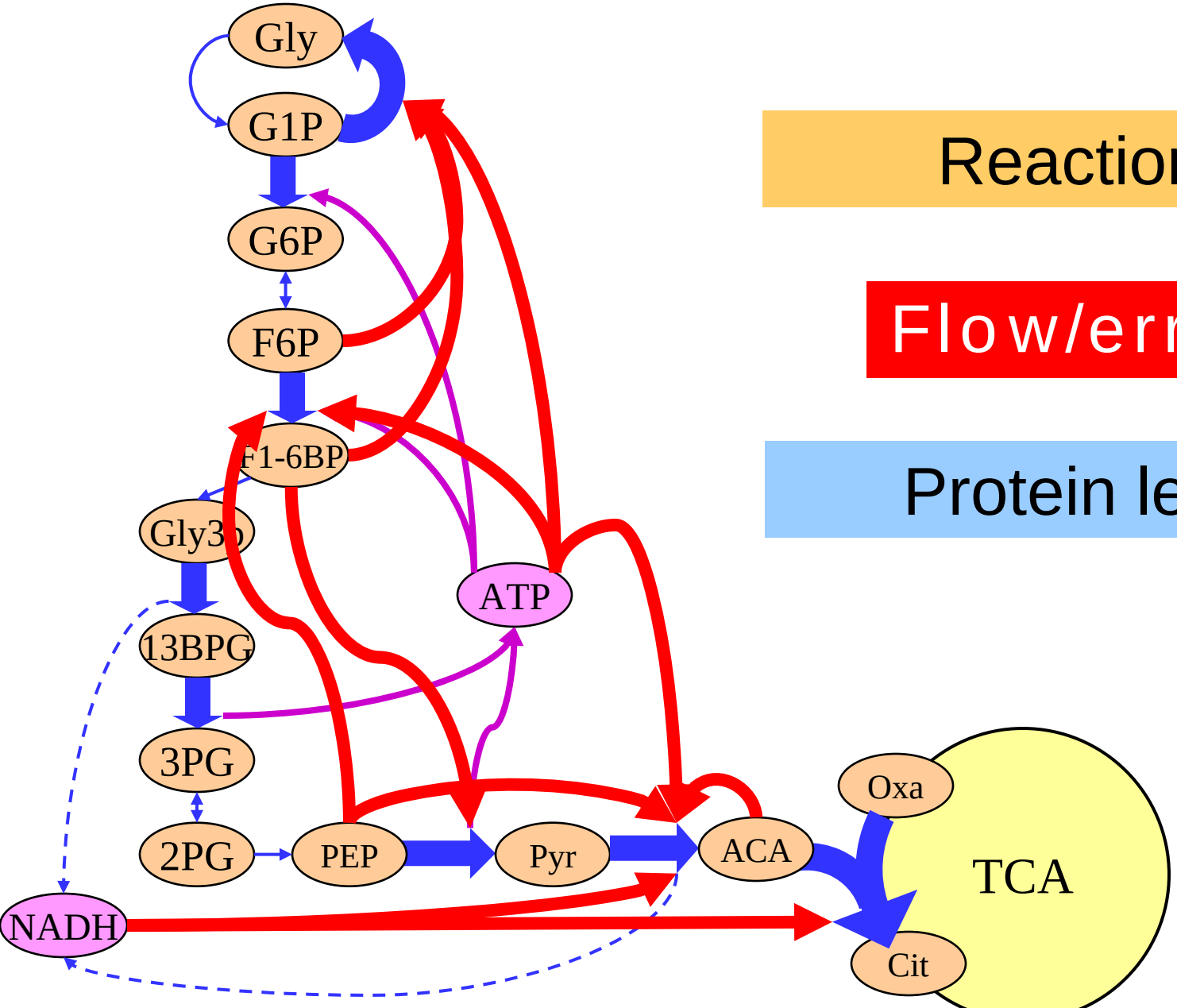
$$\frac{dx}{dt} = Sv(x) = \begin{bmatrix} \text{Mass \&} \\ \text{Energy} \\ \text{Balance} \end{bmatrix} \boxed{\begin{bmatrix} \text{Reaction} \\ \text{flux} \end{bmatrix}}$$



Reaction

Error/flow

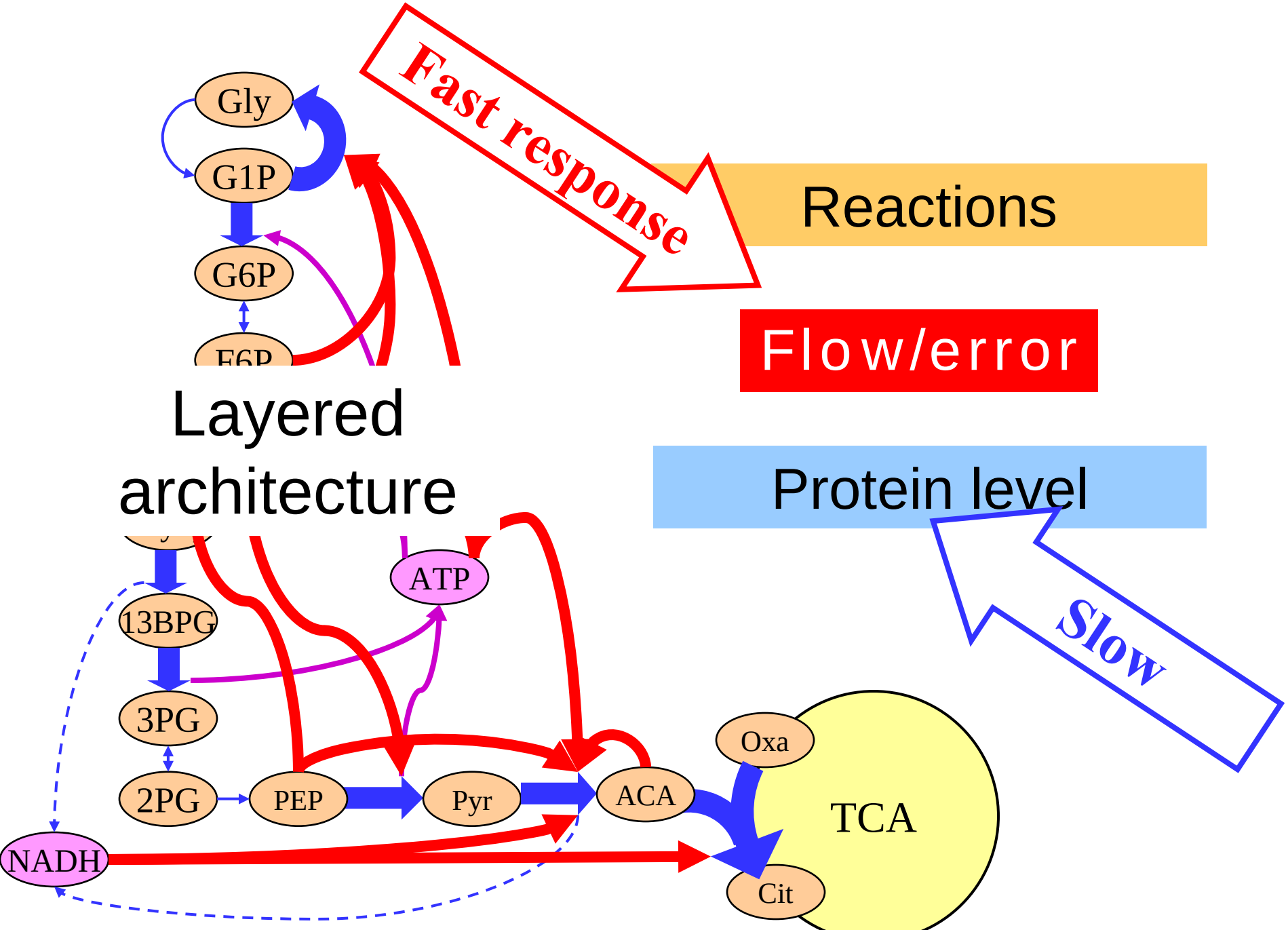
Level

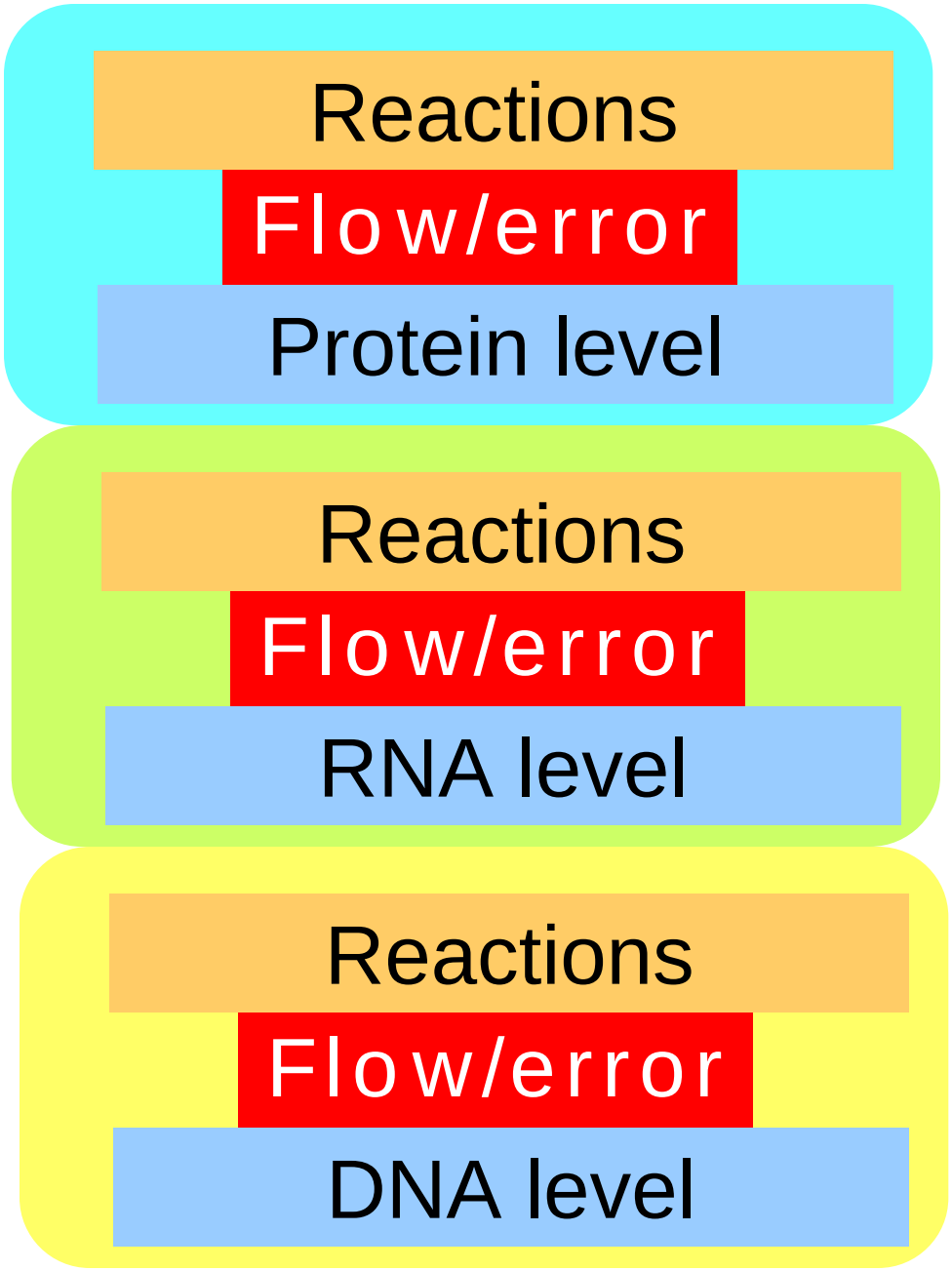


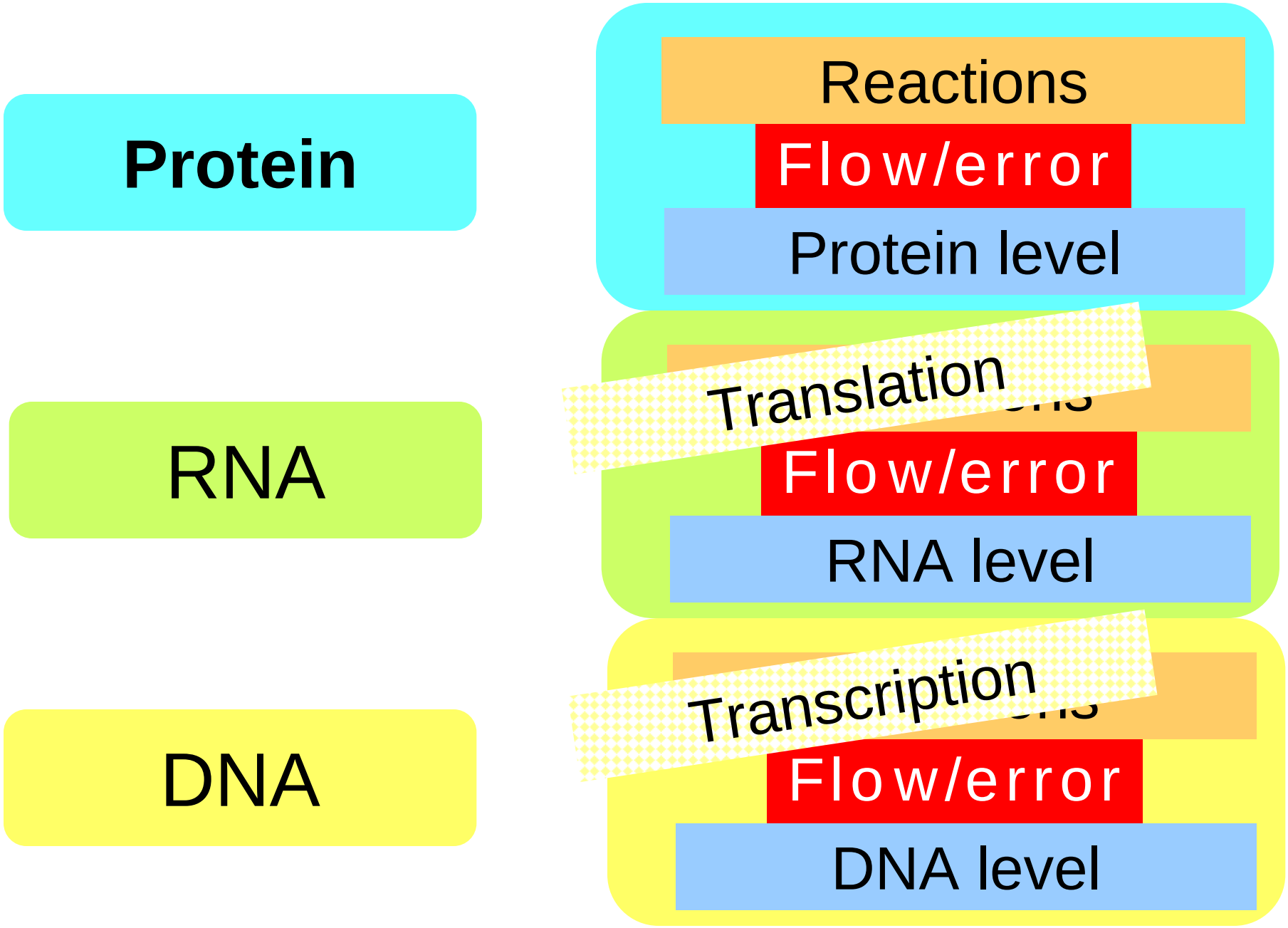
Reactions

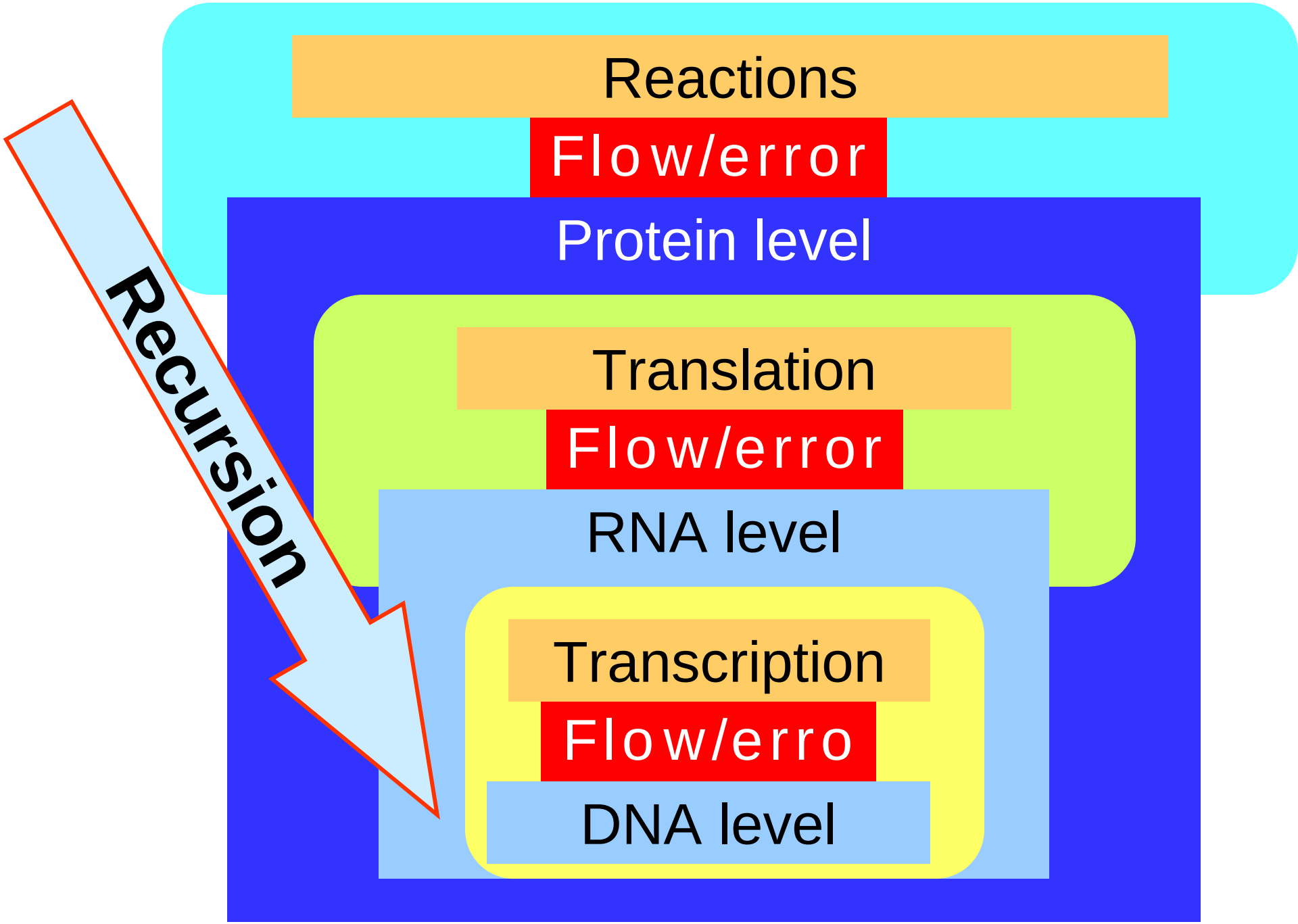
Flow/error

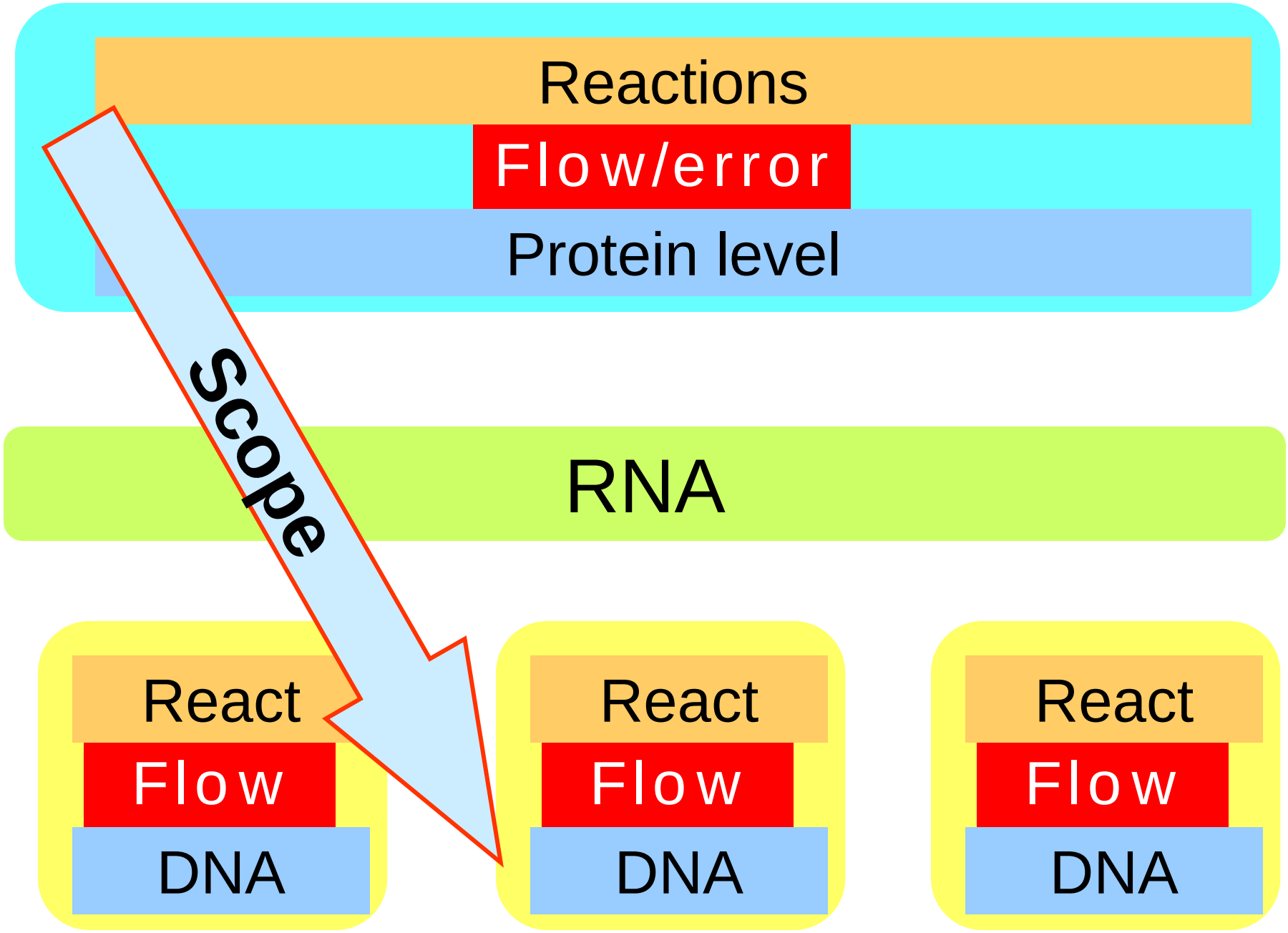
Protein level

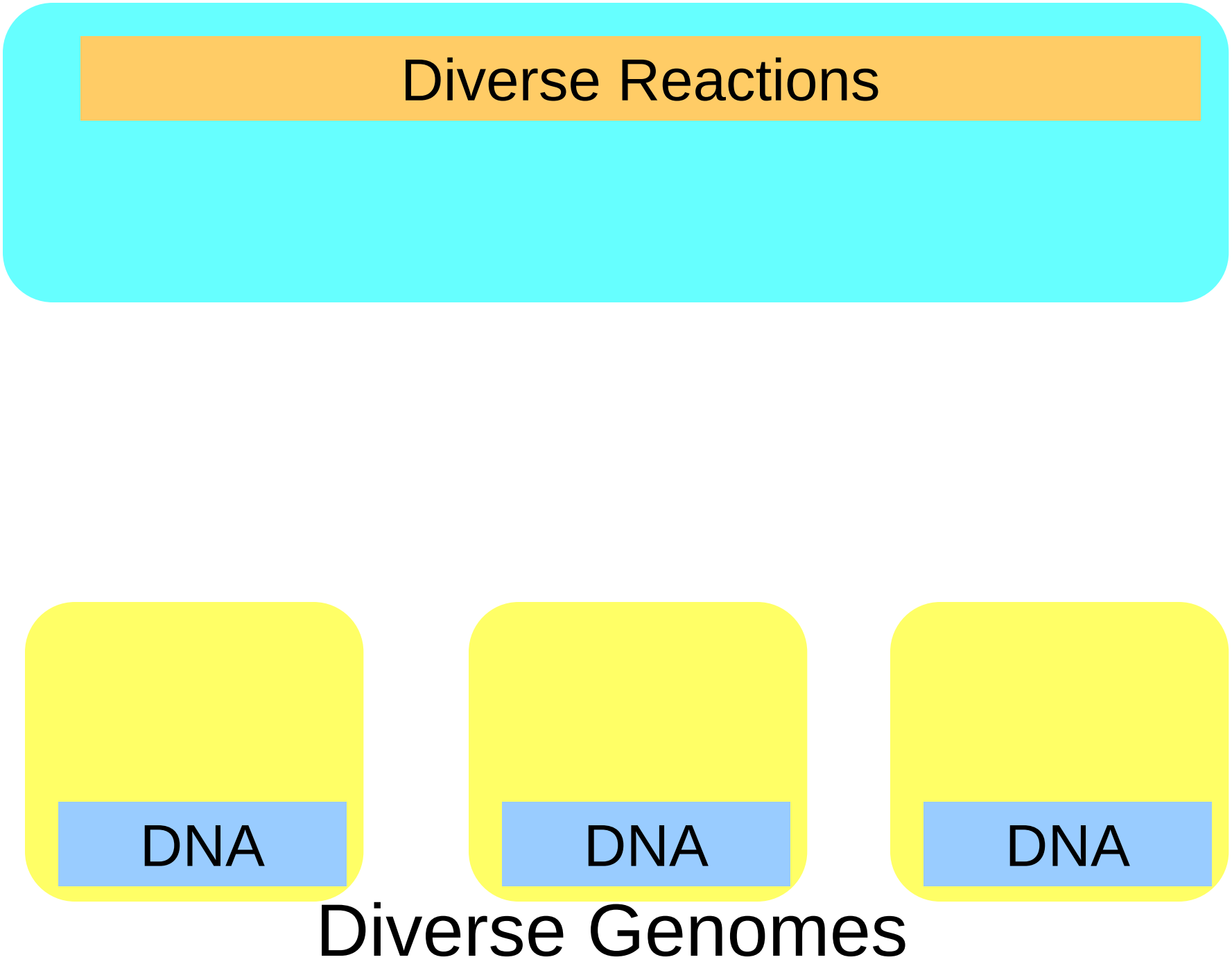

Fast response
Reactions
Flow/error
Protein level
Slow
Layered architecture
Gly
G1P
G6P
F6P
ATP
13BPG
3PG
2PG
PEP
Pyr
ACA
NADH
Oxa
TCA
Cit

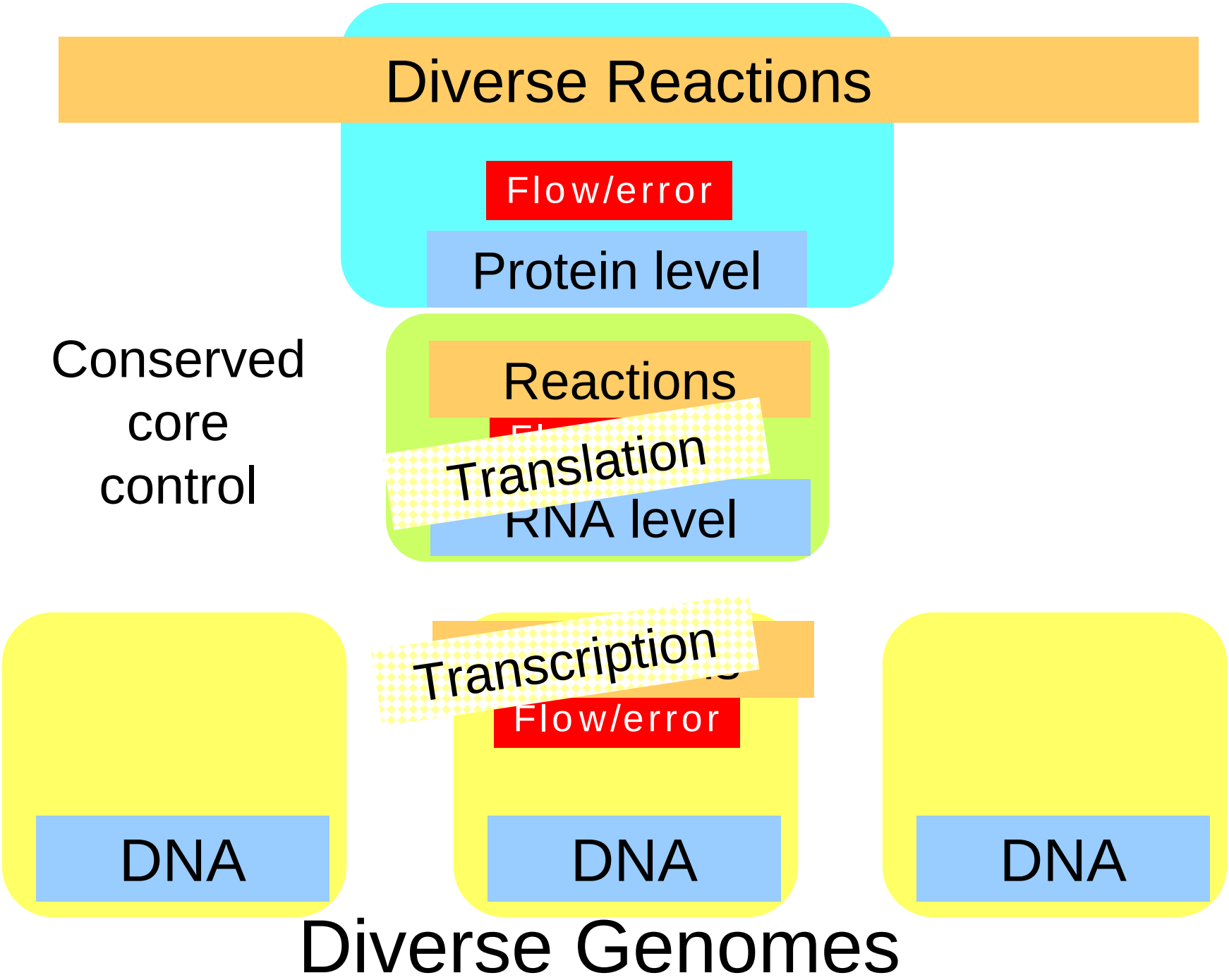

Reactions
Flow/error
Protein level
Reactions
Flow/error
RNA level
Reactions
Flow/error
DNA level

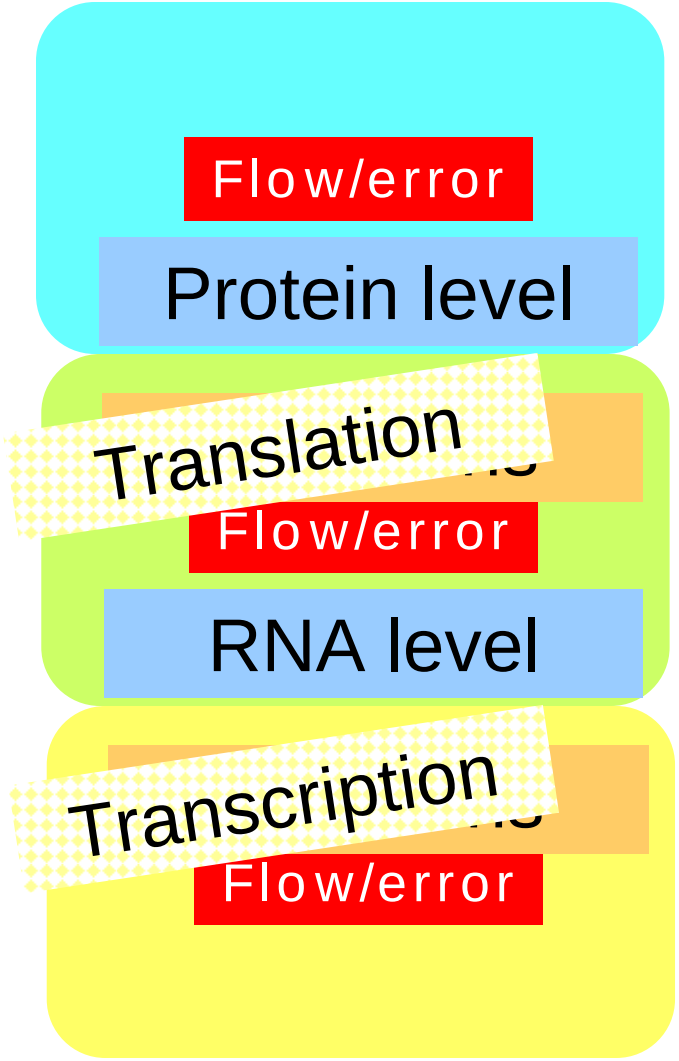

Protein
Reactions
Flow/error
Protein level
RNA
Translation
Flow/error
RNA level
DNA
Transcription
Flow/error
DNA level

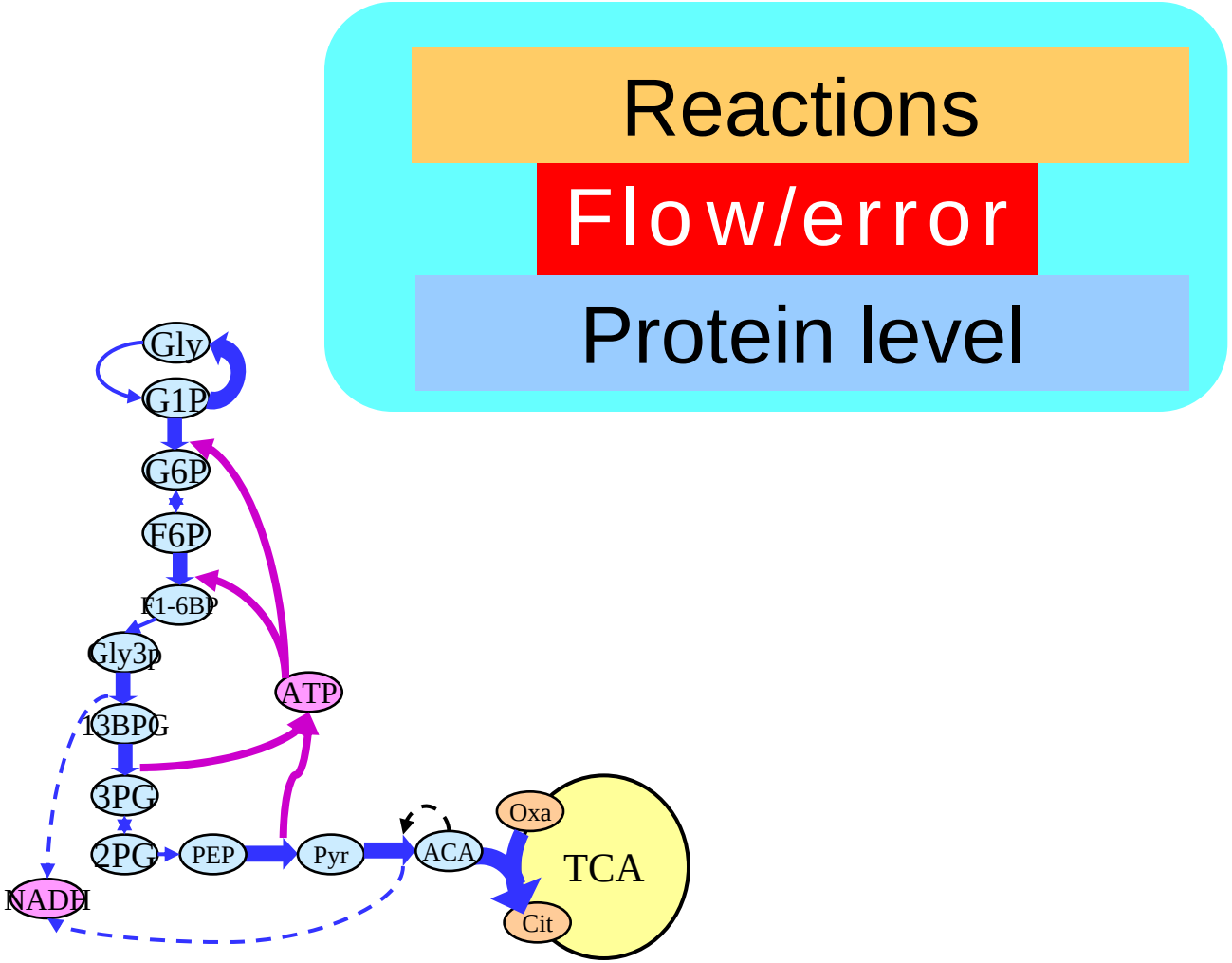

Reactions
Flow/error
Protein level
Translation
Flow/error
RNA level
Transcription
Flow/erro
DNA level
Recursion


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


Diverse Reactions
DNA
DNA
DNA
Diverse Genomes


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


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


Reactions
Flow/error
Protein level
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
Cit
TCA

Reactions

Flow/erro

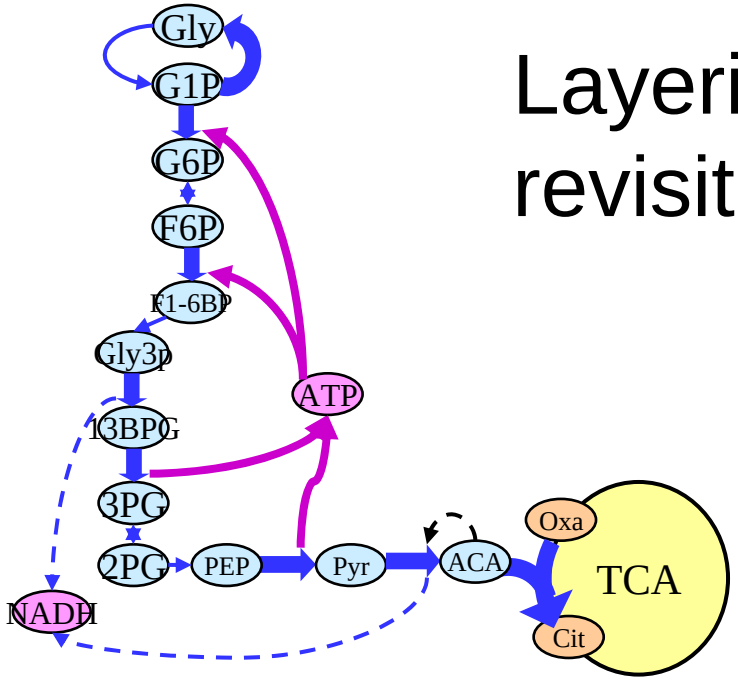
Protein level

Reactions

Flow/erro

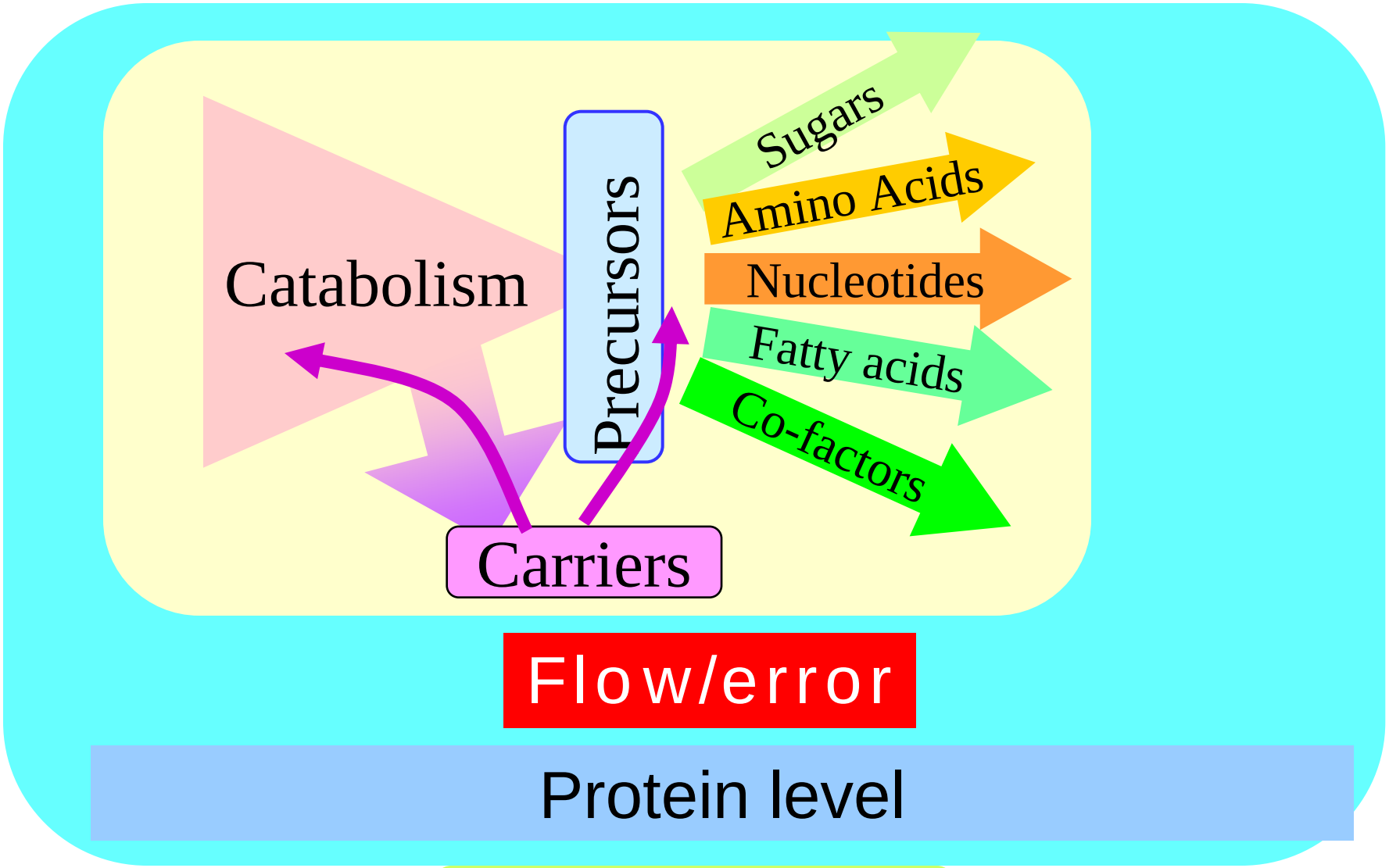
Carriers

Proteins



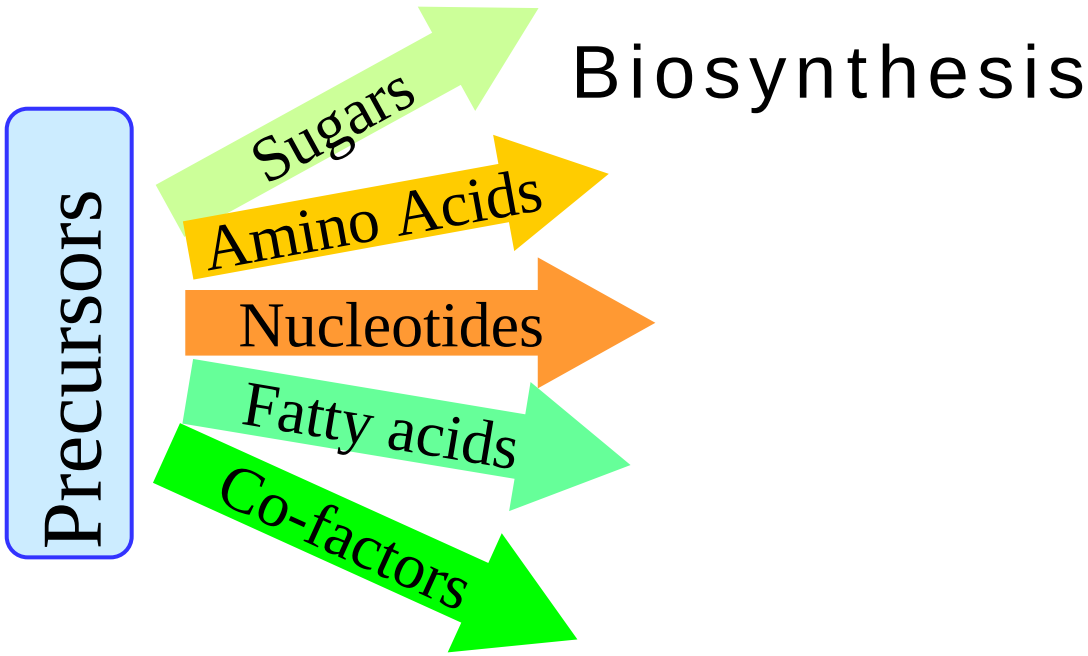
Layering revisited

More complete picture


Catabolism
Precursors
Sugars
Amino Acids
Nucleotides
Fatty acids
Co-factors
Carriers
Flow/error
Protein level

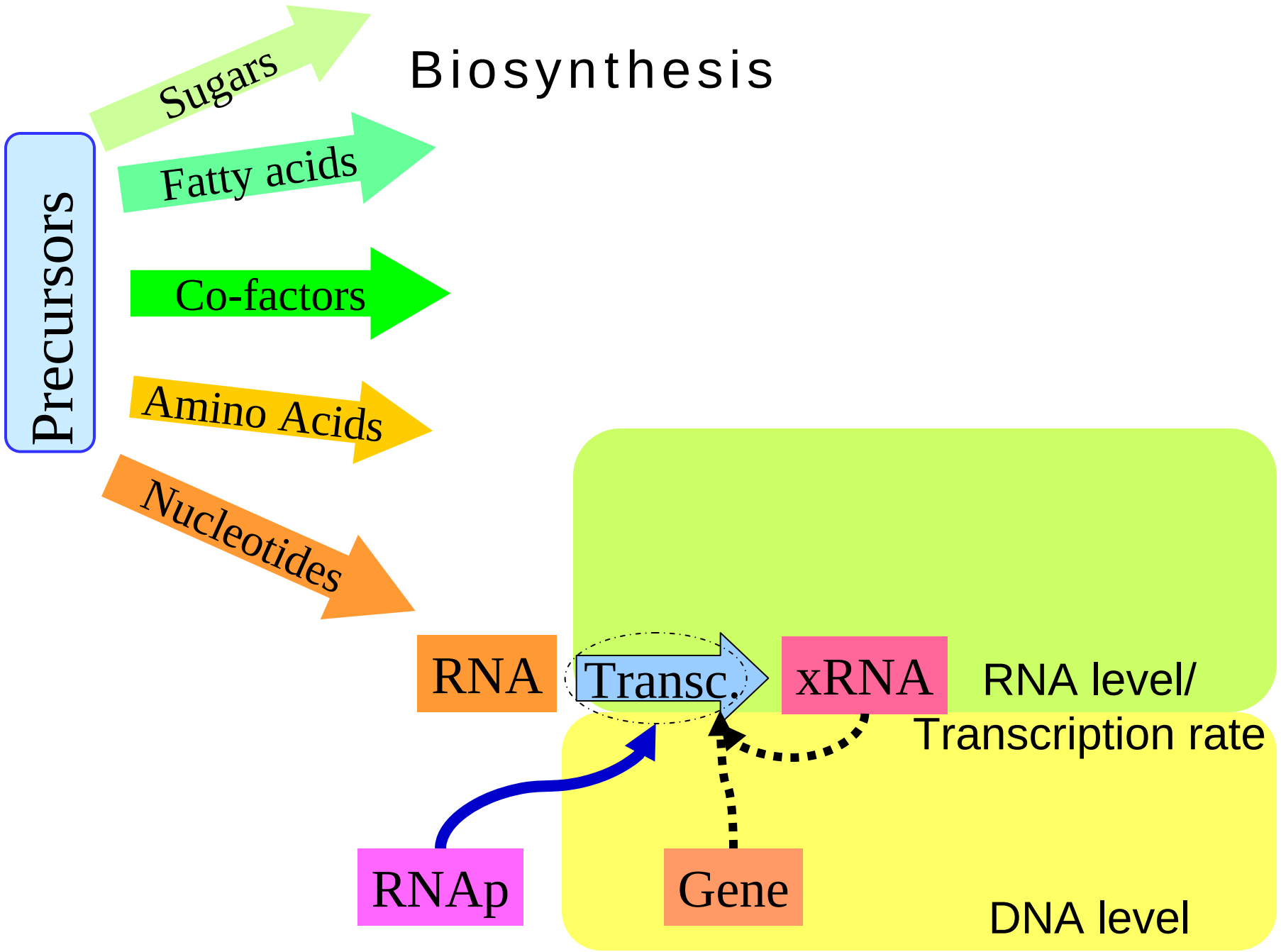
RNA

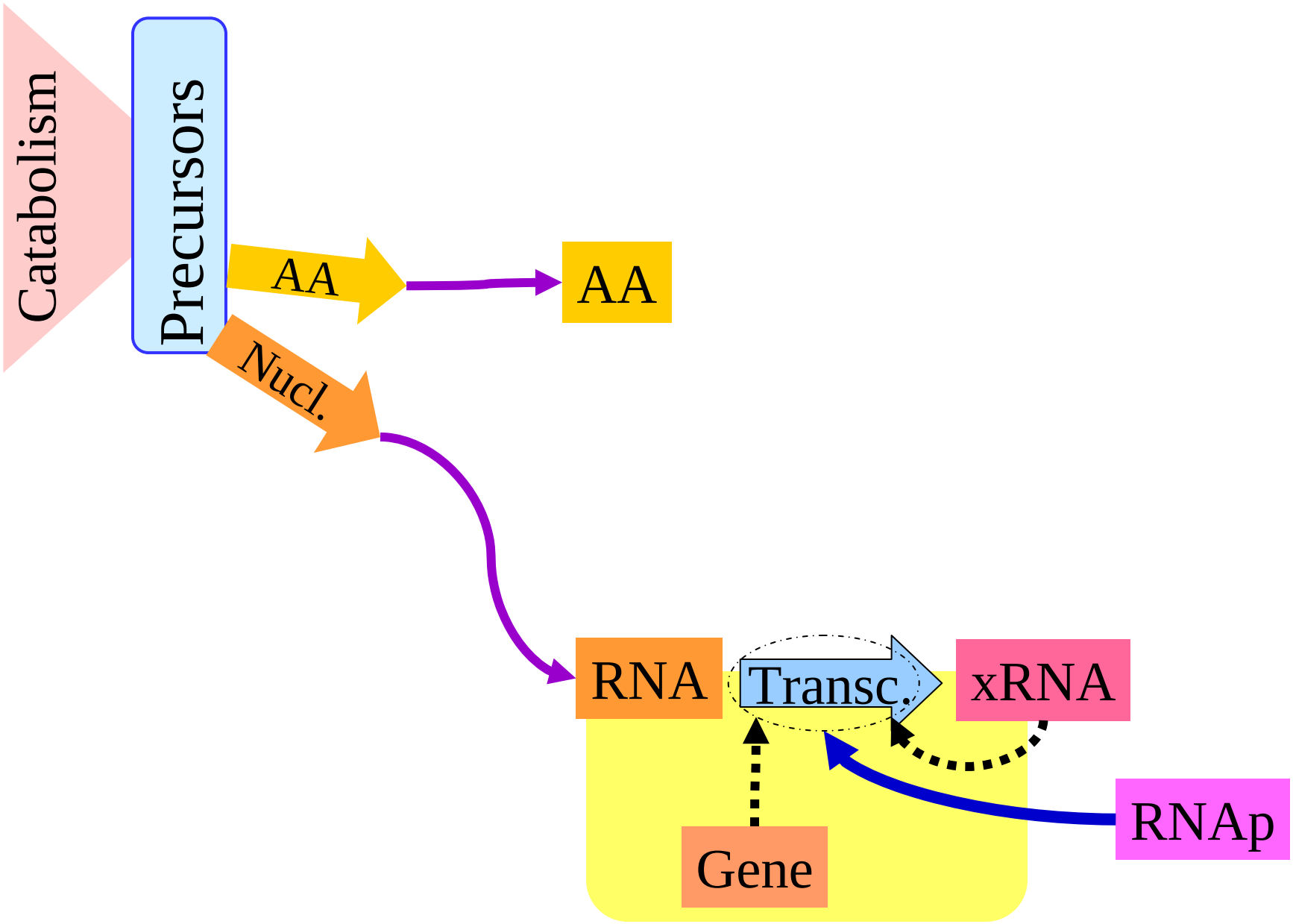
DNA

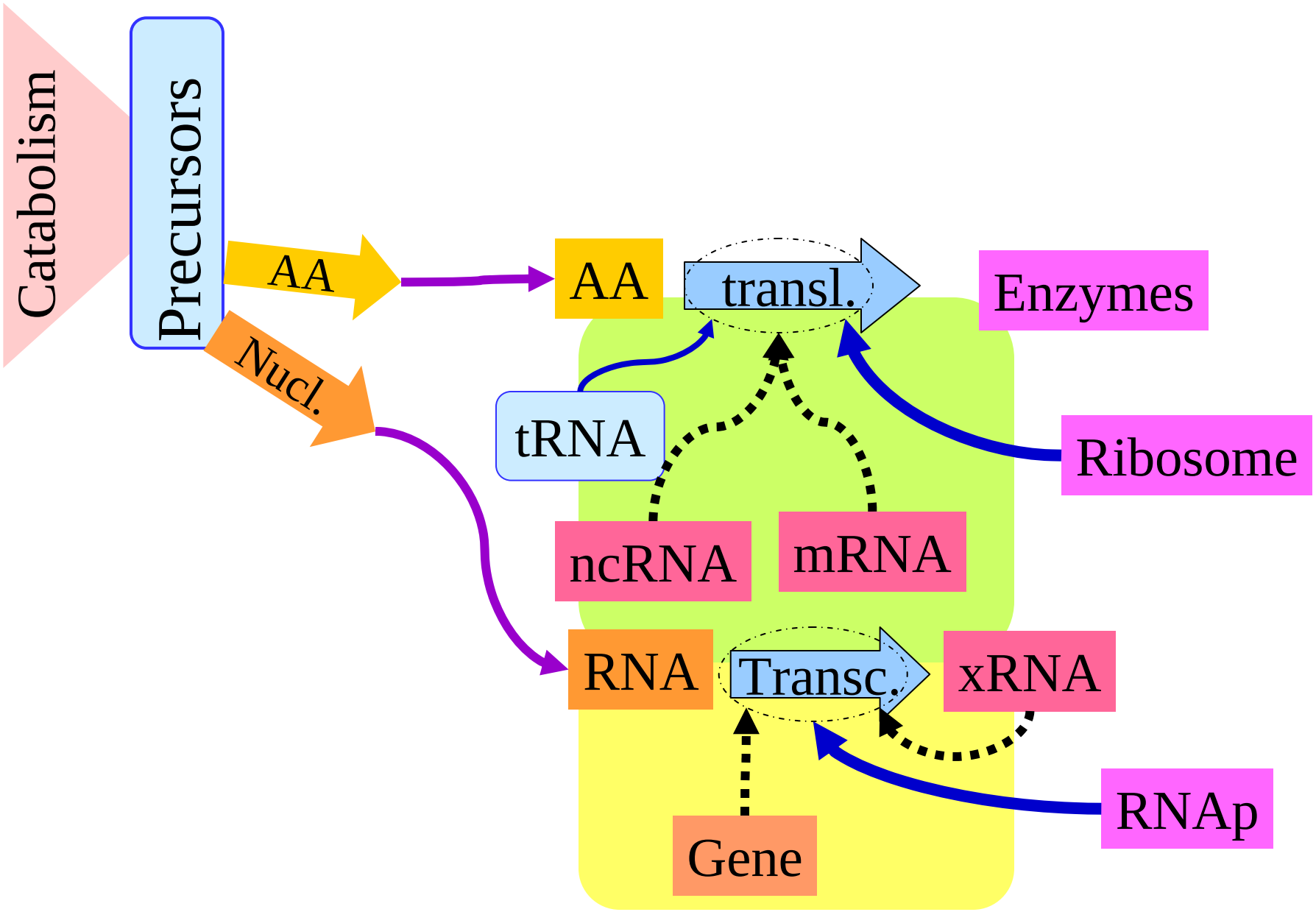

Biosynthesis
Precursors
Sugars
Amino Acids
Nucleotides
Fatty acids
Co-factors

RNA

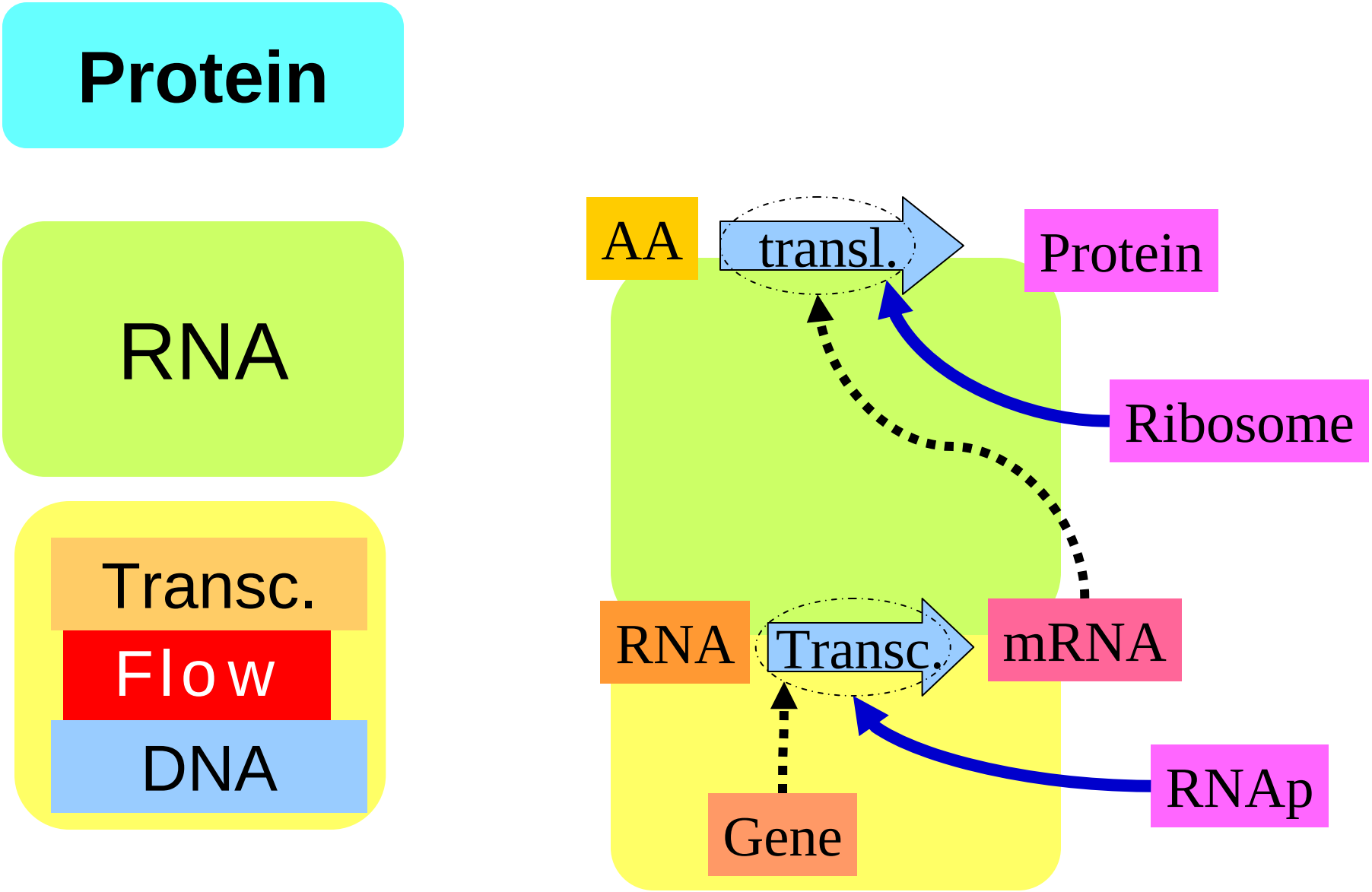
DNA

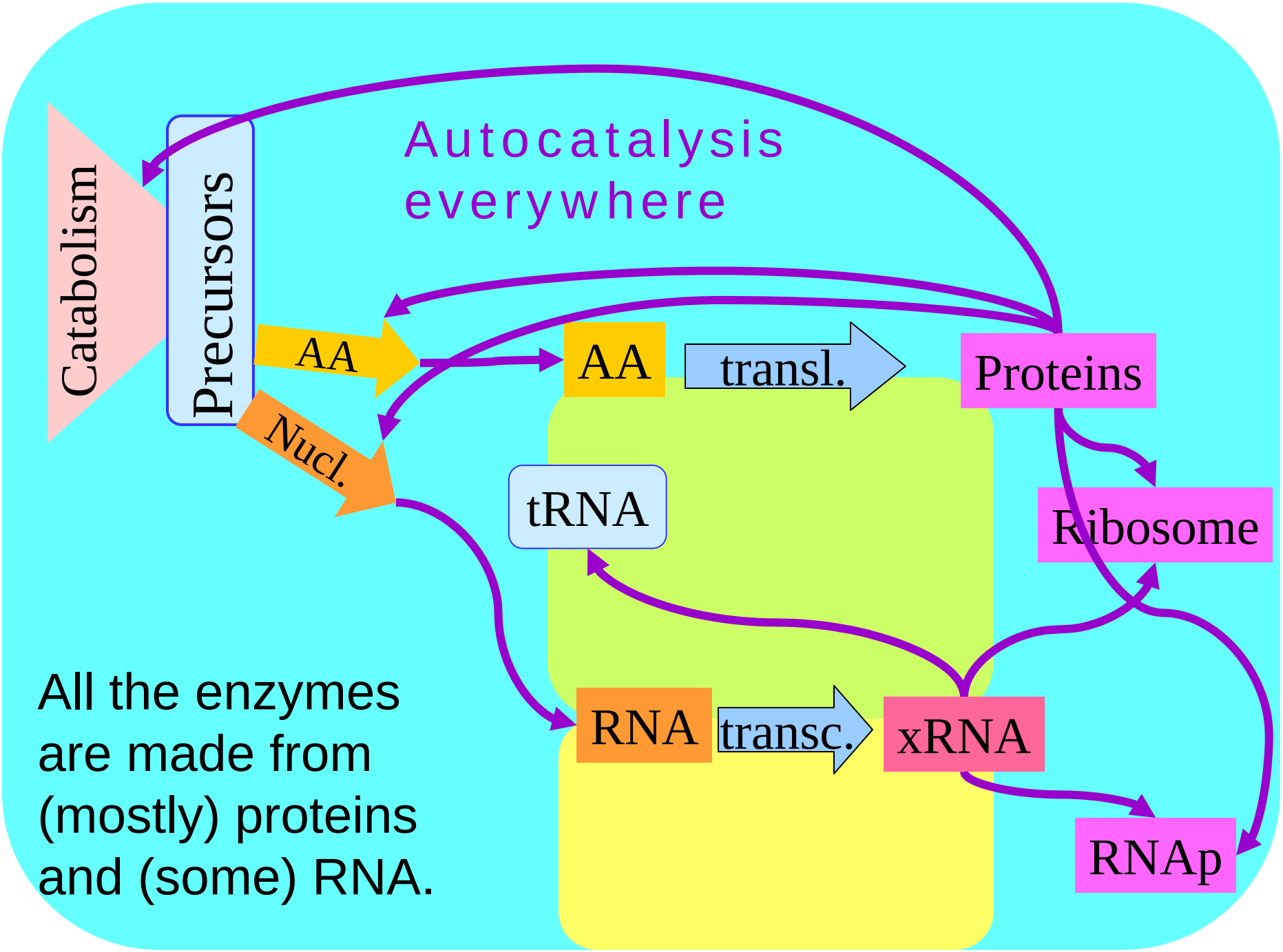

Biosynthesis
Precursors
Sugars
Fatty acids
Co-factors
Amino Acids
Nucleotides
RNA
Transc.
xRNA
RNA level/
Transcription rate
RNAp
Gene
DNA level


Catabolism
Precursors
AA
AA
Nucl.
RNA
Transc.
xRNA
RNAp
Gene


Catabolism
Precursors
AA
Nucl.
AA
transl.
Enzymes
tRNA
Ribosome
ncRNA
mRNA
RNA
Transc.
xRNA
RNAp
Gene

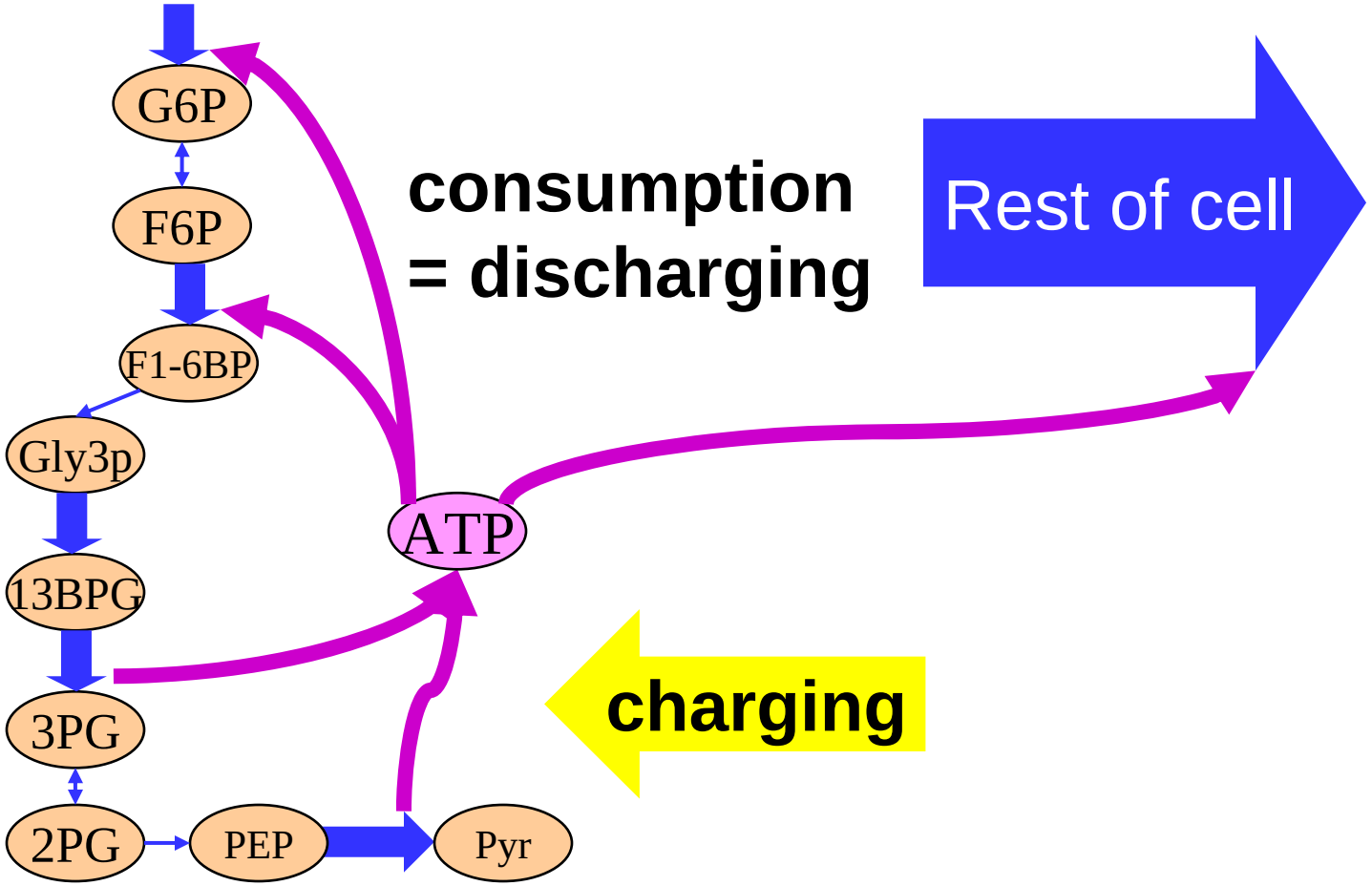
“Central dogma”

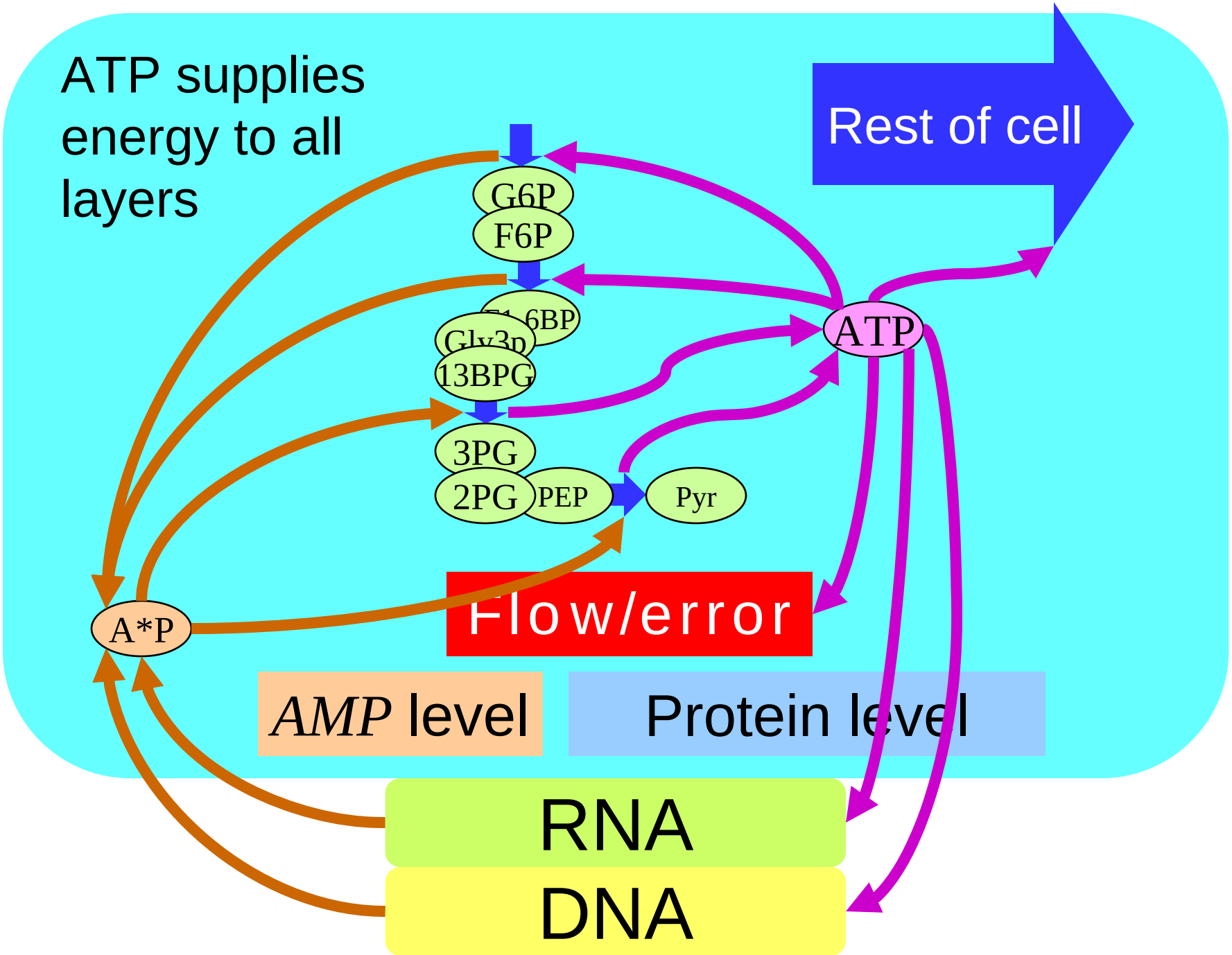


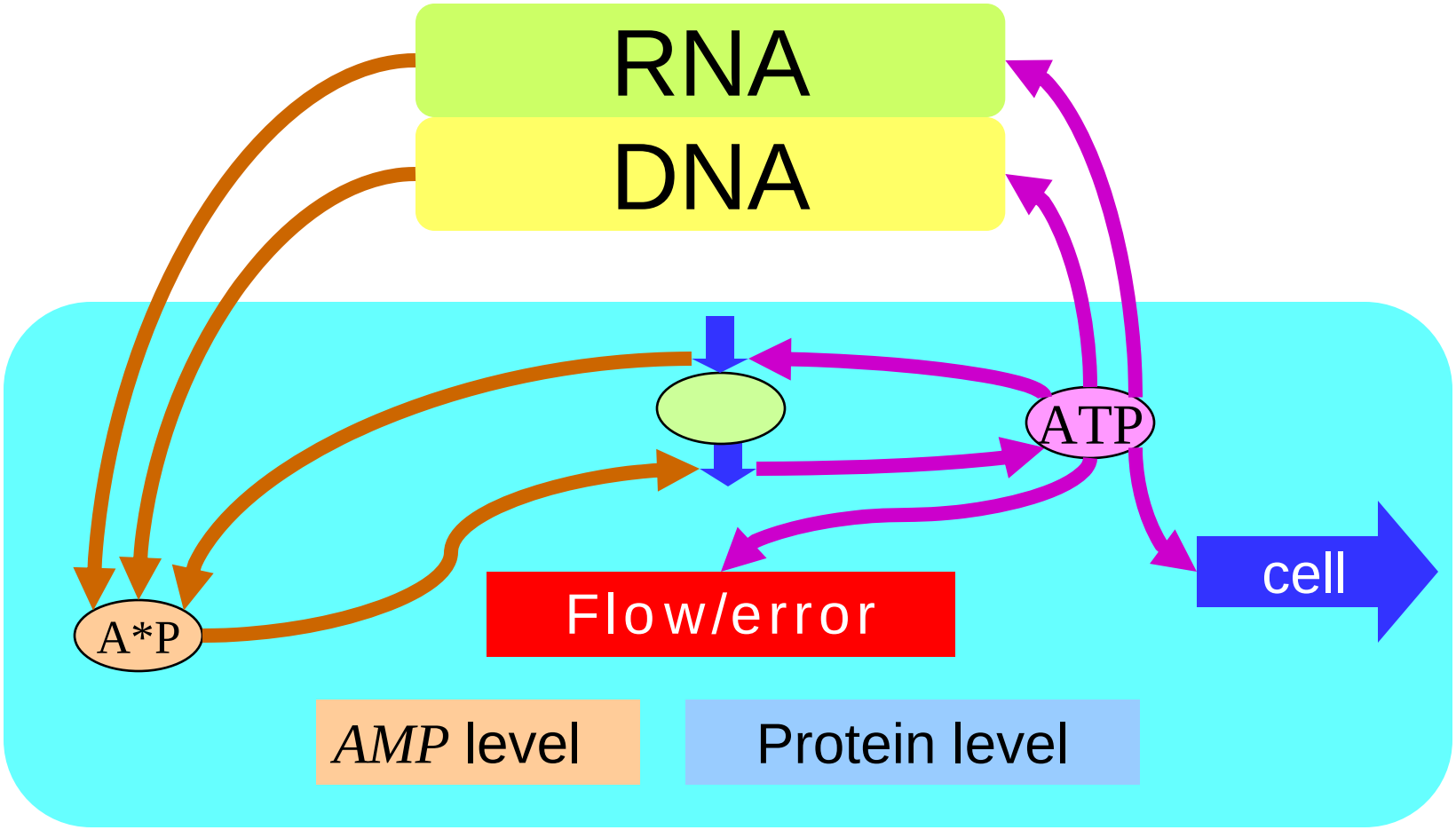


All the enzymes are made from (mostly) proteins and (some) RNA.

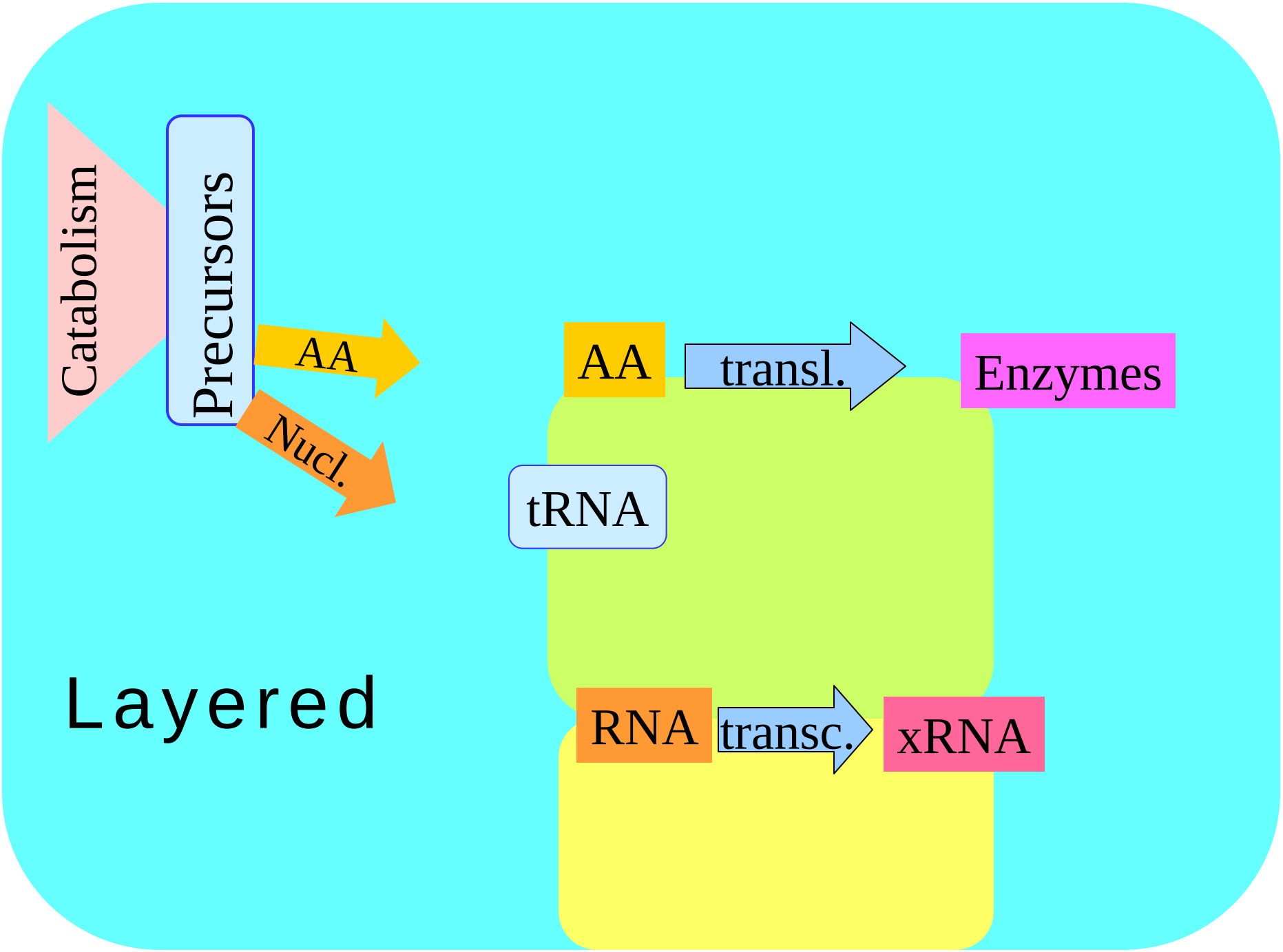
This is just charging and discharging

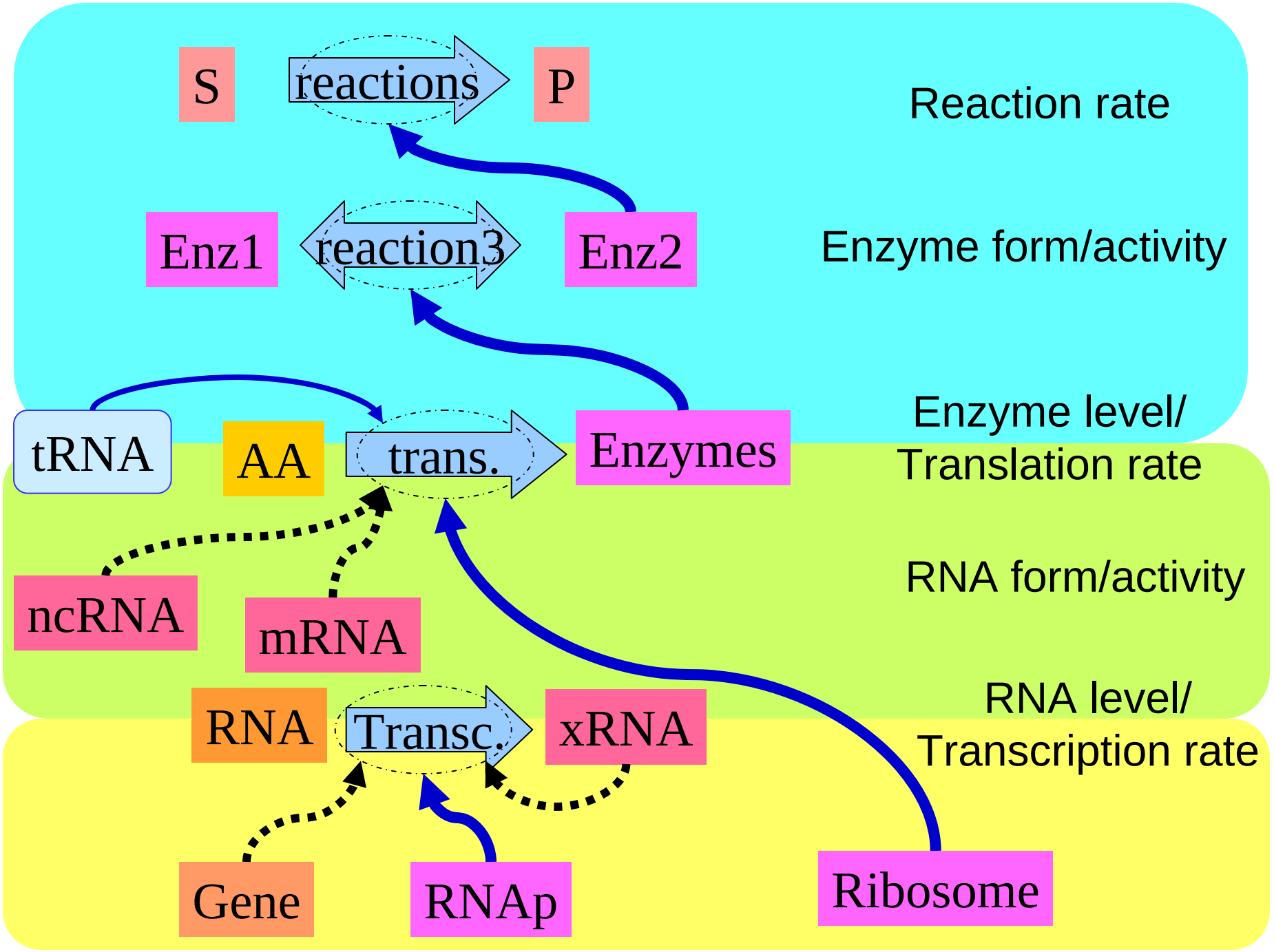



ATP supplies energy to all layers
Rest of cell
G6P
F6P
6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ATP
A*P
Flow/error
AMP level
Protein level
RNA
DNA

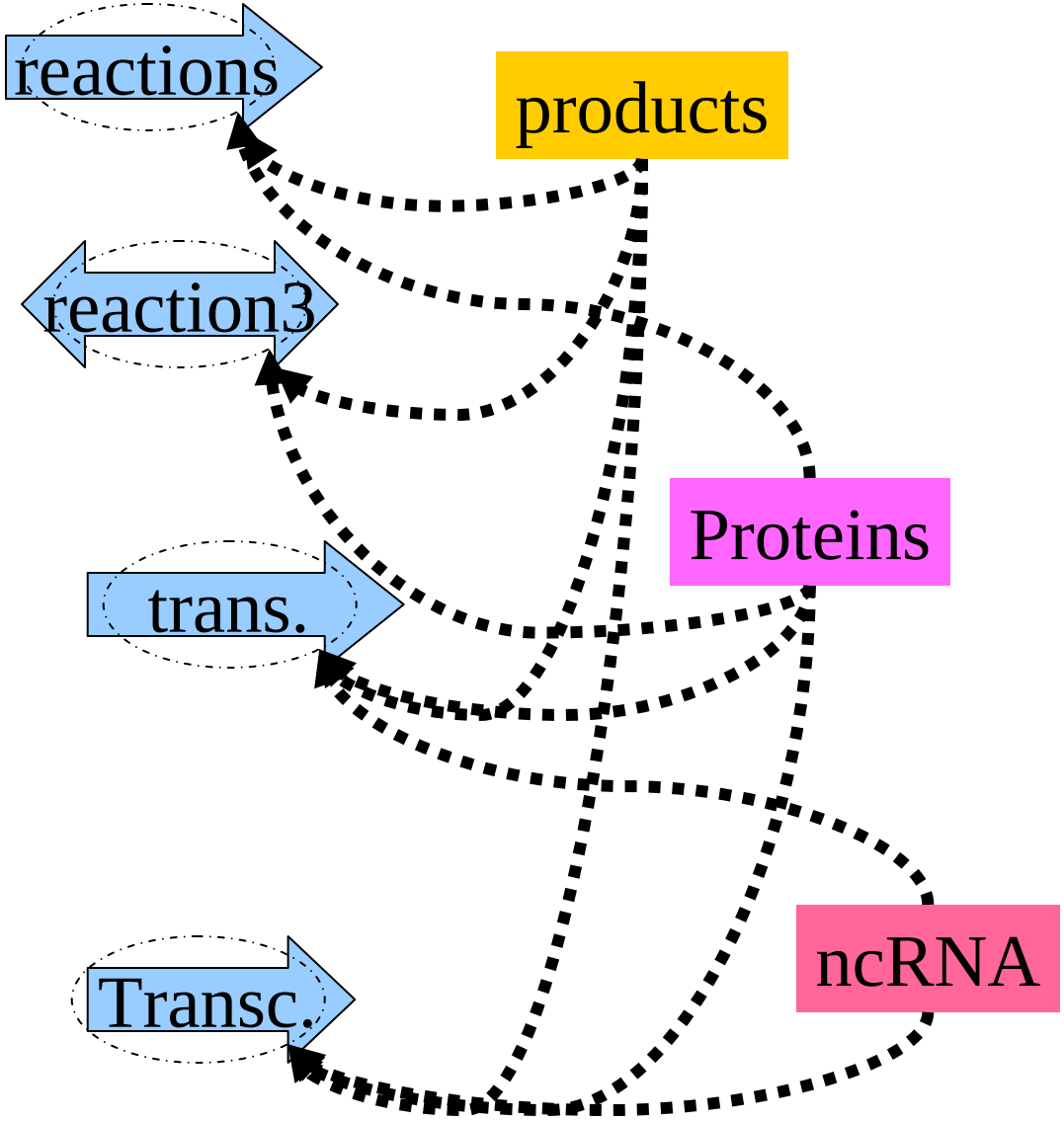


Lots of ways to draw this.


Catabolism
Precursors
AA
Nucl.
AA
transl.
Enzymes
tRNA
RNA
transc.
xRNA
Layered

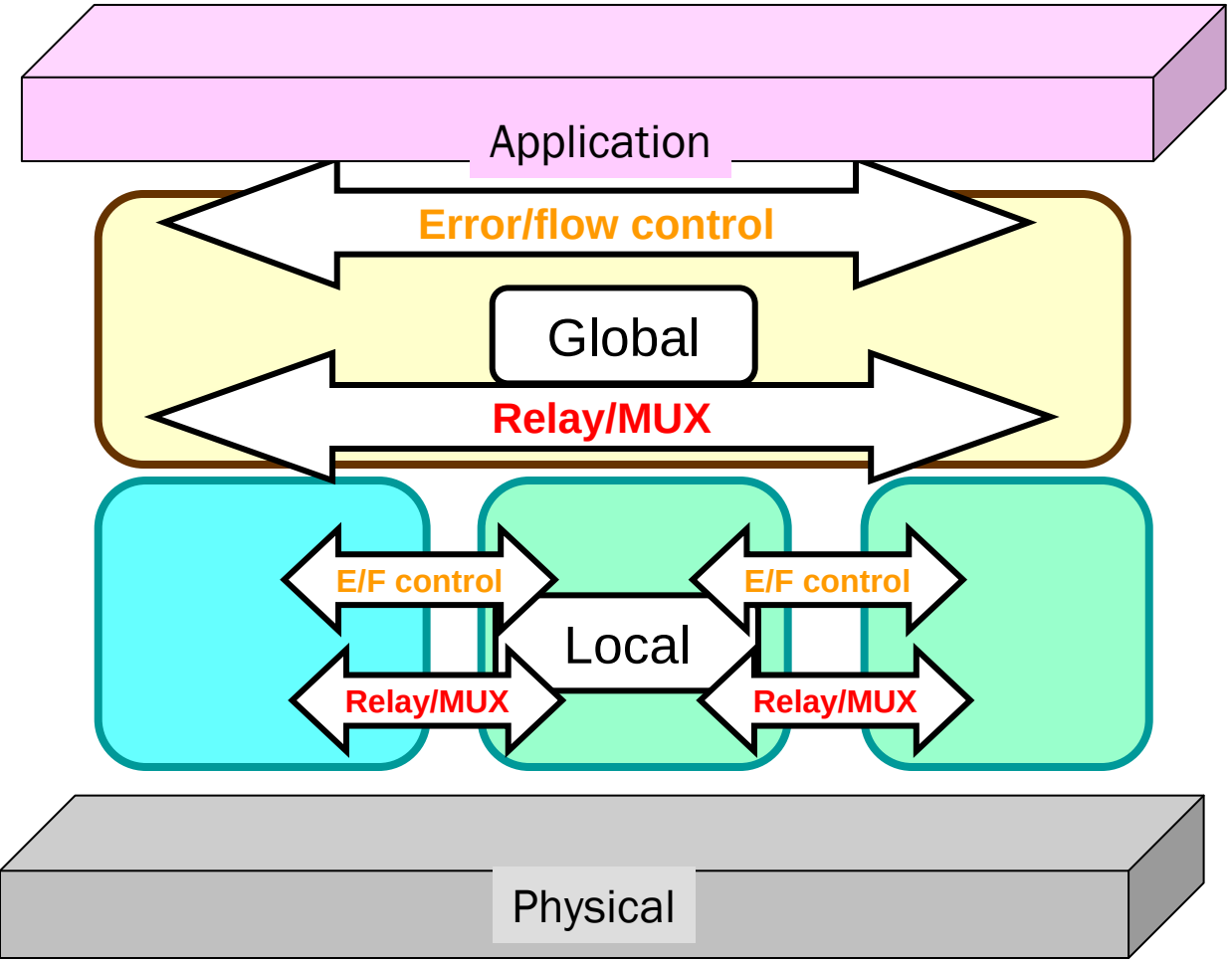

S
reactions
P
Reaction rate
Enz1
reaction3
Enz2
Enzyme form/activity
tRNA
AA
trans.
Enzymes
Enzyme level/
Translation rate
ncRNA
mRNA
RNA form/activity
RNA
Transc.
xRNA
RNA level/
Transcription rate
Gene
RNAp
Ribosome

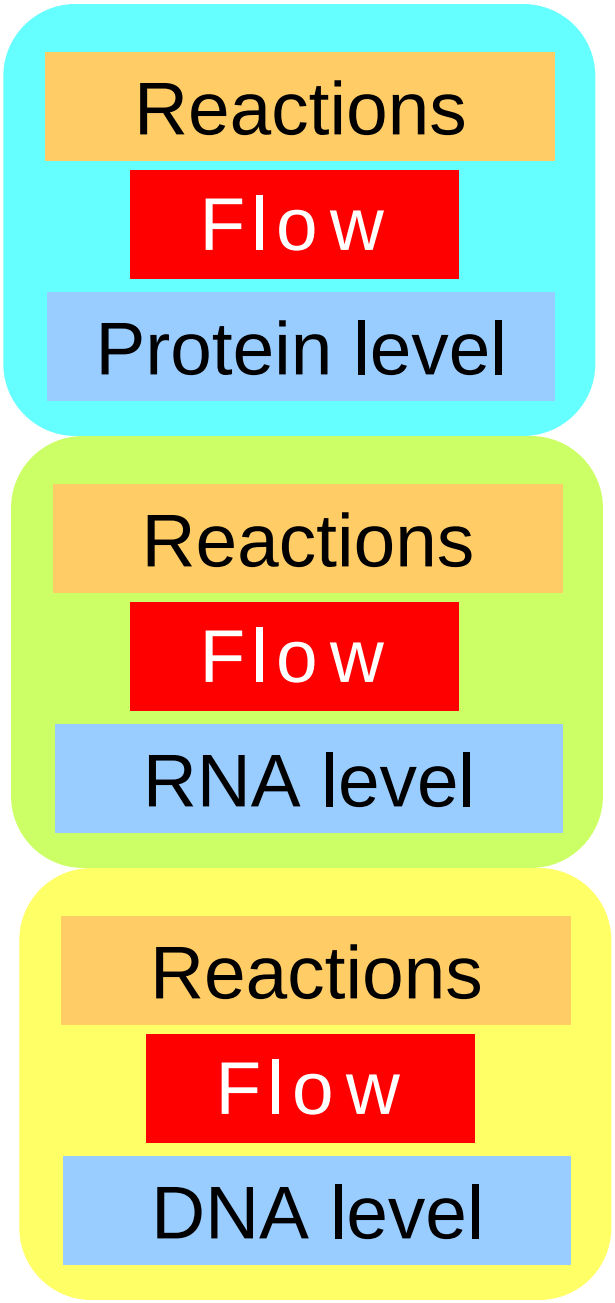
Control?



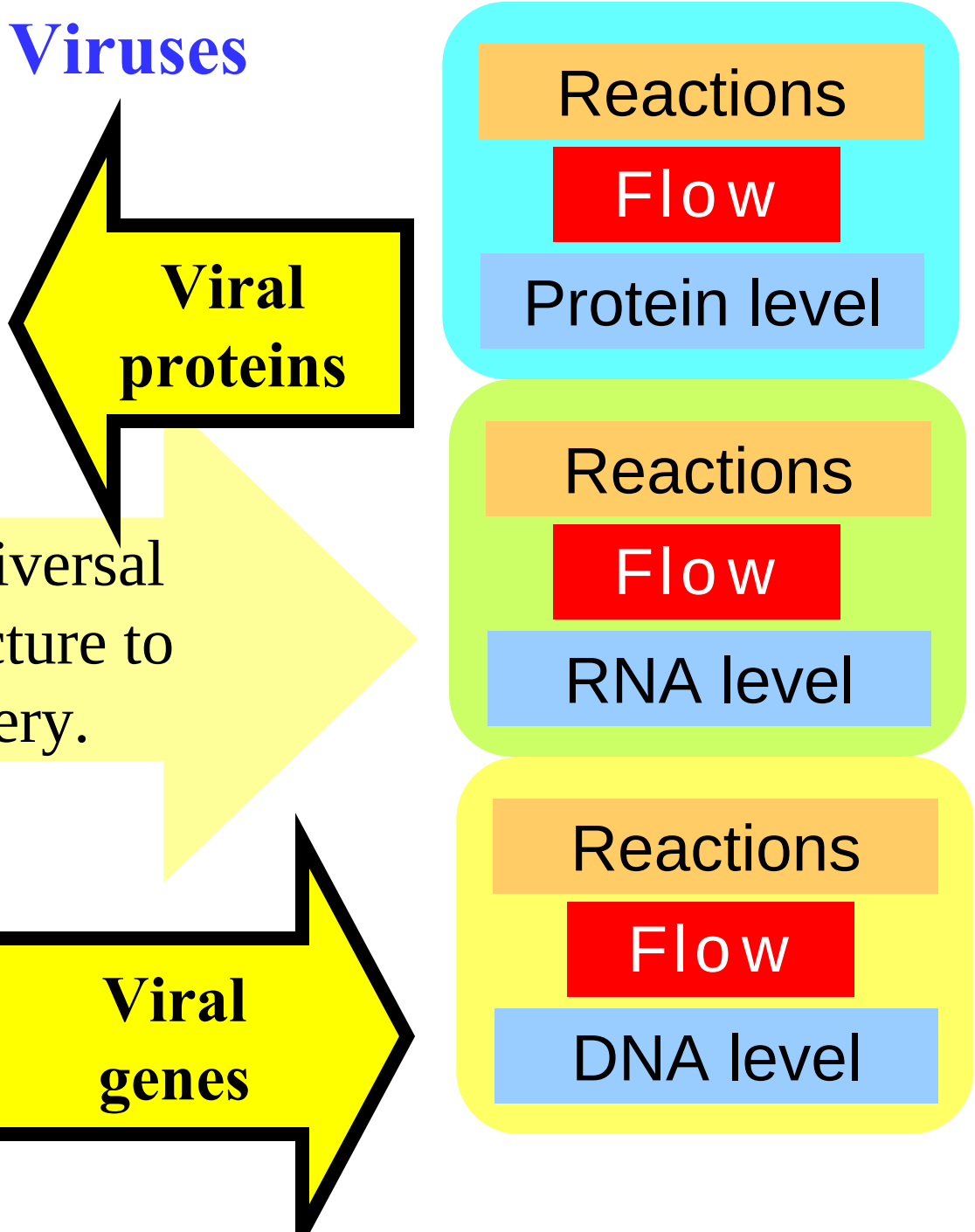
All products
feedback everywhere

Recursive control structure

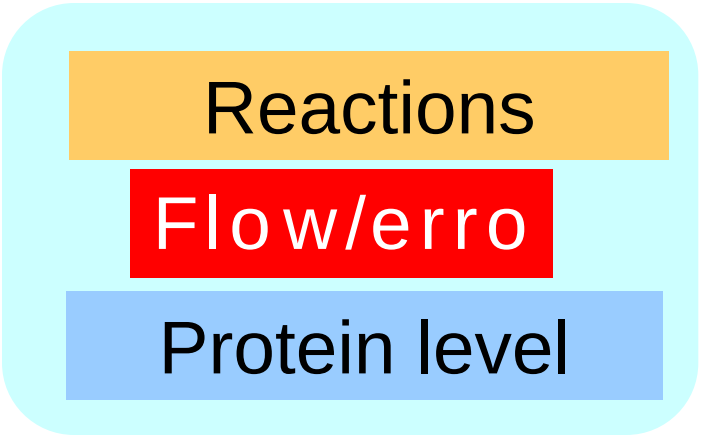


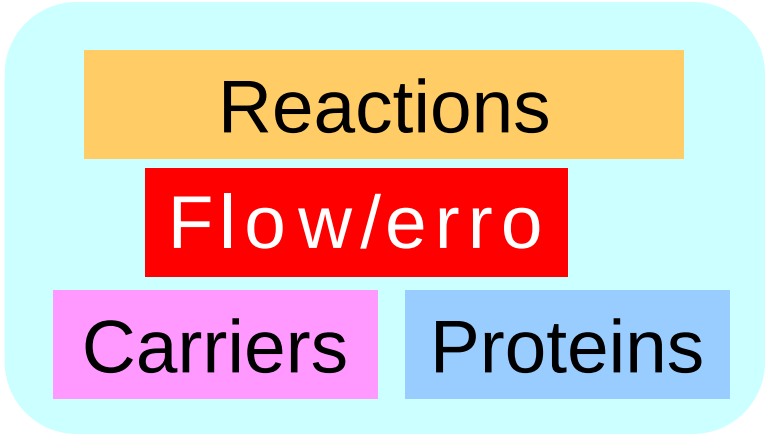


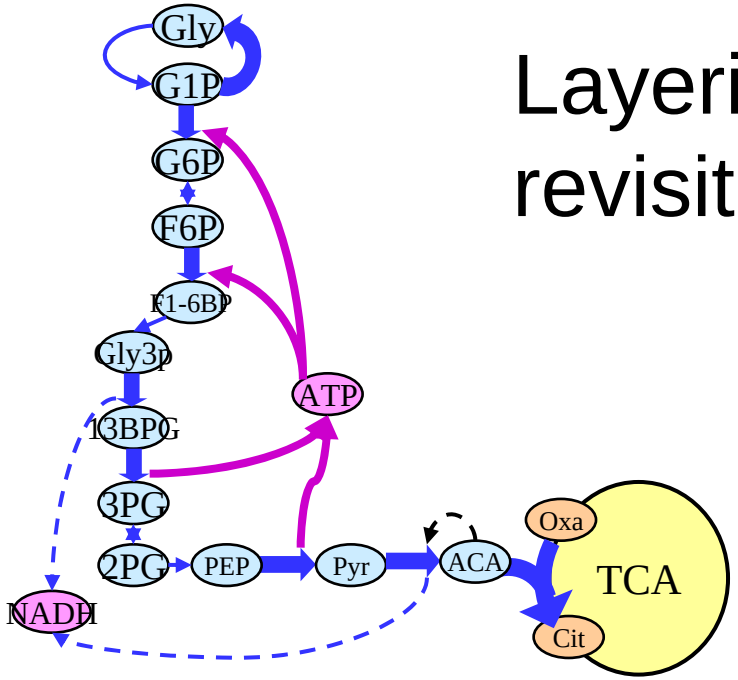
Fragility example: Viruses



Viruses exploit the universal bowtie/hourglass structure to hijack the cell machinery.

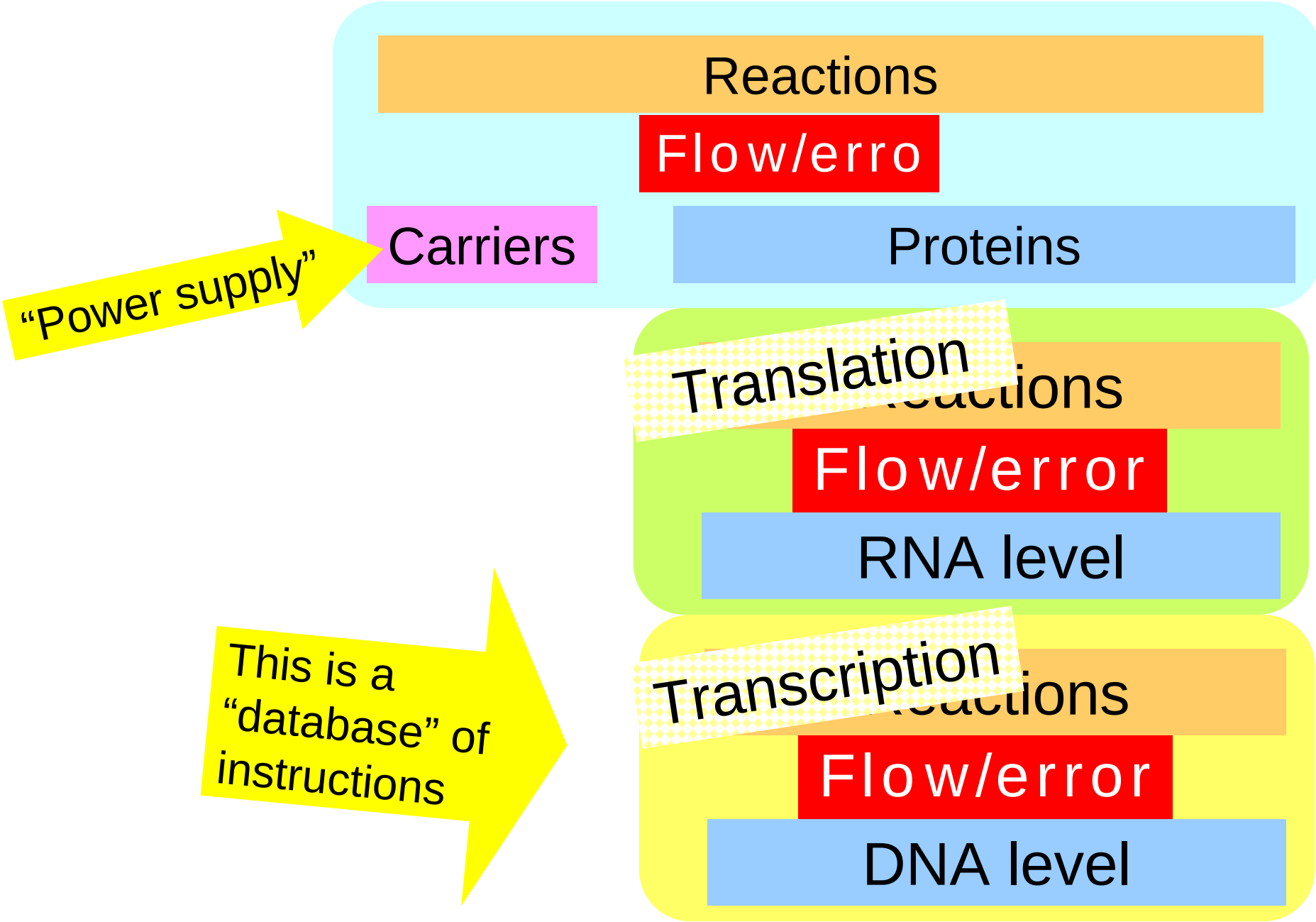


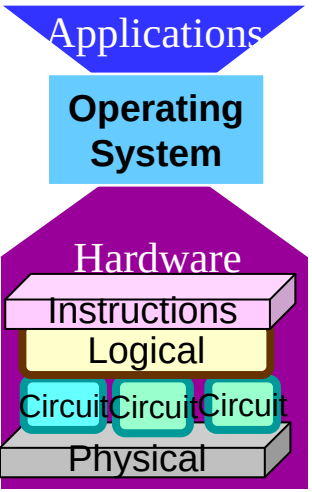


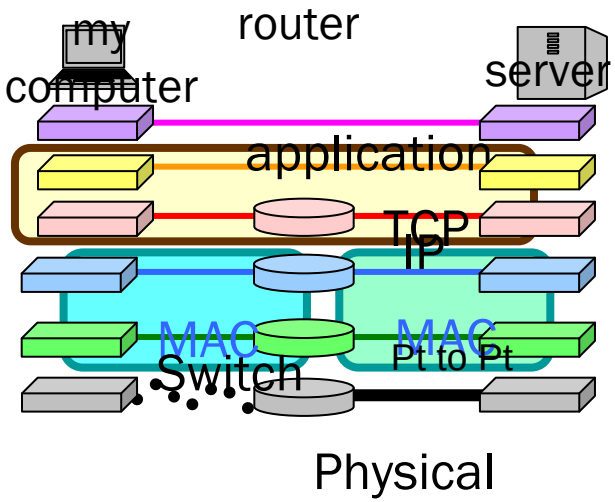


Layering revisited

More complete picture ?


Reactions
Flow/erro
Carriers
Proteins
"Power supply"
Translation
Flow/error
RNA level
This is a "database" of instructions
Transcription
Flow/error
DNA level



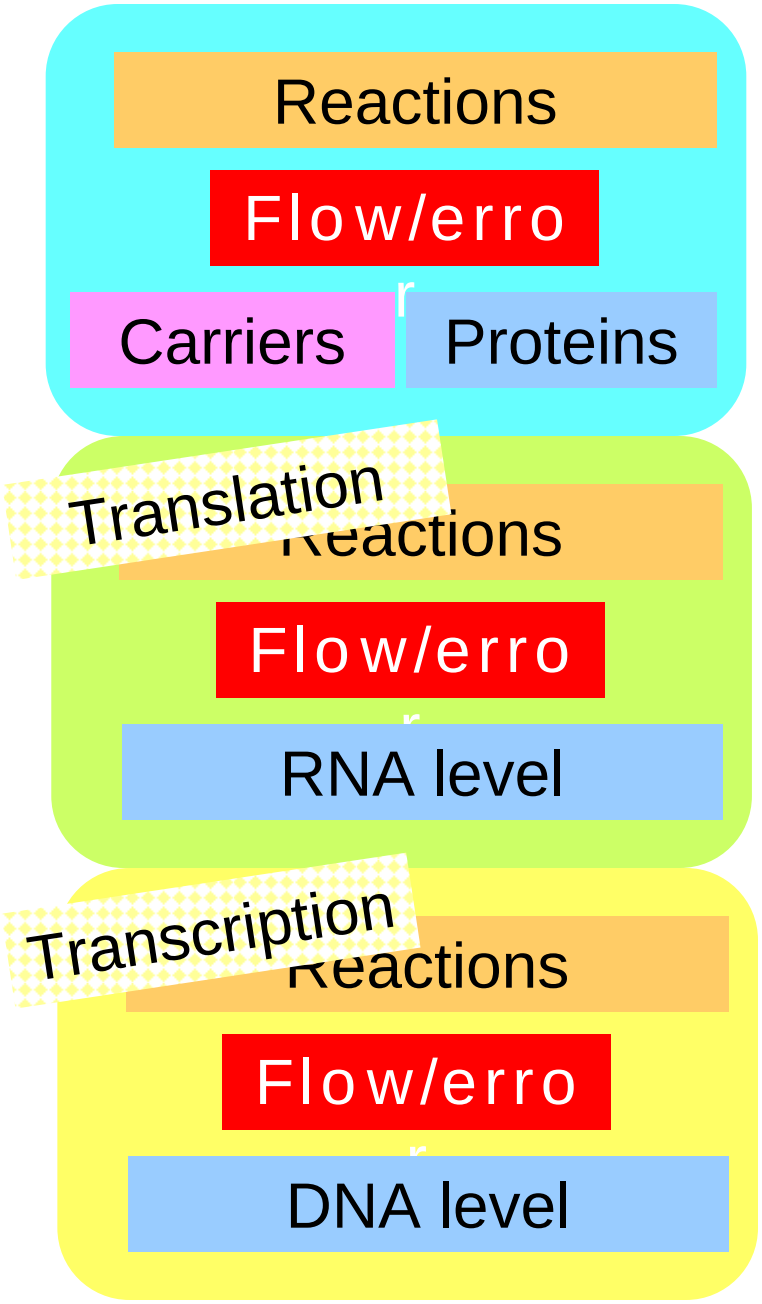


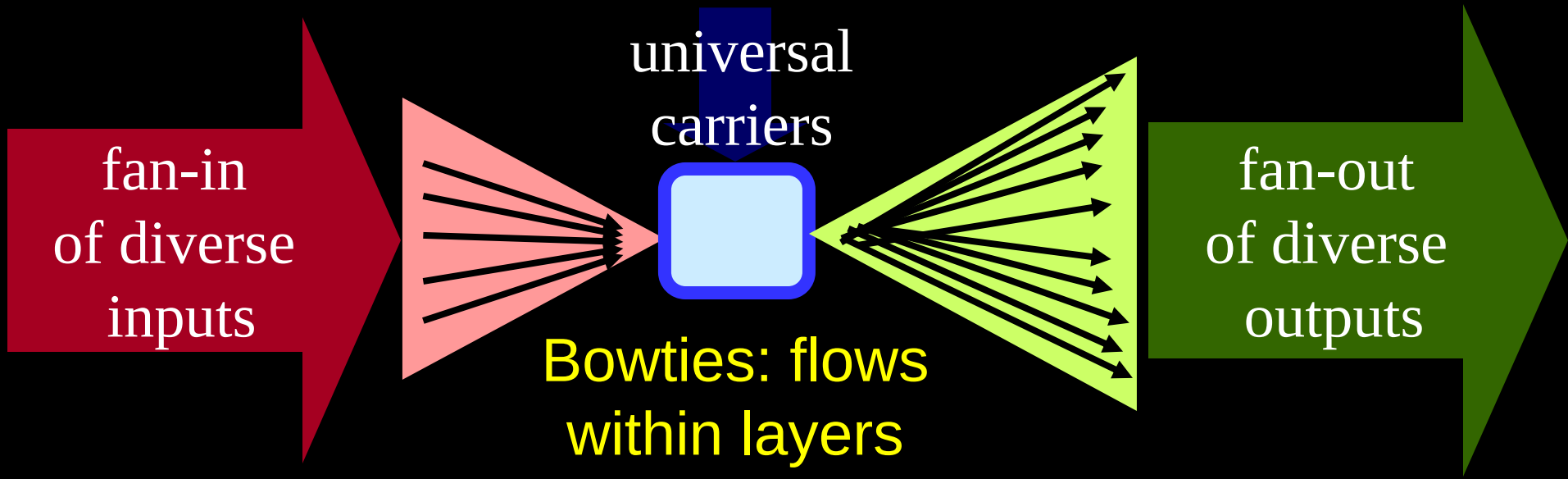
?

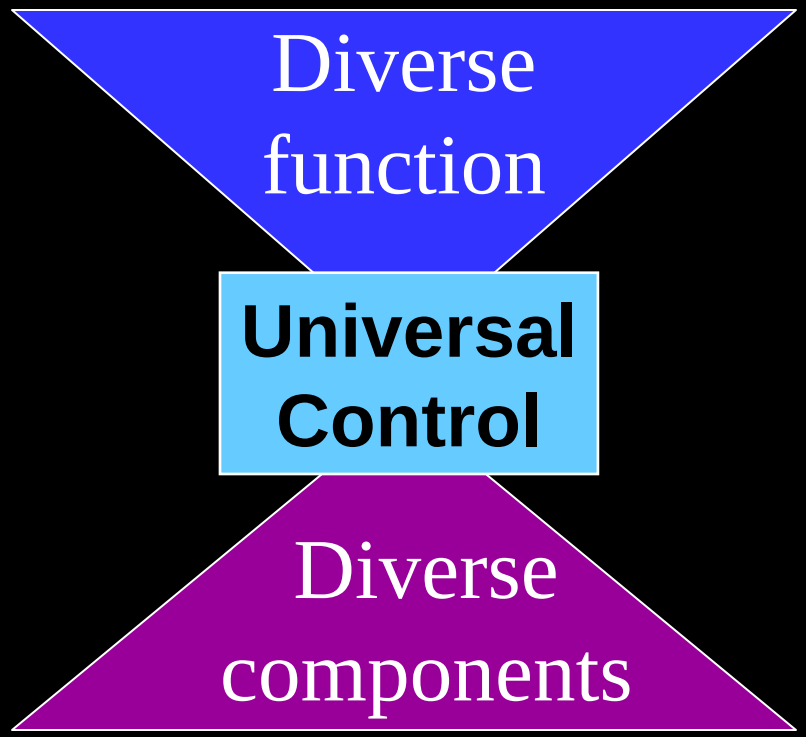
What are the additional layers?

?

- Where is the power supply?
- Where are the designs and processes that produce the chips, PCs, routers, etc?



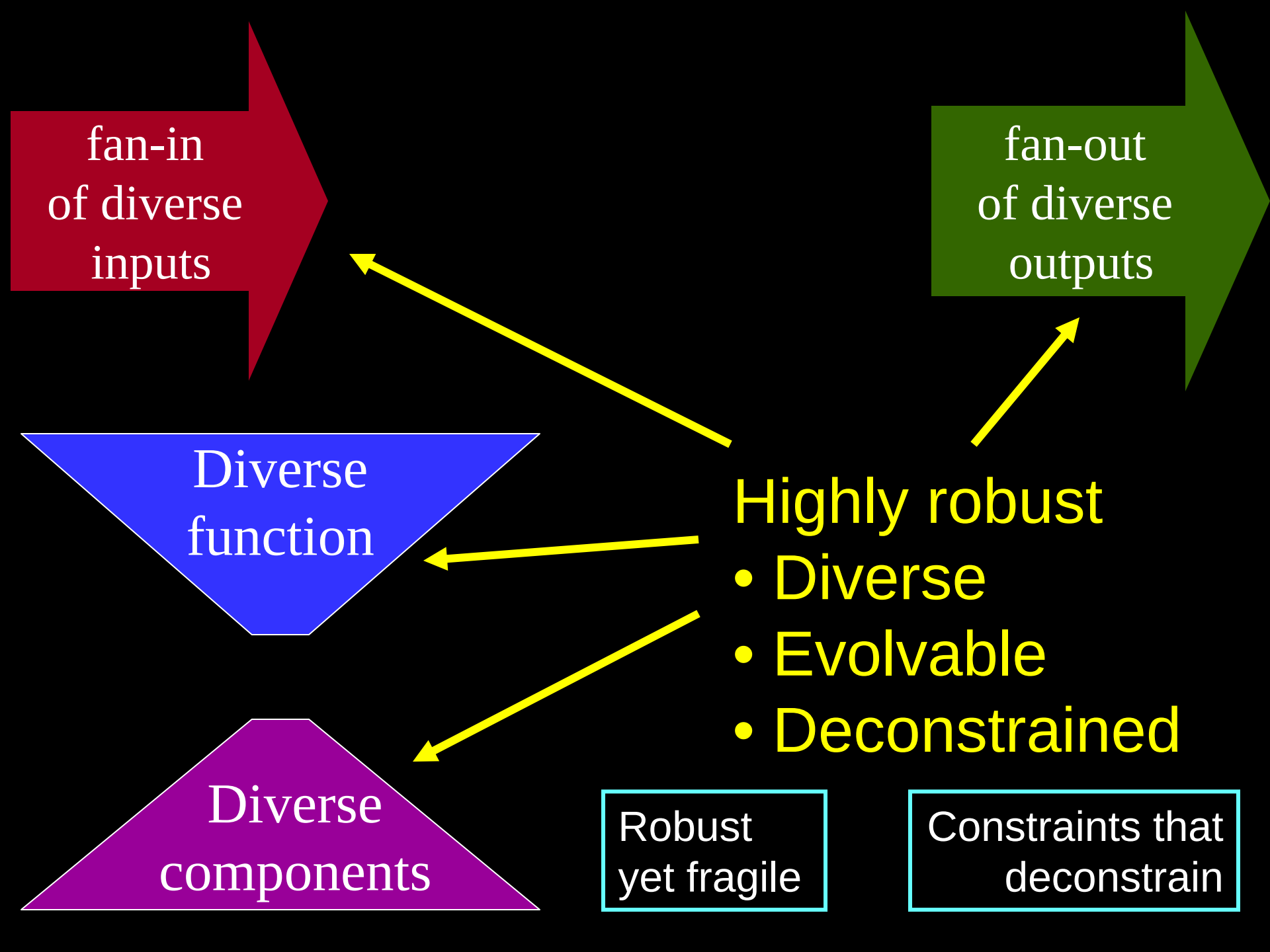




Essential ideas

Robust yet fragile

Constraints that deconstrain


fan-in
of diverse
inputs
fan-out
of diverse
outputs
Diverse
function
Highly robust
• Diverse
• Evolvable
• Deconstrained
Diverse
components
Robust
yet fragile
Constraints that
deconstrain

universal carriers

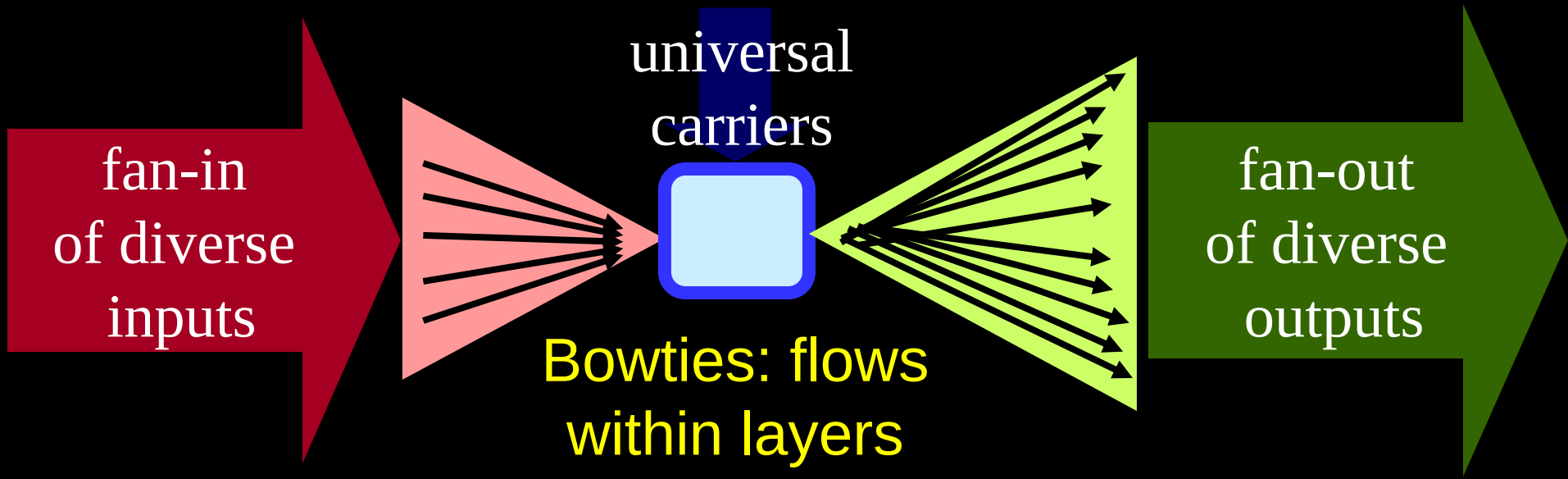
Highly fragile

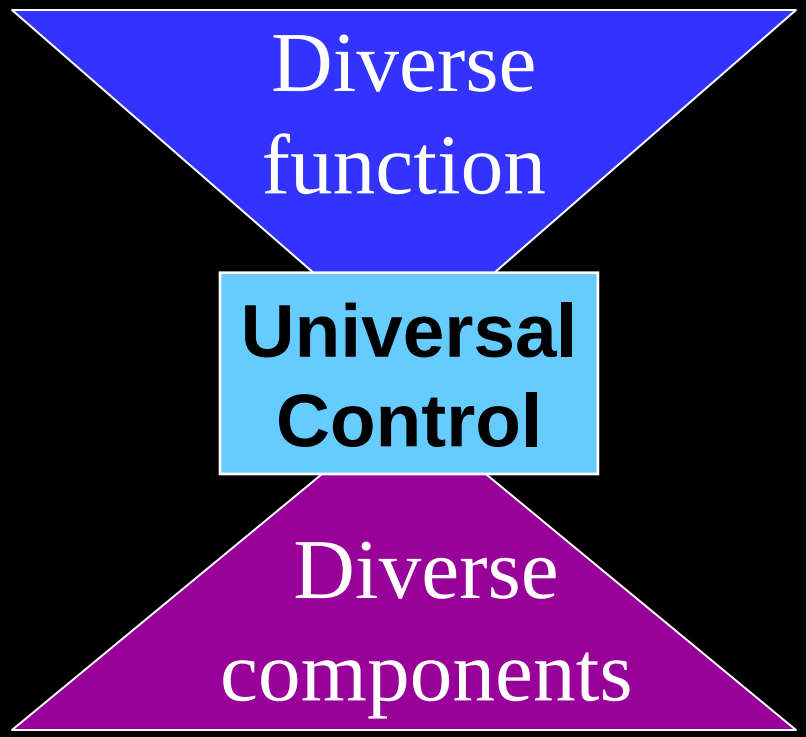
- Universal
- Frozen
- Constrained

Universal Control

Robust yet fragile

Constraints that deconstrain





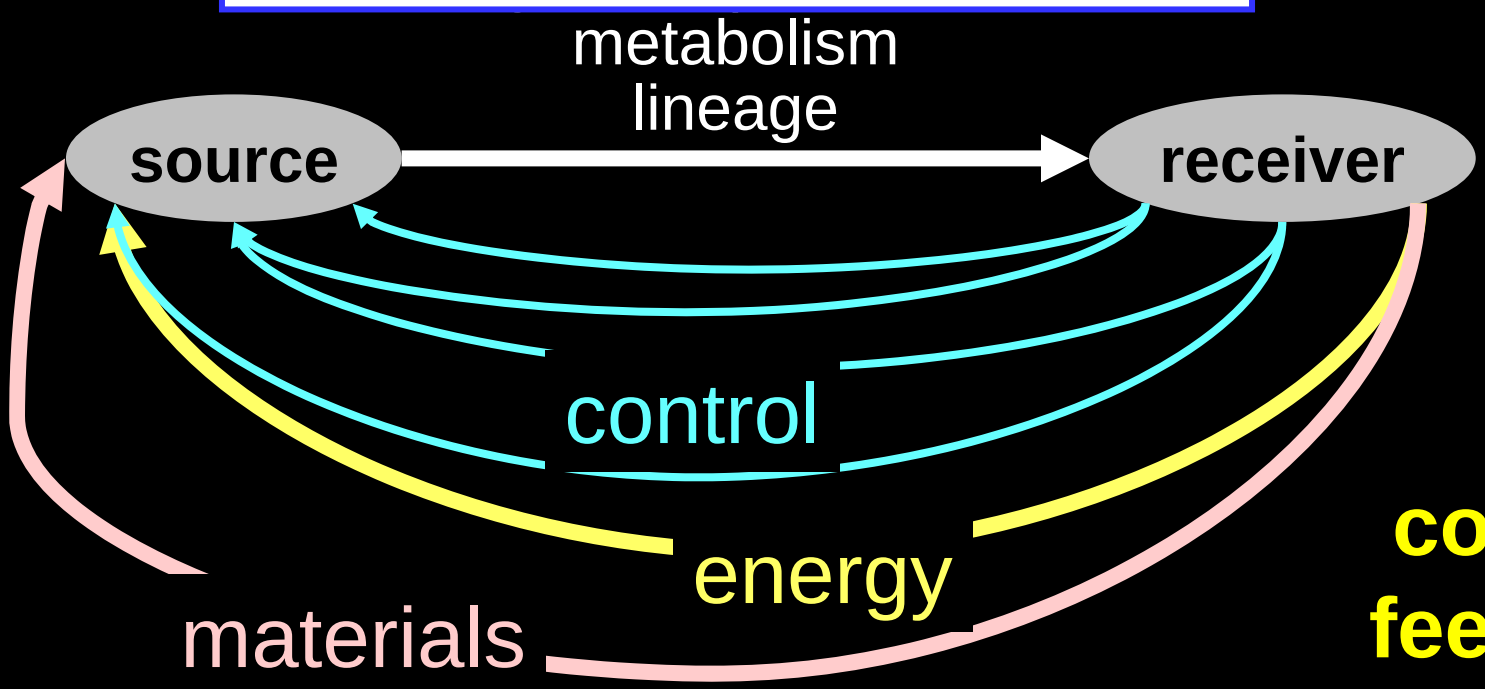
Essential ideas

Robust yet fragile

Constraints that deconstrain

What theory is relevant to these more complex feedback systems?

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



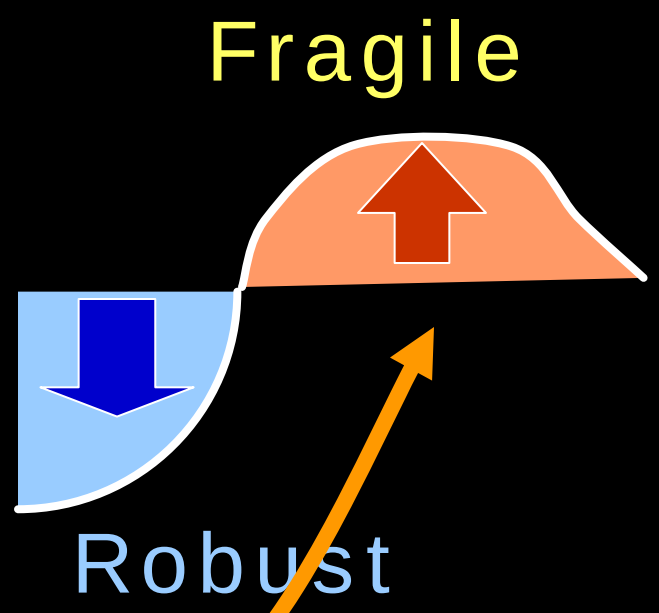
More complex feedback

[a system] can have
[a property] ***robust*** for
[a set of perturbations]

Yet be ***fragile for***

[a different property]

Or [a different perturbation]



Robust yet fragile = fragile robustness

[a system] can have
[a property] ***robust*** for
[a set of perturbations]

Apply recursively

[a property]

[property] = ***robust*** for
[one set of perturbations]

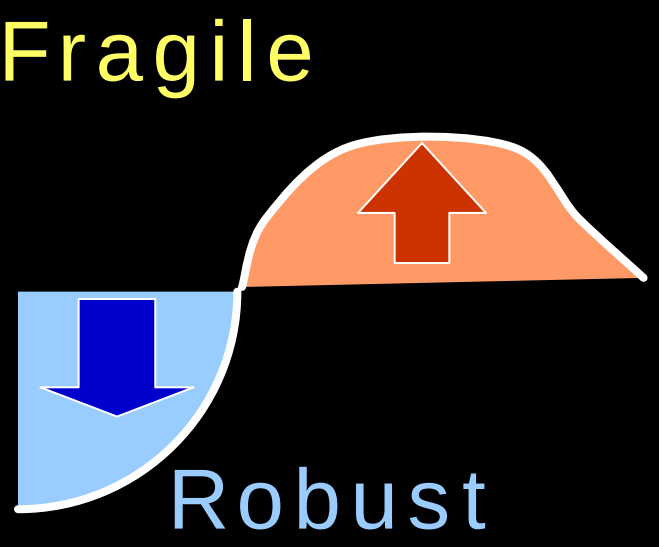
fragile for

[another property] or
[another set of perturbations]

[a perturbation]

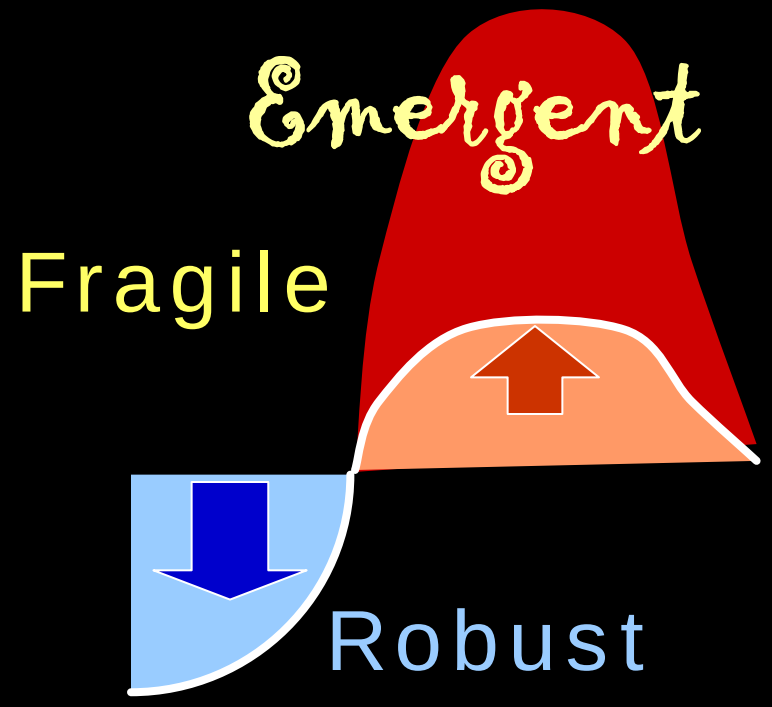
Robust yet fragile = fragile robustness

[a system] can have
[a property] ***robust*** for
[a set of perturbations]



- Some fragilities are inevitable in robust complex systems.

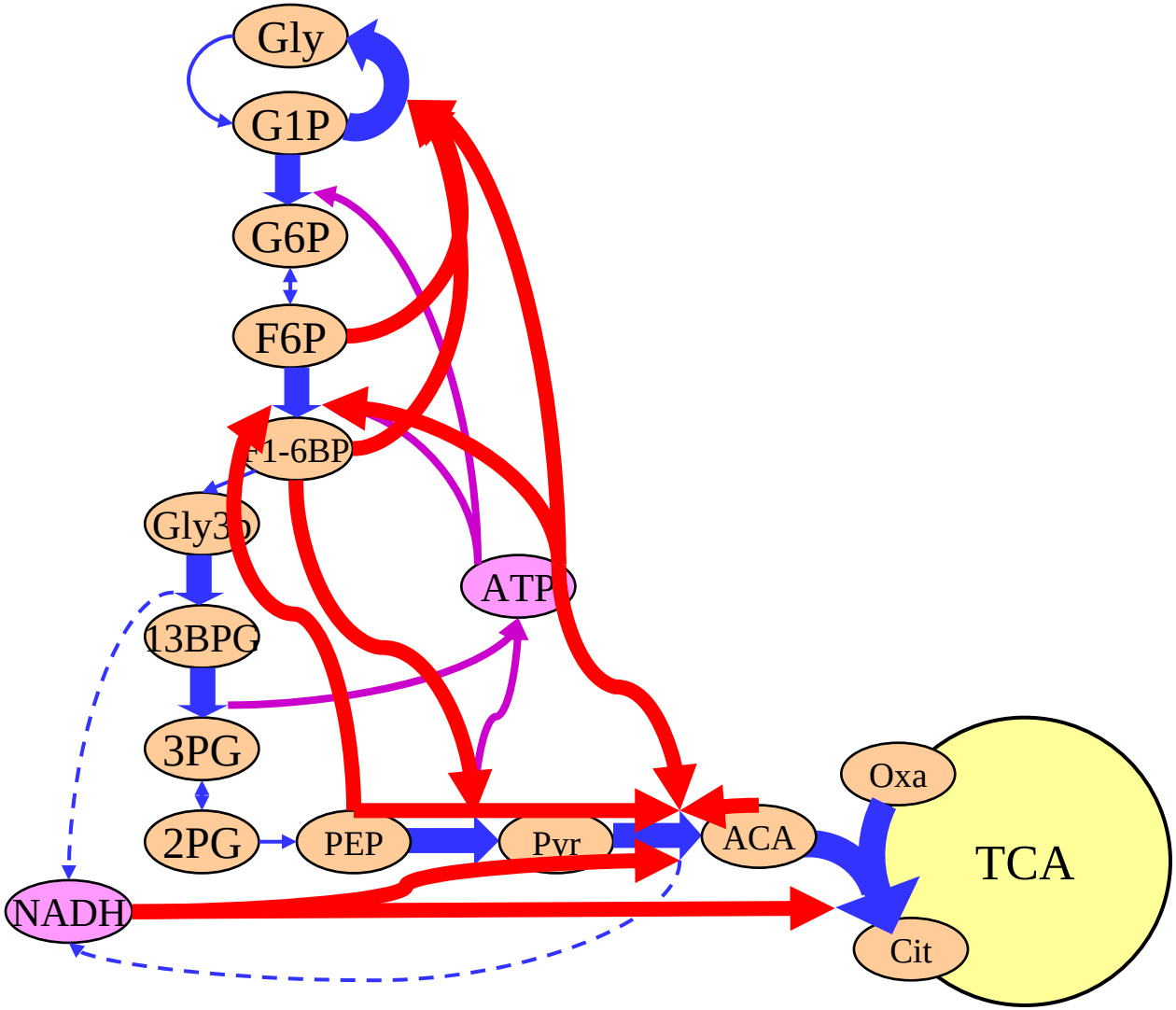
- But if robustness/fragility are ***conserved***, what does it mean for a ***system*** to be robust or fragile?

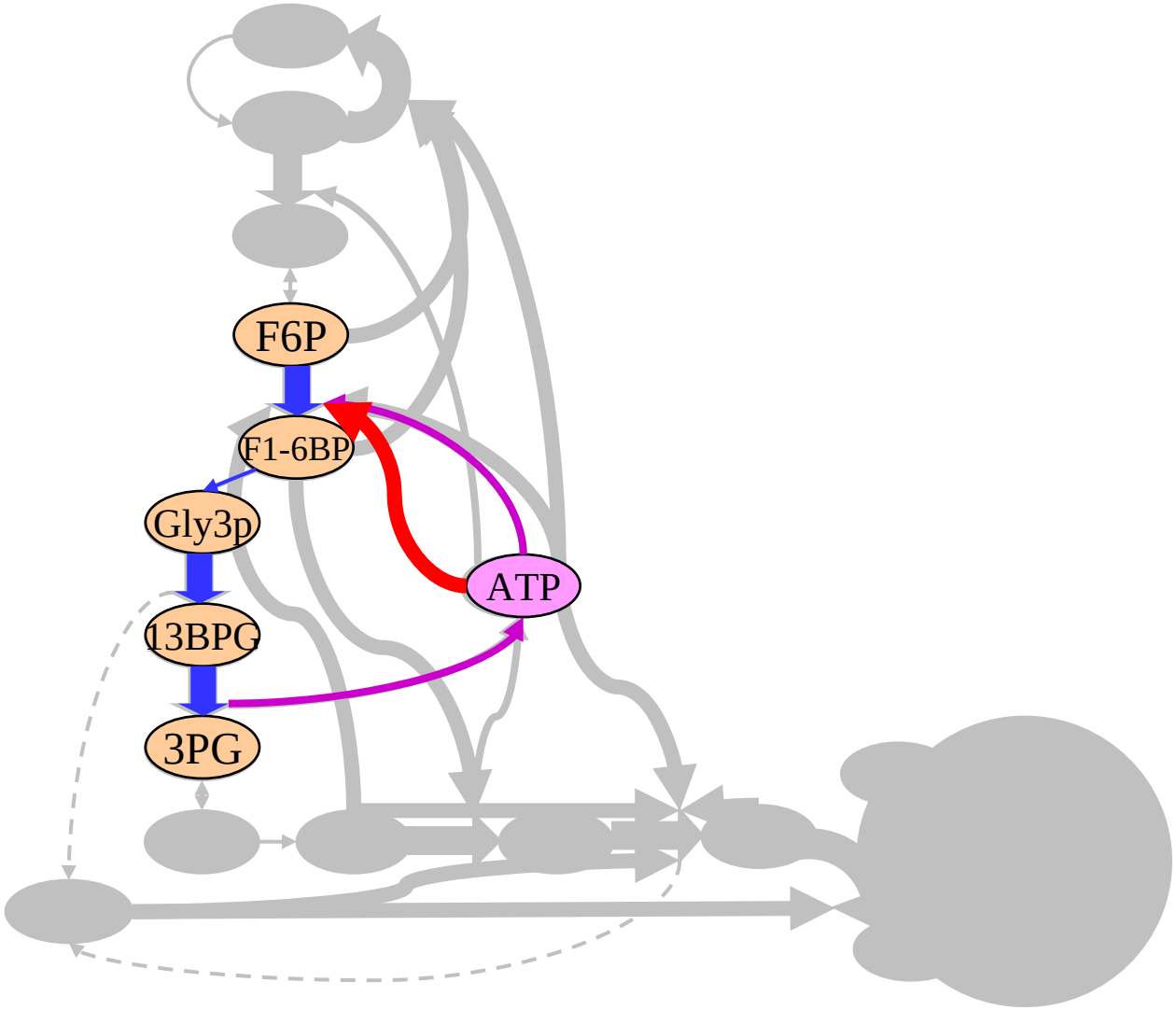


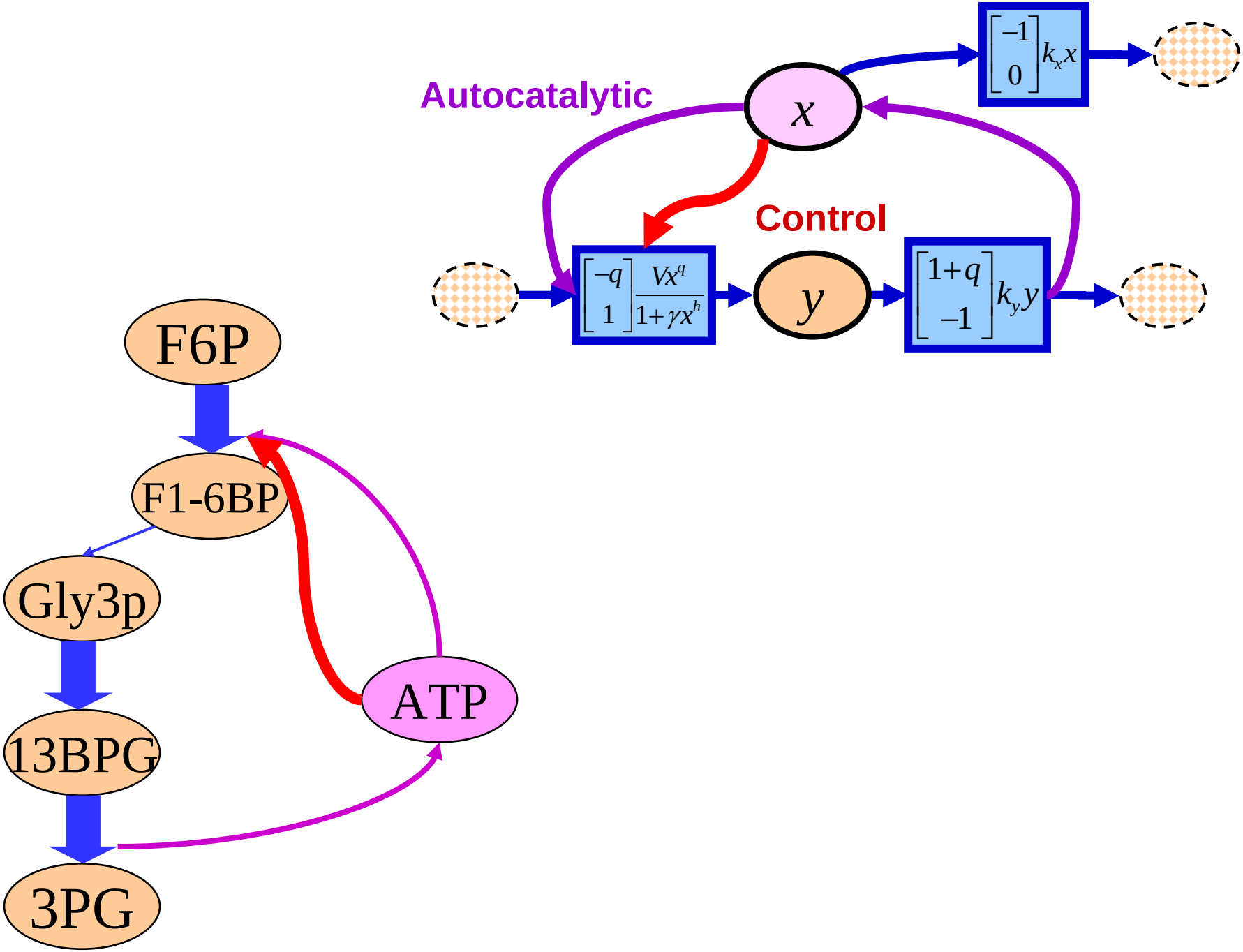
- Some fragilities are inevitable in robust complex systems.

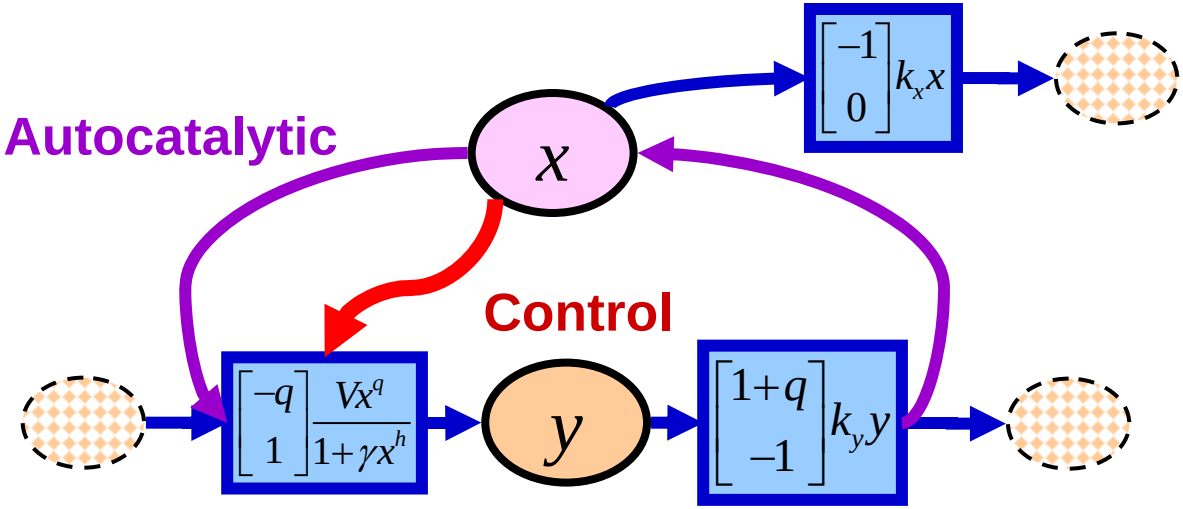
- But if robustness/fragility are ***conserved***, what does it mean for a ***system*** to be robust or fragile?

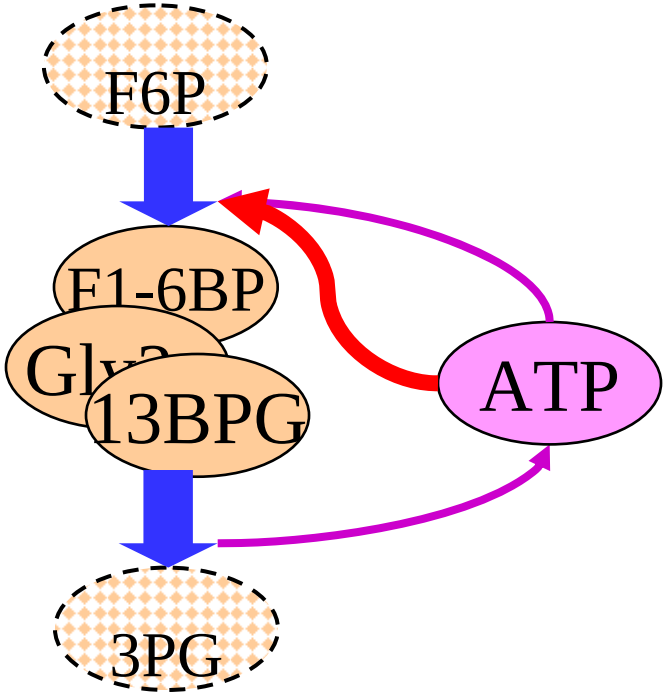
- Robust ***systems*** systematically manage this tradeoff.
- Fragile ***systems*** waste robustness.

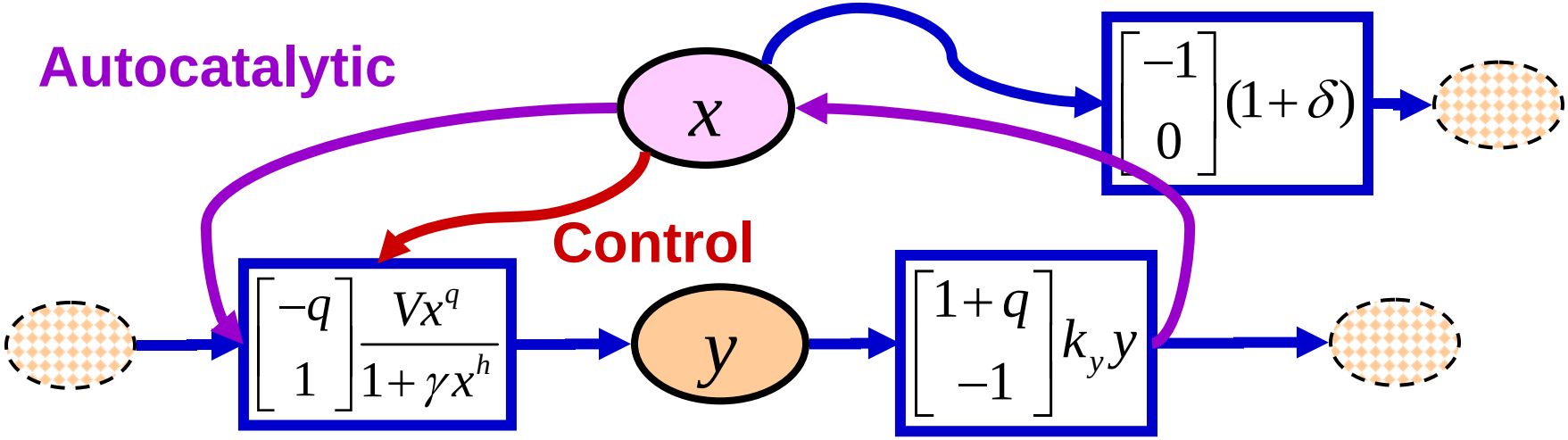

Gly
G1P
G6P
F6P
F1-6BP
Gly3p
ATP
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit
NADH


F6P
F1-6BP
Gly3p
13BPG
3PG
ATP


Autocatalytic
Control
x
y
$\begin{bmatrix}-1\\0\end{bmatrix} k_x x$
$\begin{bmatrix}-q\\1\end{bmatrix} \frac{Vx^q}{1+\gamma x^h}$
$\begin{bmatrix}1+q\\-1\end{bmatrix} k_y y$
F6P
F1-6BP
Gly3p
13BPG
3PG
ATP


Autocatalytic
Control
x
y
$\begin{bmatrix} -1 \\ 0 \end{bmatrix} k_x x$
$\begin{bmatrix} -q \\ 1 \end{bmatrix} \frac{Vx^q}{1+\gamma x^h}$
$\begin{bmatrix} 1+q \\ -1 \end{bmatrix} k_y y$


F6P
F1-6BP
Gly3
13BPG
ATP
3PG



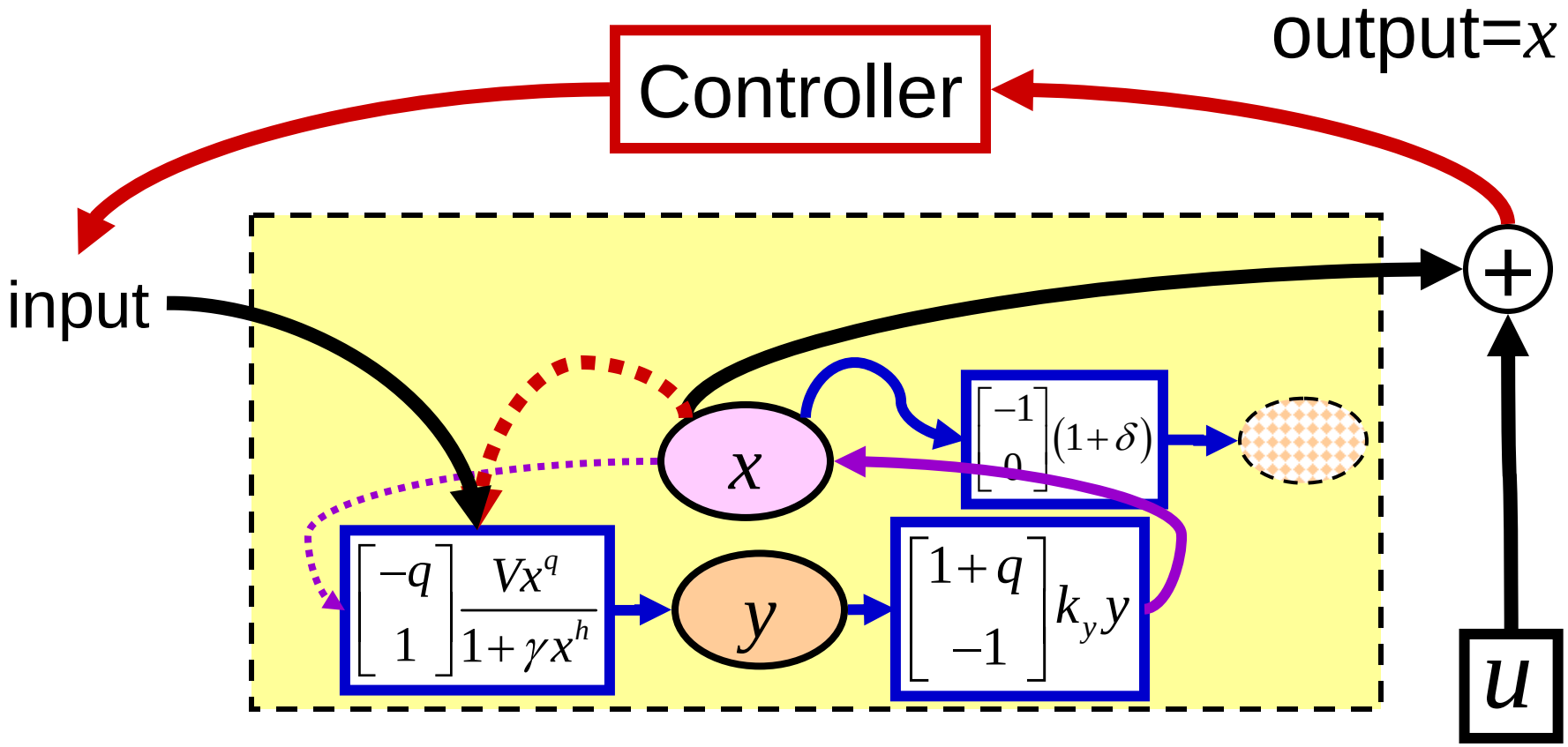
Autocatalytic

$$\begin{bmatrix} \dot{x} \\ \dot{y} \end{bmatrix} = \begin{bmatrix} -q \\ 1 \end{bmatrix} \left(\frac{Vx^q}{1+\gamma x^h} \right) + \begin{bmatrix} 1+q \\ -1 \end{bmatrix} ky + \begin{bmatrix} -1 \\ 0 \end{bmatrix} (1+\delta)$$

Control

Control theory cartoon

$$S(j\omega) = \frac{x}{u}$$



Caution: mixed cartoon

Hard limits

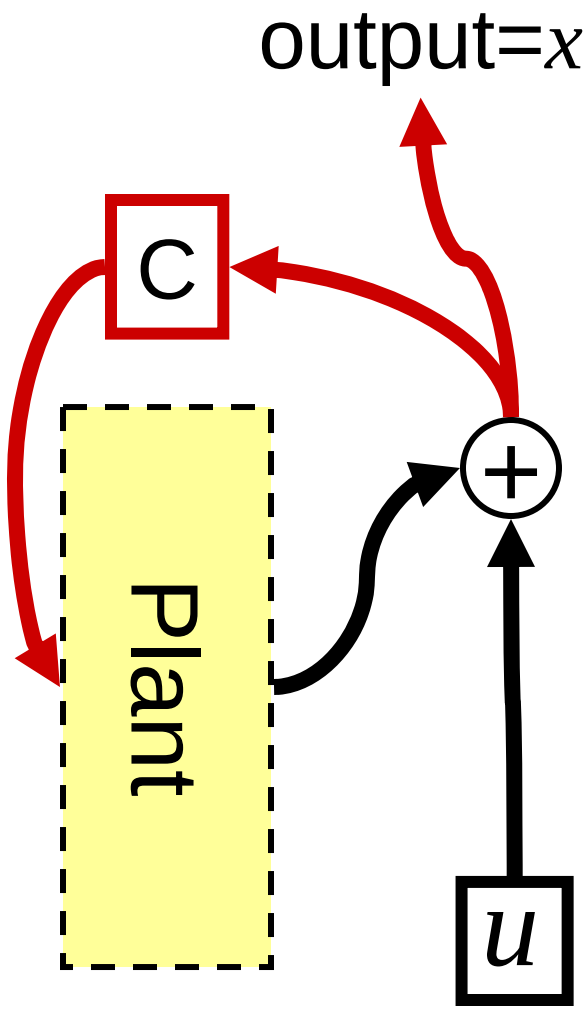
$$\boxed{S(j\omega) = \frac{X(j\omega)}{U(j\omega)}}$$

$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq 0$$

$$\int_{-\infty}^{\infty} \ln\left|S(j\omega)\right| d\omega = \int_{-\infty}^{\infty} \ln\left|\frac{X(j\omega)}{U(j\omega)}\right| d\omega$$

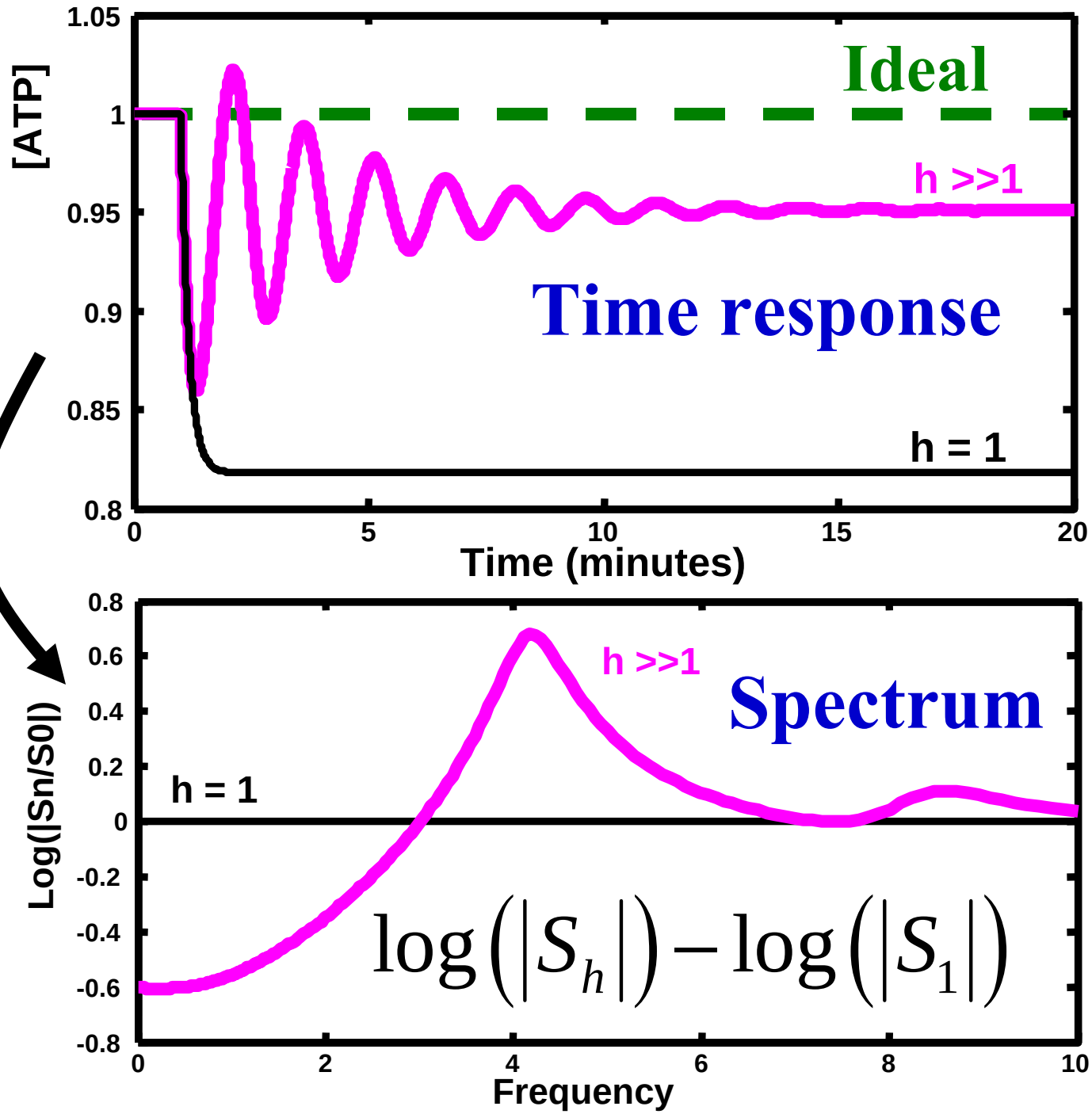
$$= \int_{-\infty}^{\infty} \ln\left|X(j\omega)\right| d\omega - \int_{-\infty}^{\infty} \ln\left|U(j\omega)\right| d\omega$$

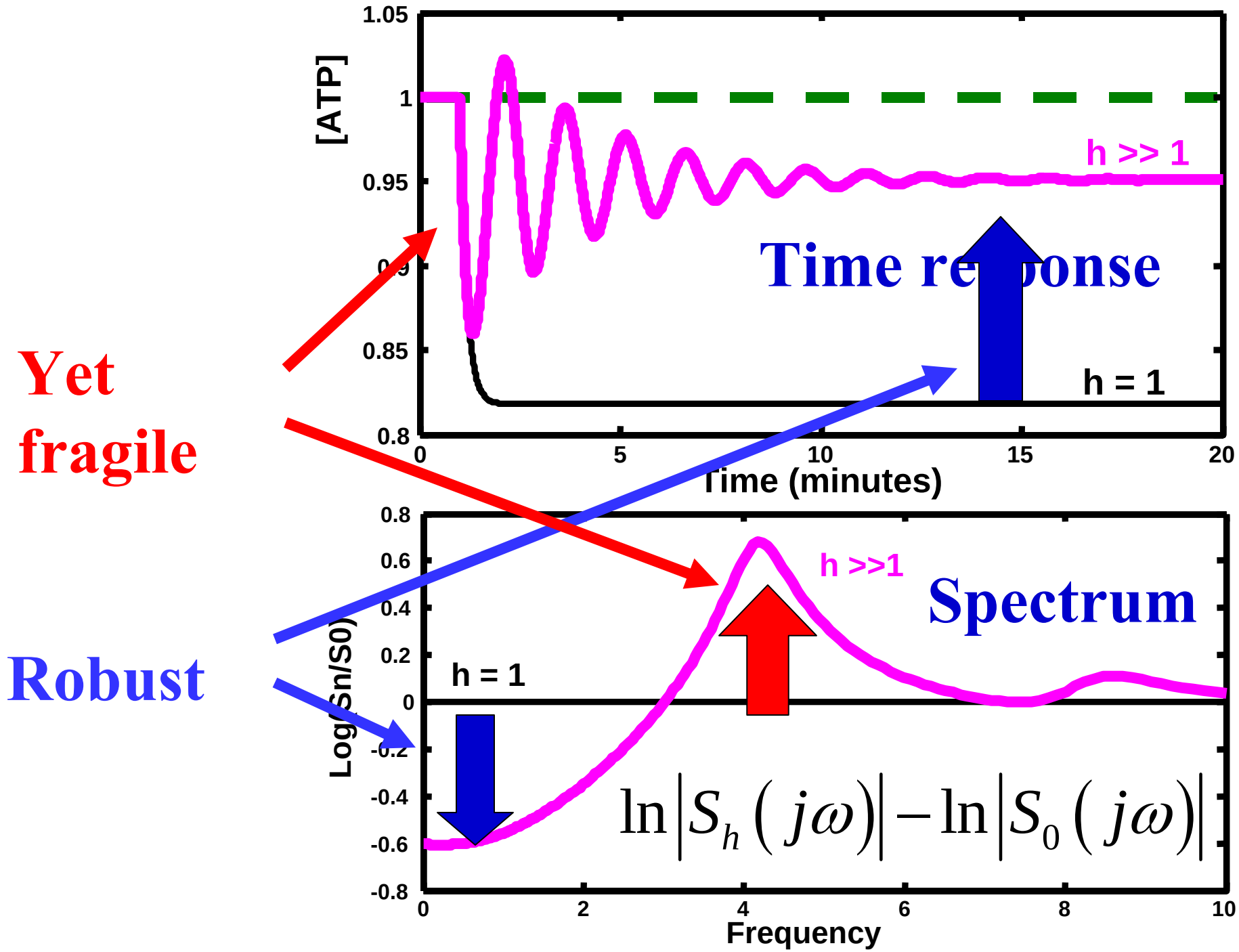
Entropy rates



$$S_h = \mathrm{F}(x)\big|_h$$

Fourier Transform of error

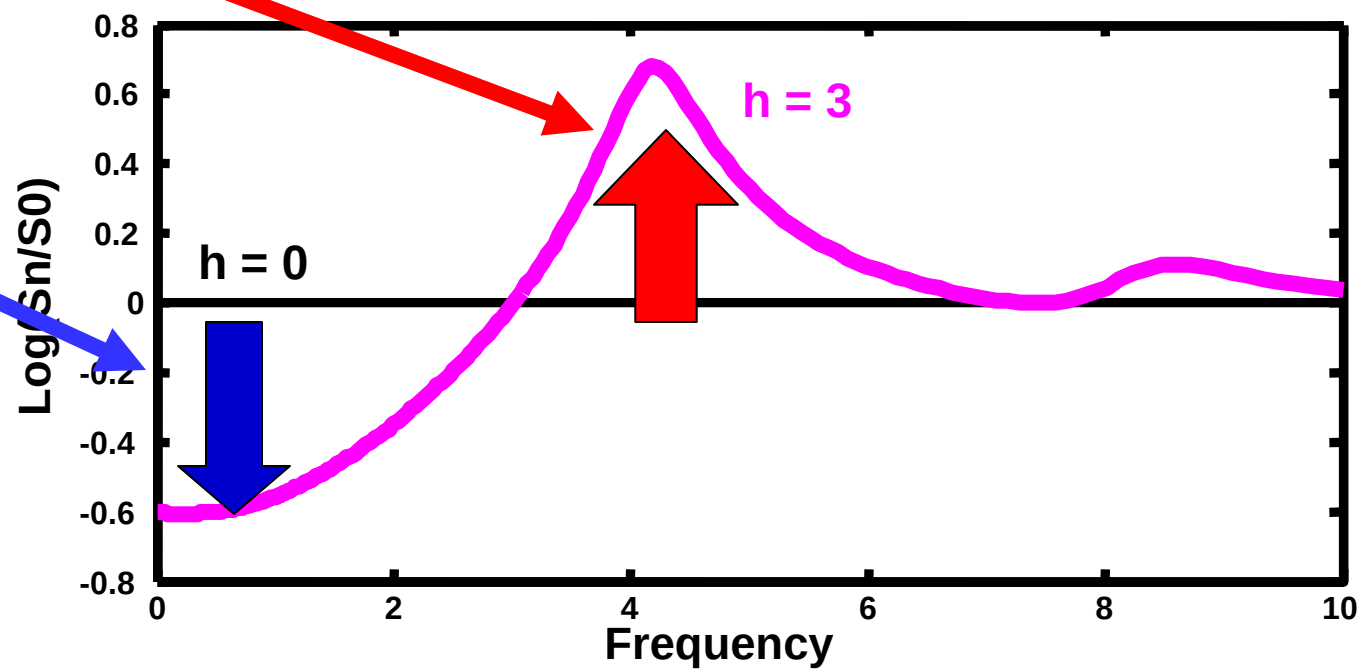



Yet fragile
Robust
[ATP]
1.05
1
0.95
0.9
0.85
0.8
0
5
10
15
20
Time (minutes)
h >> 1
h = 1
Time response
Log(Sn/S0)
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
0
2
4
6
8
10
Frequency
h >>1
h = 1
Spectrum
$\ln\left|S_h(j\omega)\right| - \ln\left|S_0(j\omega)\right|$

$$\int_0^\infty \Delta \ln \left| S(j\omega) \right| d\omega = 0$$

Yet fragile

Robust

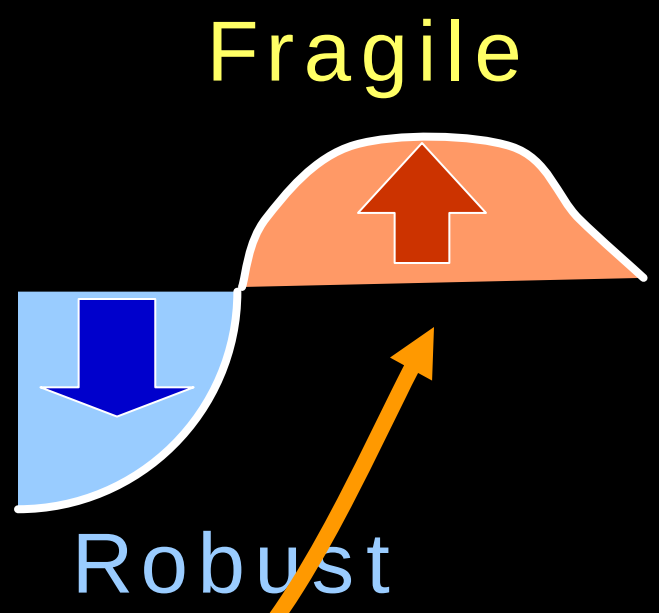


[a system] can have
[a property] ***robust*** for
[a set of perturbations]

Yet be ***fragile for***

[a different property]

Or [a different perturbation]



Robust yet fragile = fragile robustness

Hard limits

$$S(j\omega) = \frac{X(j\omega)}{U(j\omega)}$$

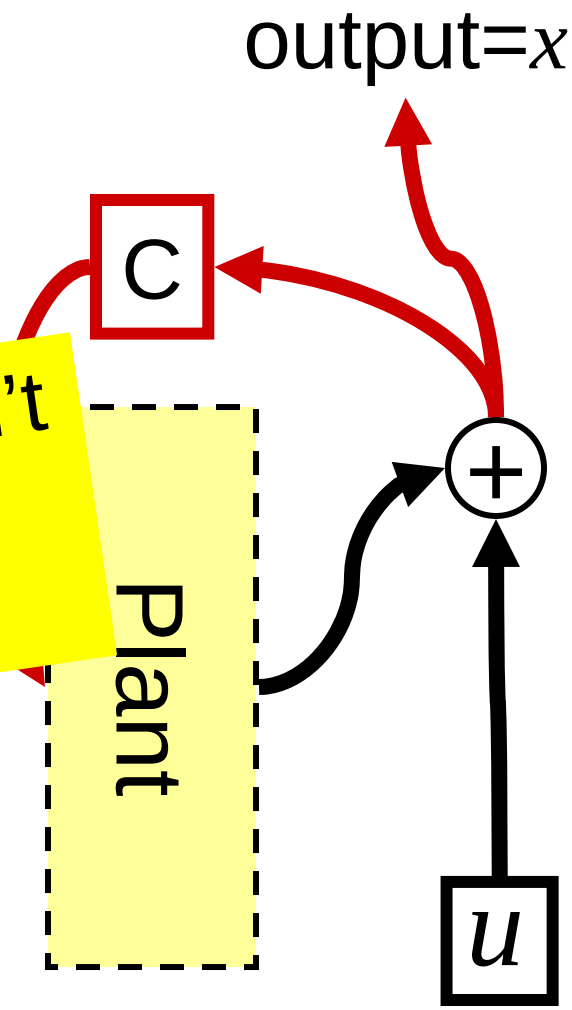
$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq 0$$

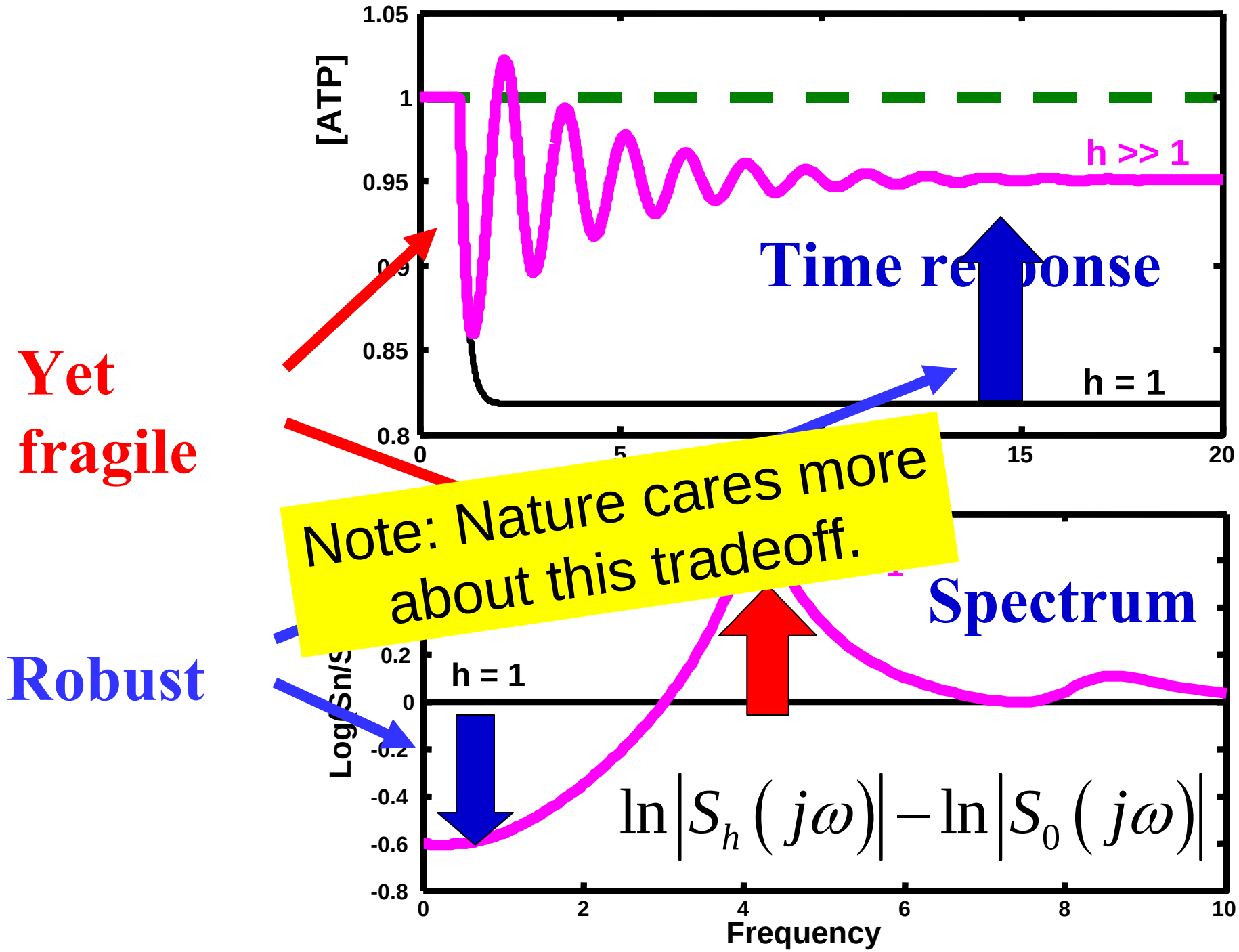
$$\int_{-\infty}^{\infty} \ln\left|S(j\omega)\right| d\omega$$

$$= \int_{-\infty}^{\infty} \ln\left|X(j\omega)\right| d\omega - \int_{-\infty} \ln\left|U(j\omega)\right| d\omega$$

Entropy rates

Note: Nature doesn't care much about entropy rates.

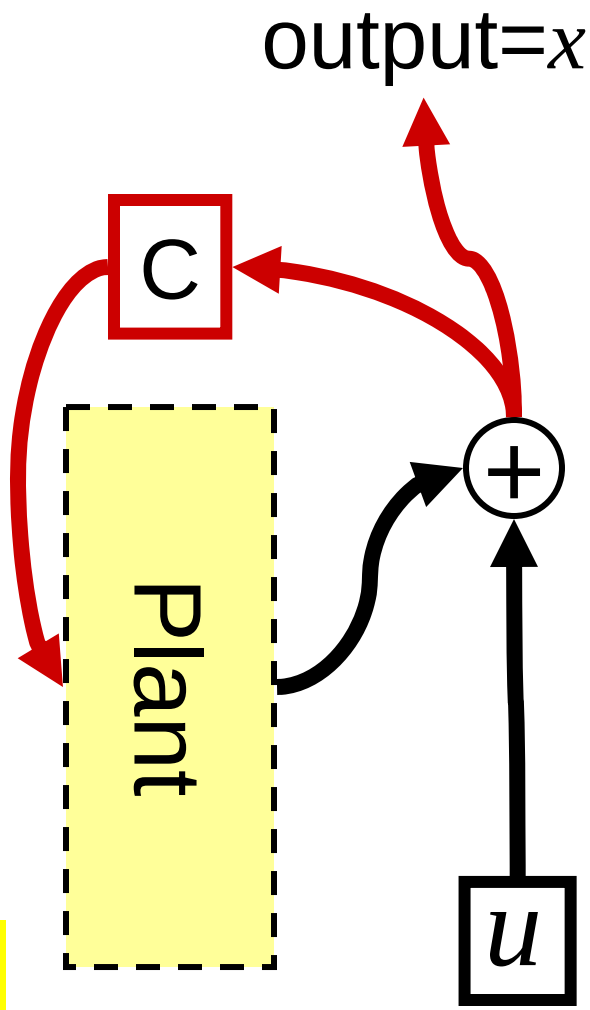



[ATP]
1.05
1
0.95
0.9
0.85
0.8
0
5
15
20
h >> 1
h = 1
Time response
Yet fragile
Note: Nature cares more about this tradeoff.
Spectrum
Robust
Log|Sn/S
0.2
0
-0.2
-0.4
-0.6
-0.8
h = 1
0
2
4
6
8
10
Frequency
$\ln\left|S_h(j\omega)\right| - \ln\left|S_0(j\omega)\right|$

$$\boxed{S(j\omega) = \frac{X(j\omega)}{U(j\omega)}}$$

$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq 0$$

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



The plant can make this tradeoff worse.

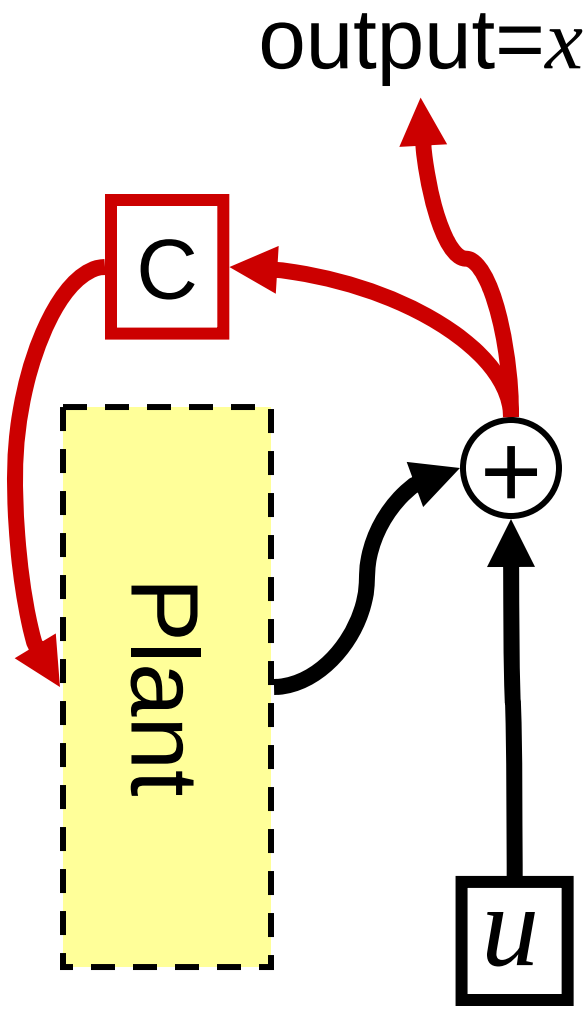
$$S(j\omega) = \frac{X(j\omega)}{U(j\omega)}$$

$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq 0$$

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

All controllers: $\geq$

Biological cells: $=$



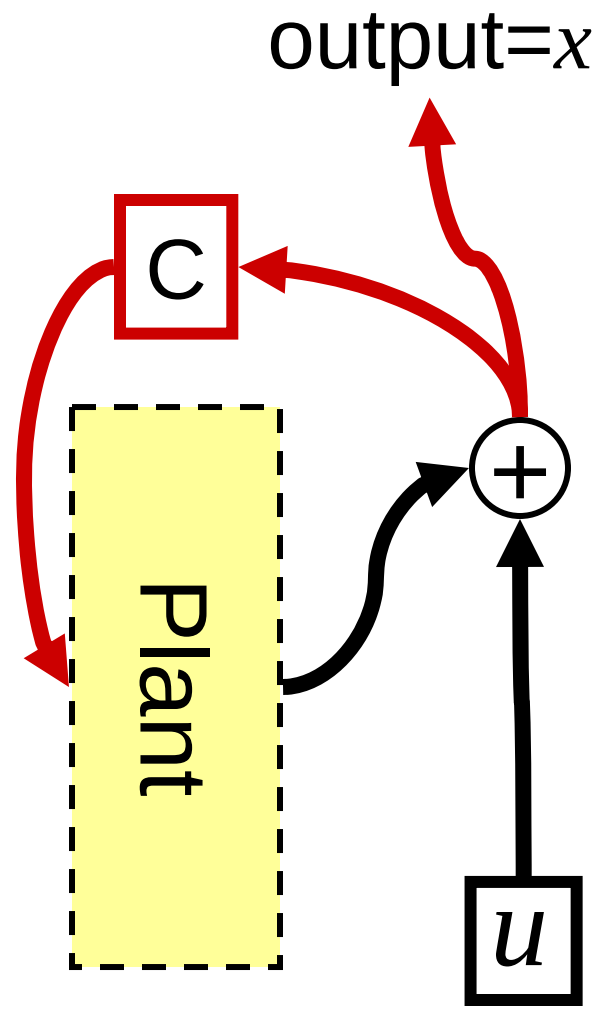
$$z = \frac{k}{q} \qquad p = RHPzero\left\{s^2 + (q\alpha + k)s - \alpha k\right\}$$

$$\boxed{S(j\omega) = \frac{X(j\omega)}{U(j\omega)}}$$

$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq 0$$

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

Small *z* is *bad*.



$$\boxed{z = \frac{k}{q}}$$

$$p = RHPzero\left\{s^2 + (q\alpha + k)s - \alpha k\right\}$$

Small z is *bad*
(oscillations and crashes)

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

Small z =

- **small k and/or**
- **large q**

Efficiency =

- **small k and/or**
- **large q**

$$\boxed{z = \frac{k}{q}}$$

Correctly predicts conditions with “glycolytic oscillations”

Hard limits

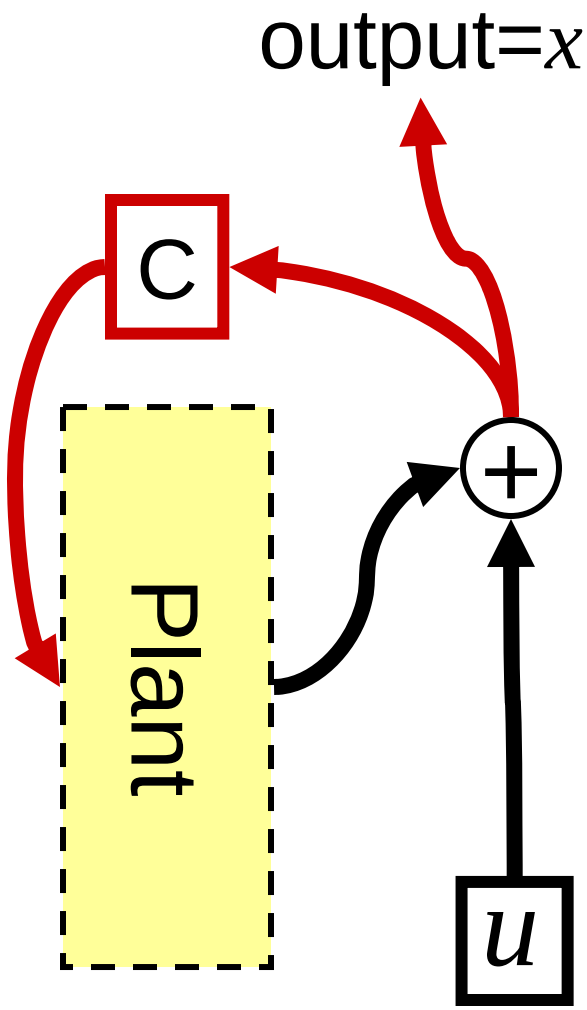
$$\boxed{S(j\omega) = \frac{X(j\omega)}{U(j\omega)}}$$

$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq 0$$

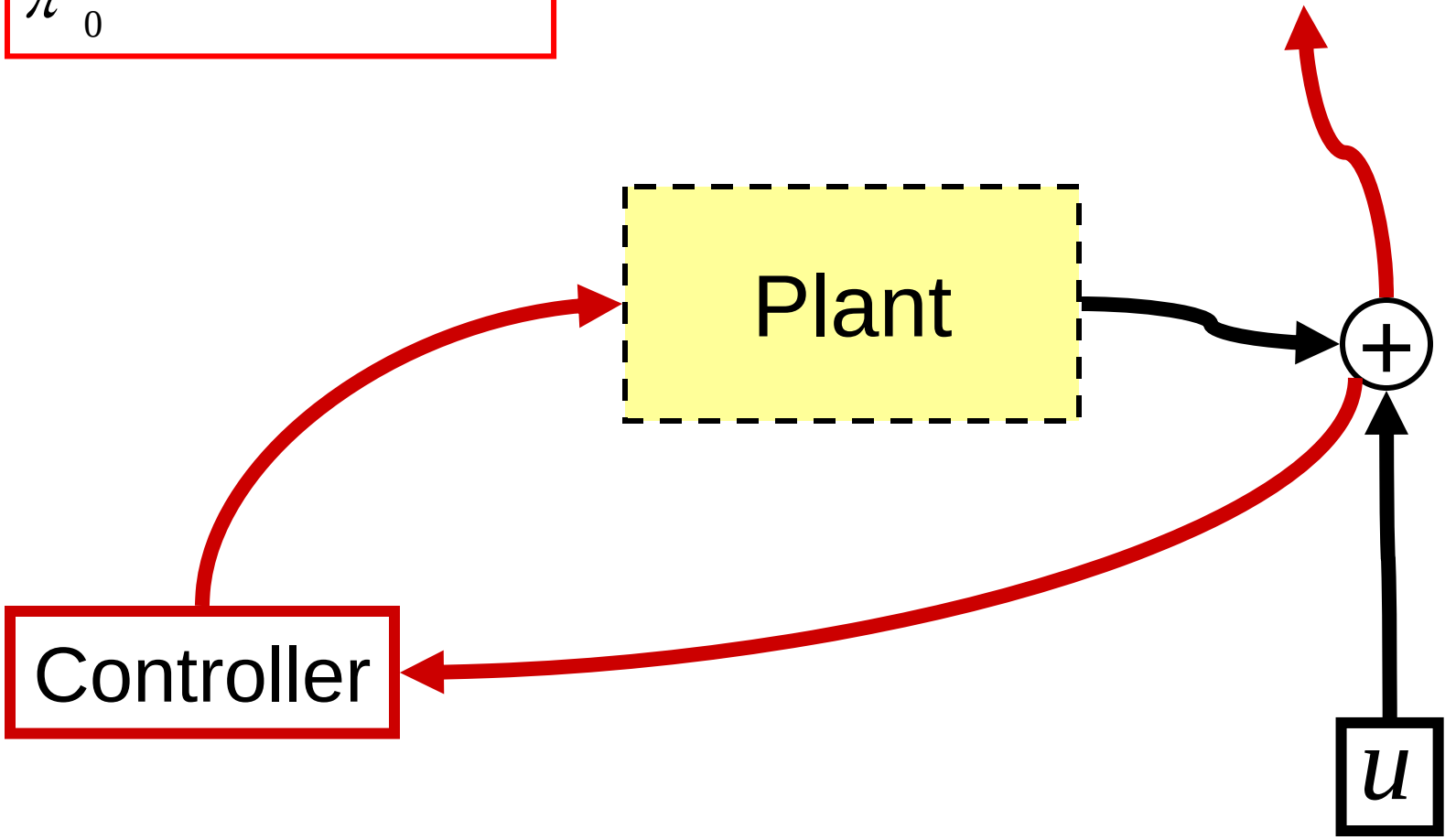
$$\int_{-\infty}^{\infty} \ln\left|S(j\omega)\right| d\omega = \int_{-\infty}^{\infty} \ln\left|\frac{X(j\omega)}{U(j\omega)}\right| d\omega$$

$$= \int_{-\infty}^{\infty} \ln\left|X(j\omega)\right| d\omega - \int_{-\infty}^{\infty} \ln\left|U(j\omega)\right| d\omega$$

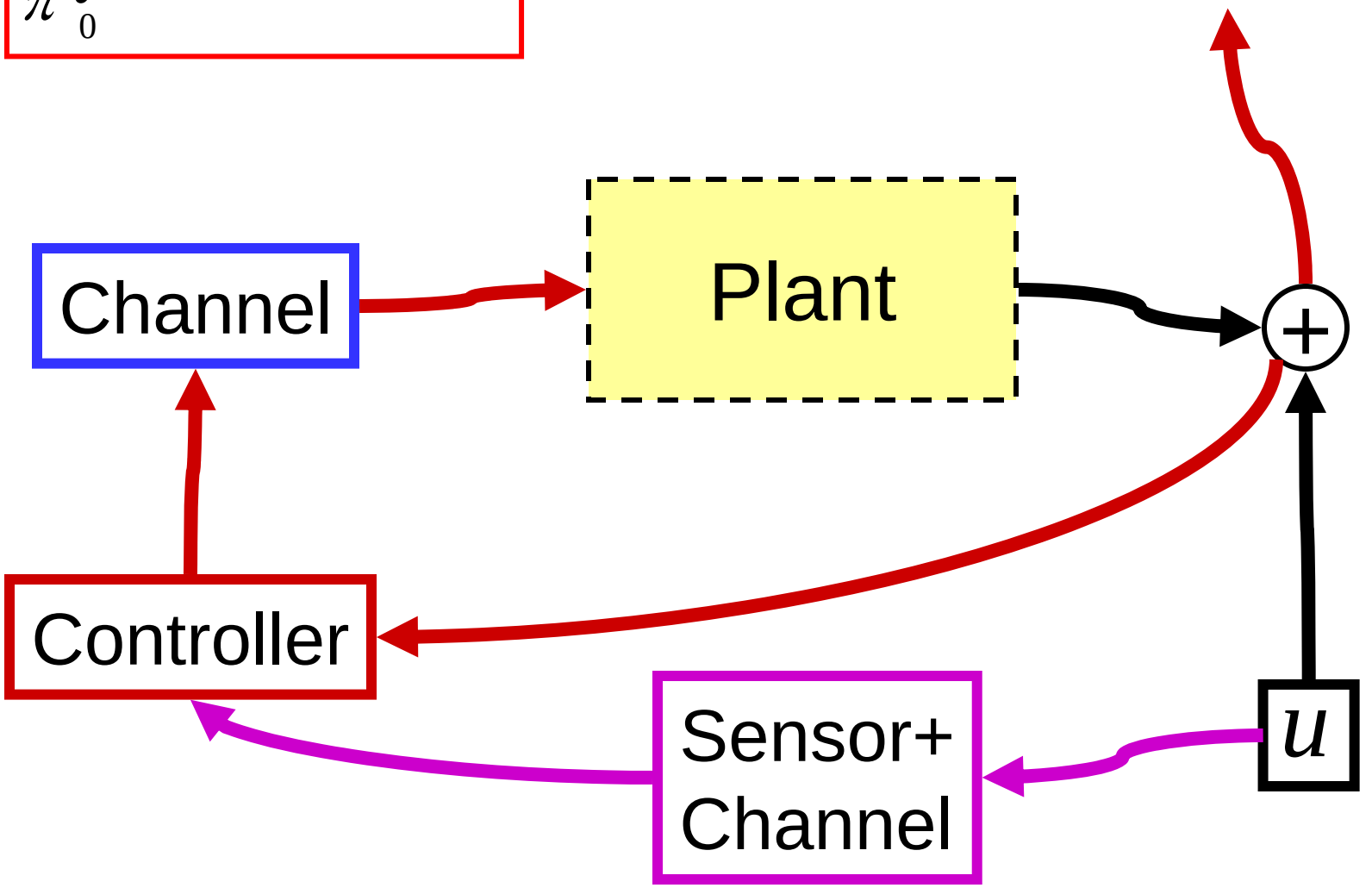
Entropy rates



$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq 0$$



$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq 0$$

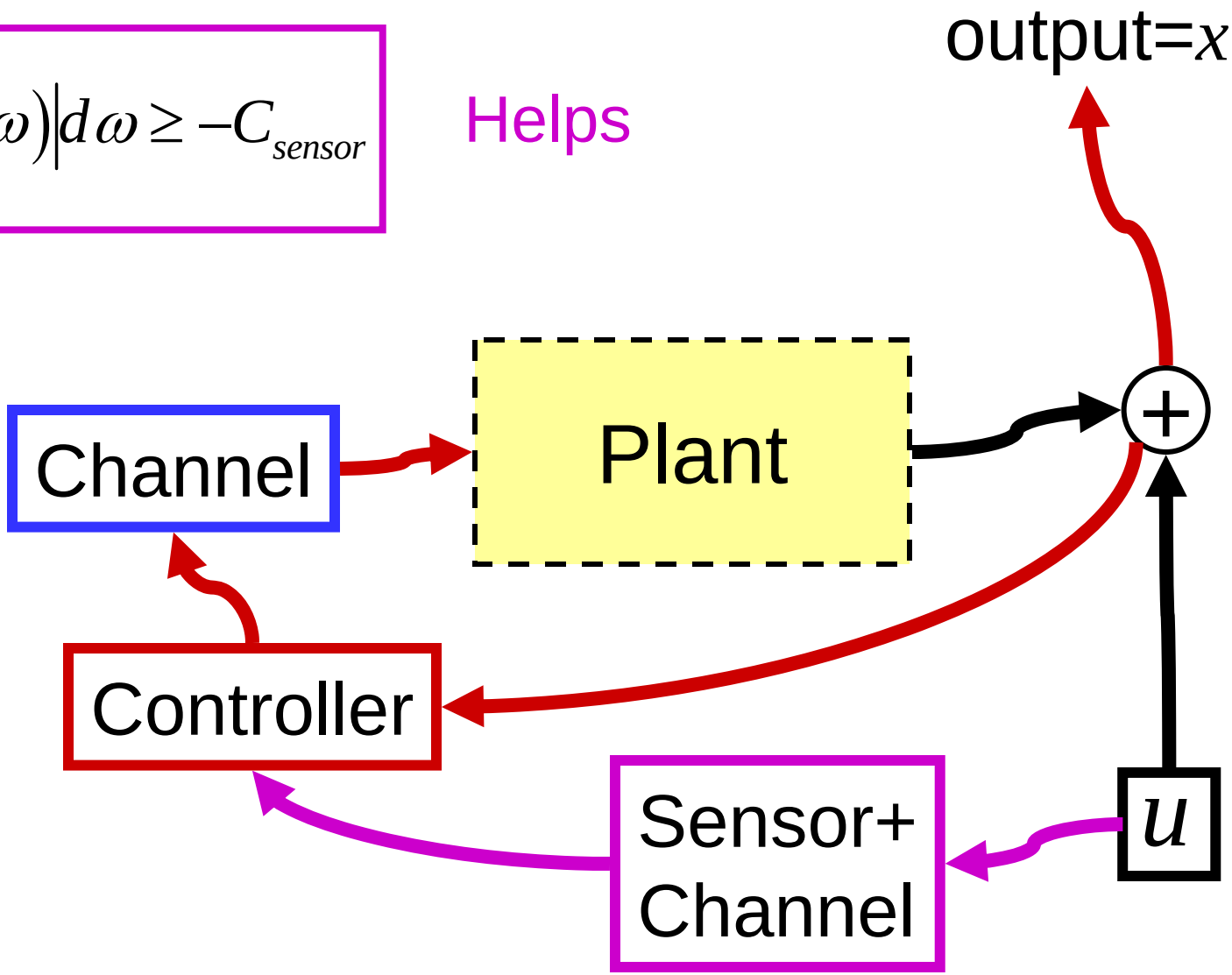


$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right|_\, d\omega \geq -C_{FB}$$

Hurts

$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq -C_{sensor}$$

Helps

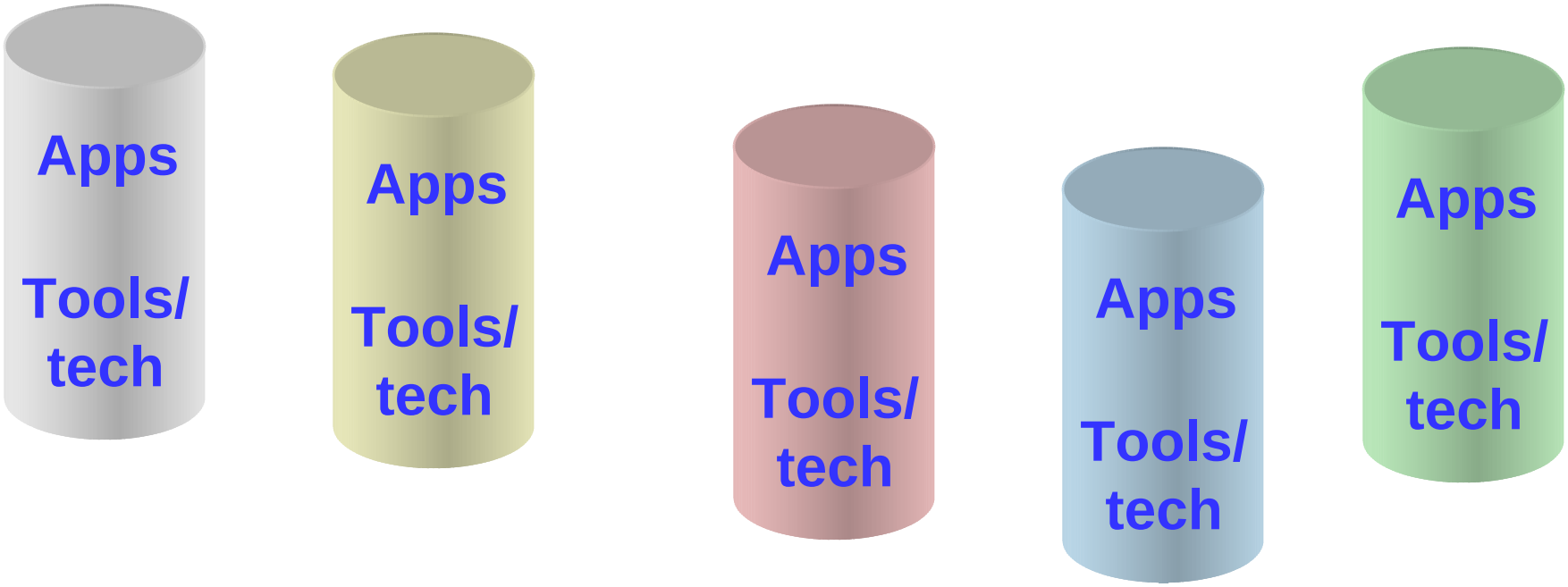


	Small	Large
Robust	Simple	Organized
Fragile	Chaocritical	Irreducible

- Taxonomy covers standard usages
- Unified picture
- Can make the definitions more precise
- Have “hand crafted” theorems in every major complexity class (but lack a unified theory)

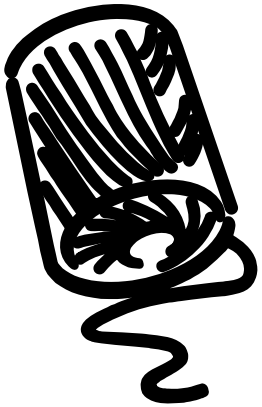
Academic stovepipes

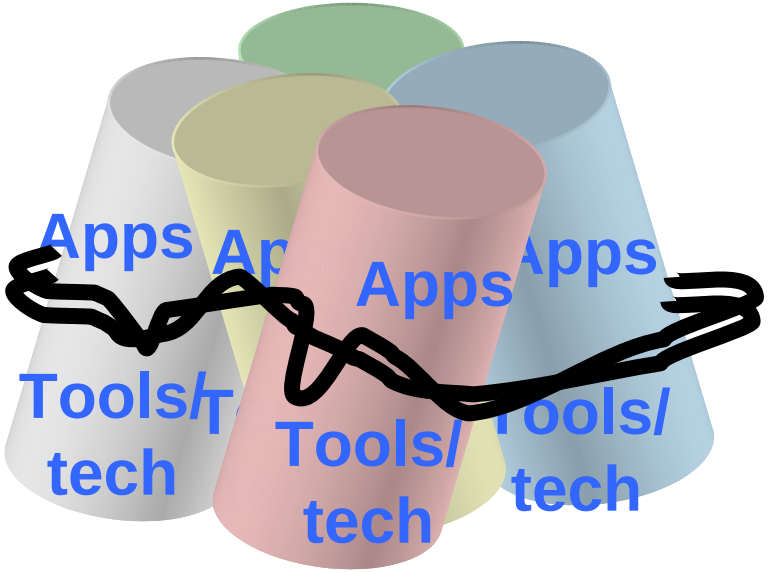
EE, CS, ME, MS, APh, ChE, Bio, Geo, Eco, …



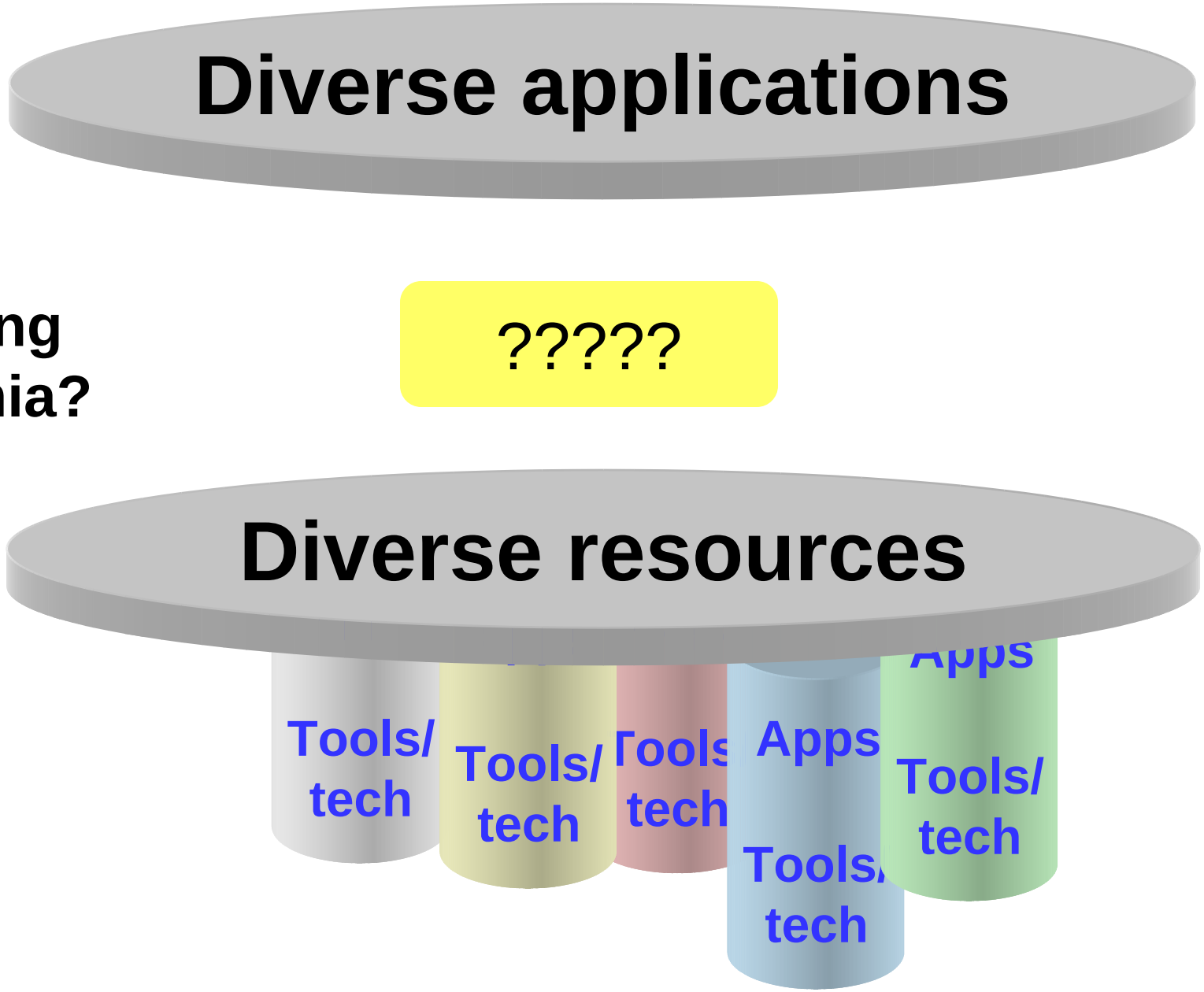
Diverse applications

Funding twine



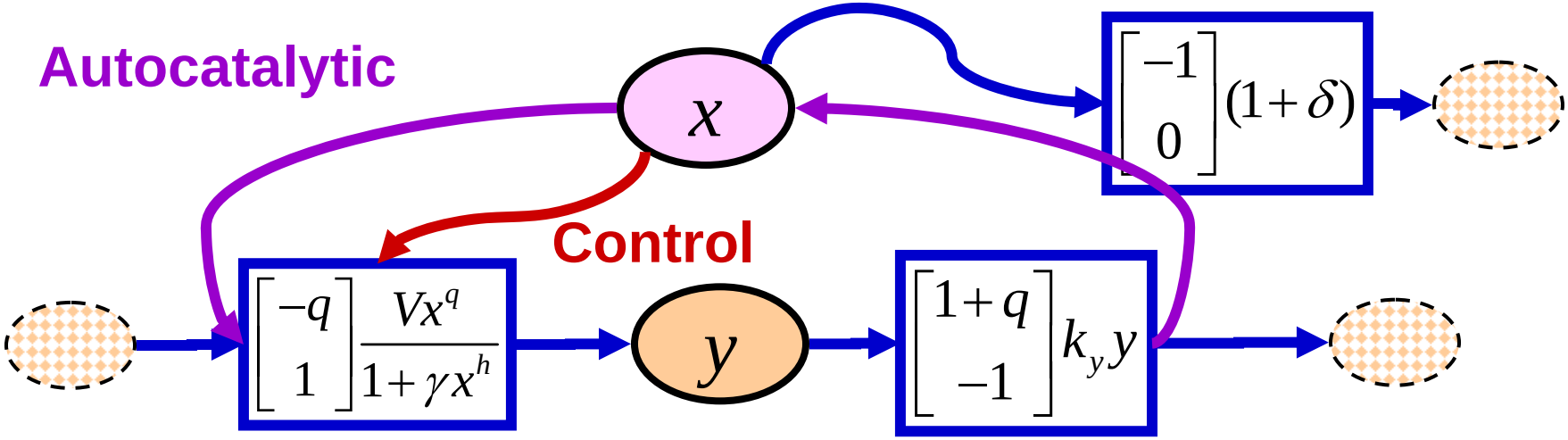


“Multidisciplinary cross-sterilization”


Diverse applications
Layering academia?
?????
Diverse resources
Tools/ tech
Tools/ tech
Tools tech
Apps
Tools/ tech
Apps
Tools/ tech

End

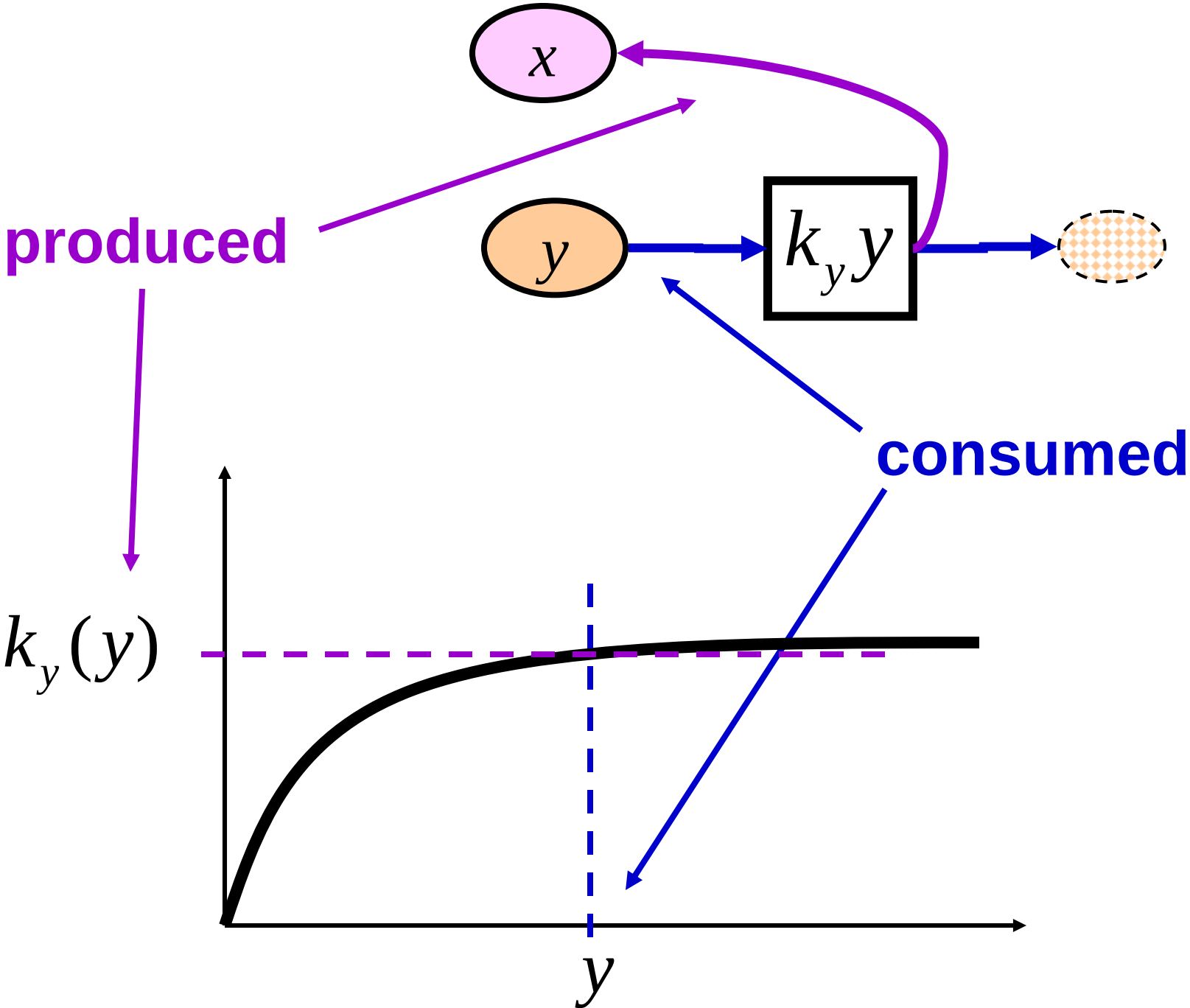
What follows are additional details on the glycolysis fragility example.



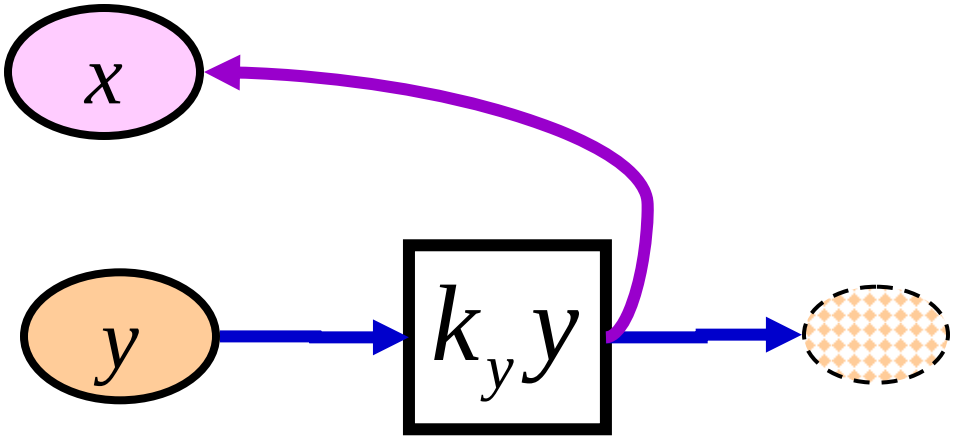
Autocatalytic

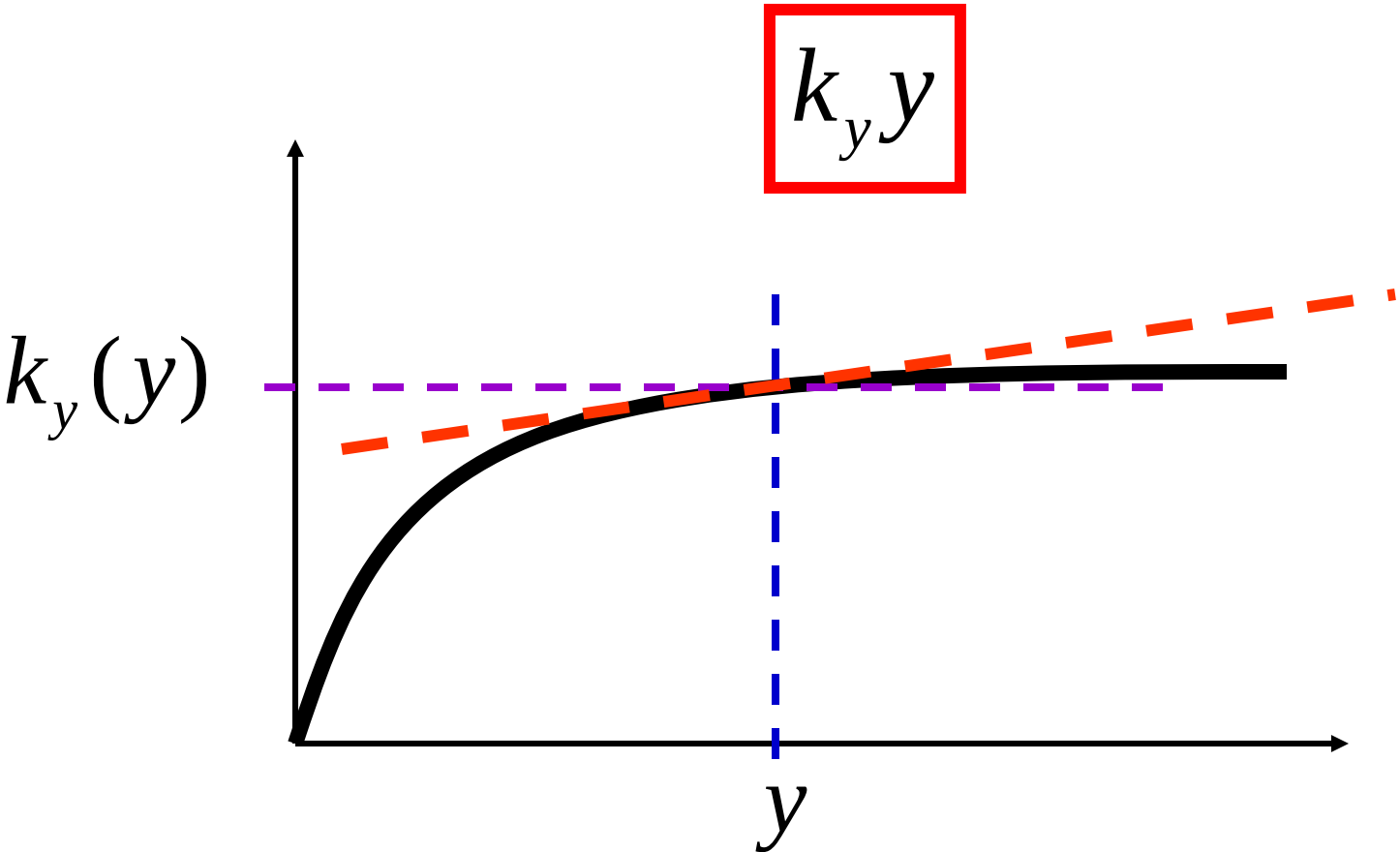
$$\begin{bmatrix} \dot{x} \\ \dot{y} \end{bmatrix} = \begin{bmatrix} -q \\ 1 \end{bmatrix} \left(\frac{Vx^q}{1+\gamma x^h} \right) + \begin{bmatrix} 1+q \\ -1 \end{bmatrix} ky + \begin{bmatrix} -1 \\ 0 \end{bmatrix} (1+\delta)$$

Control


x
produced
y
$k_y y$
consumed
$k_y(y)$
y

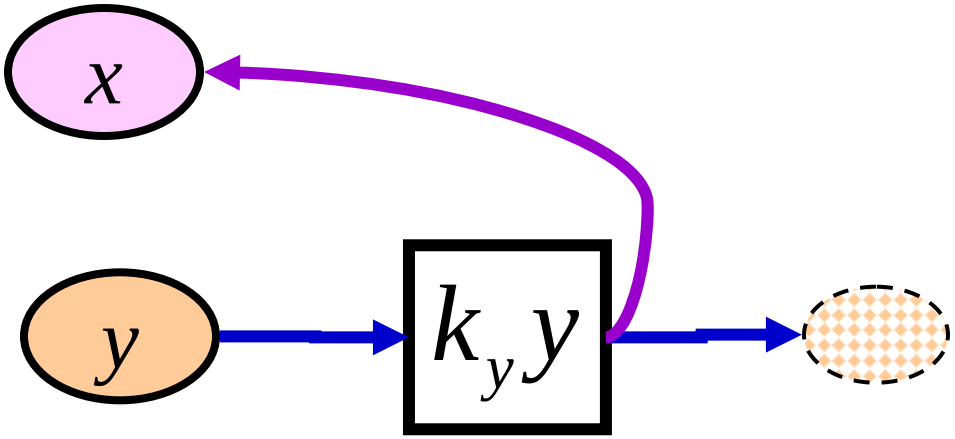
rate

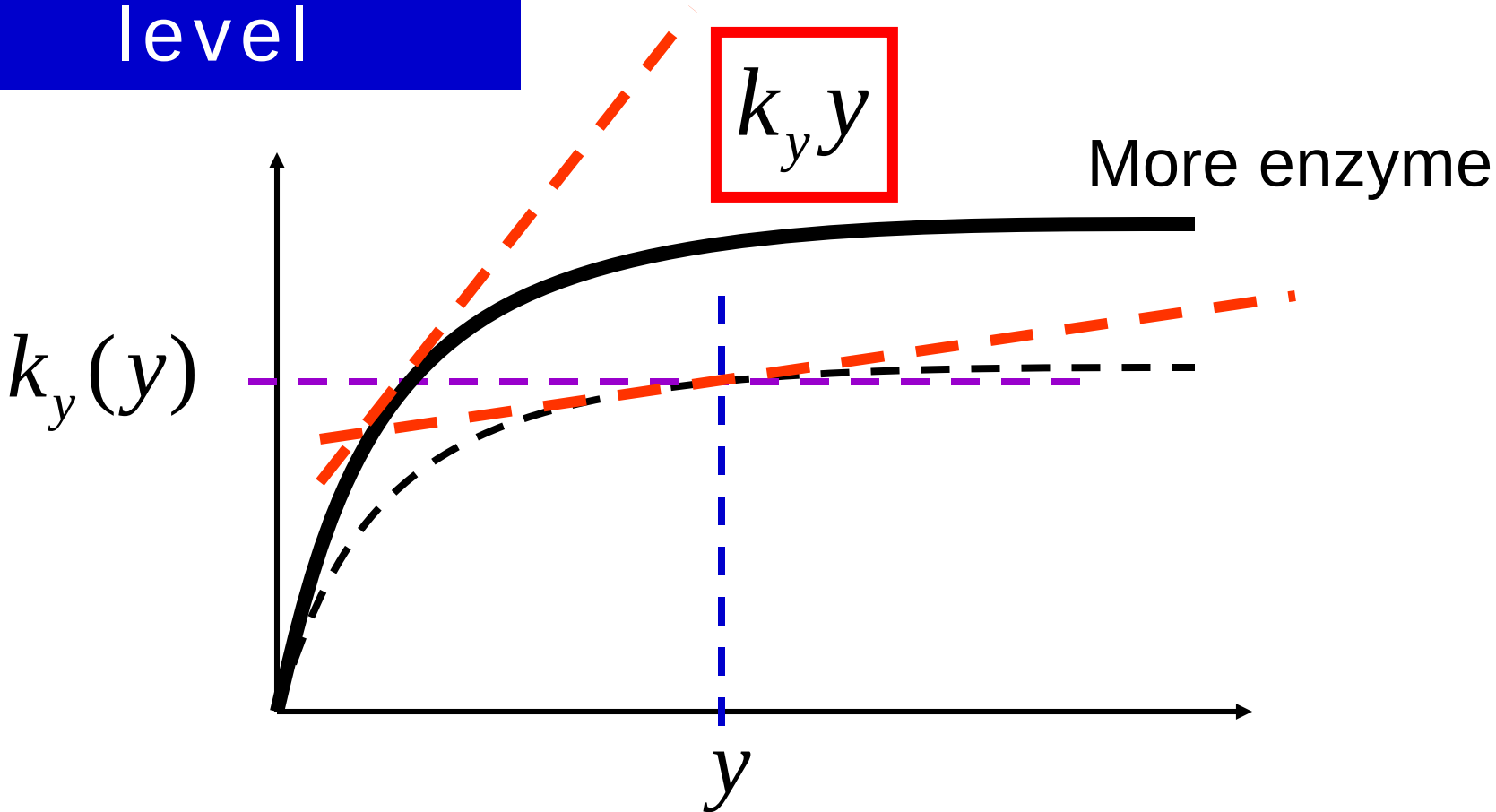


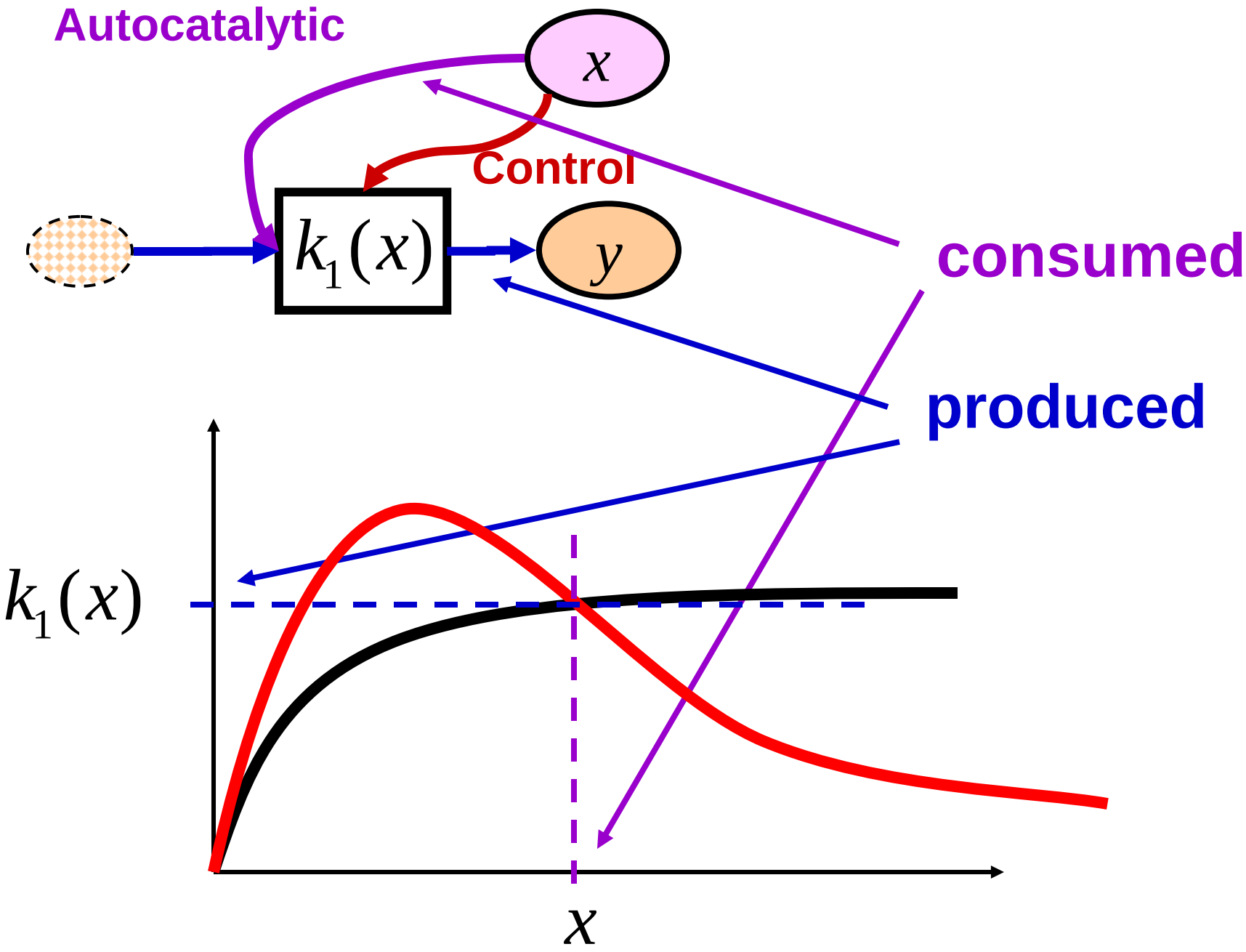


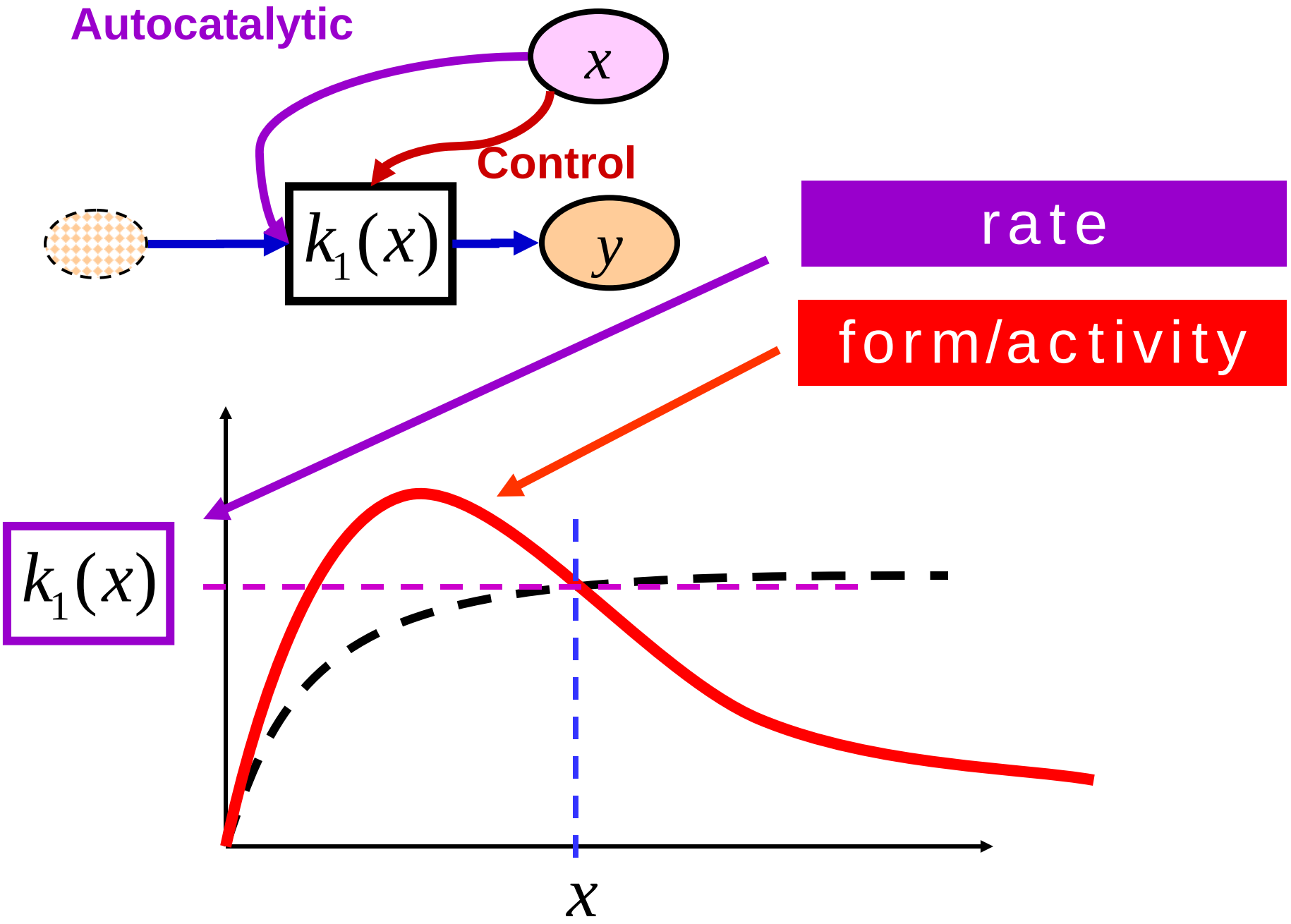
rate

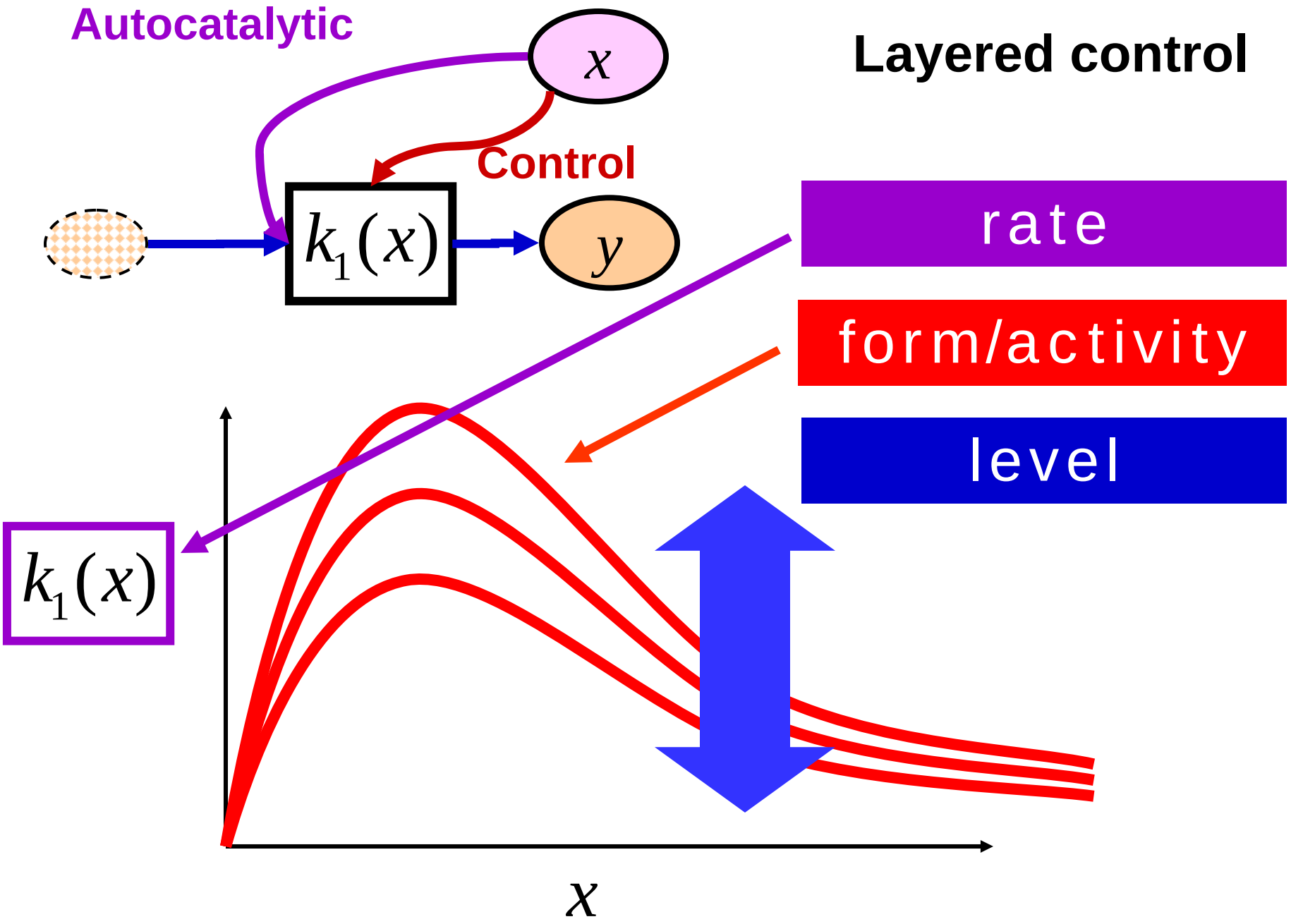
level

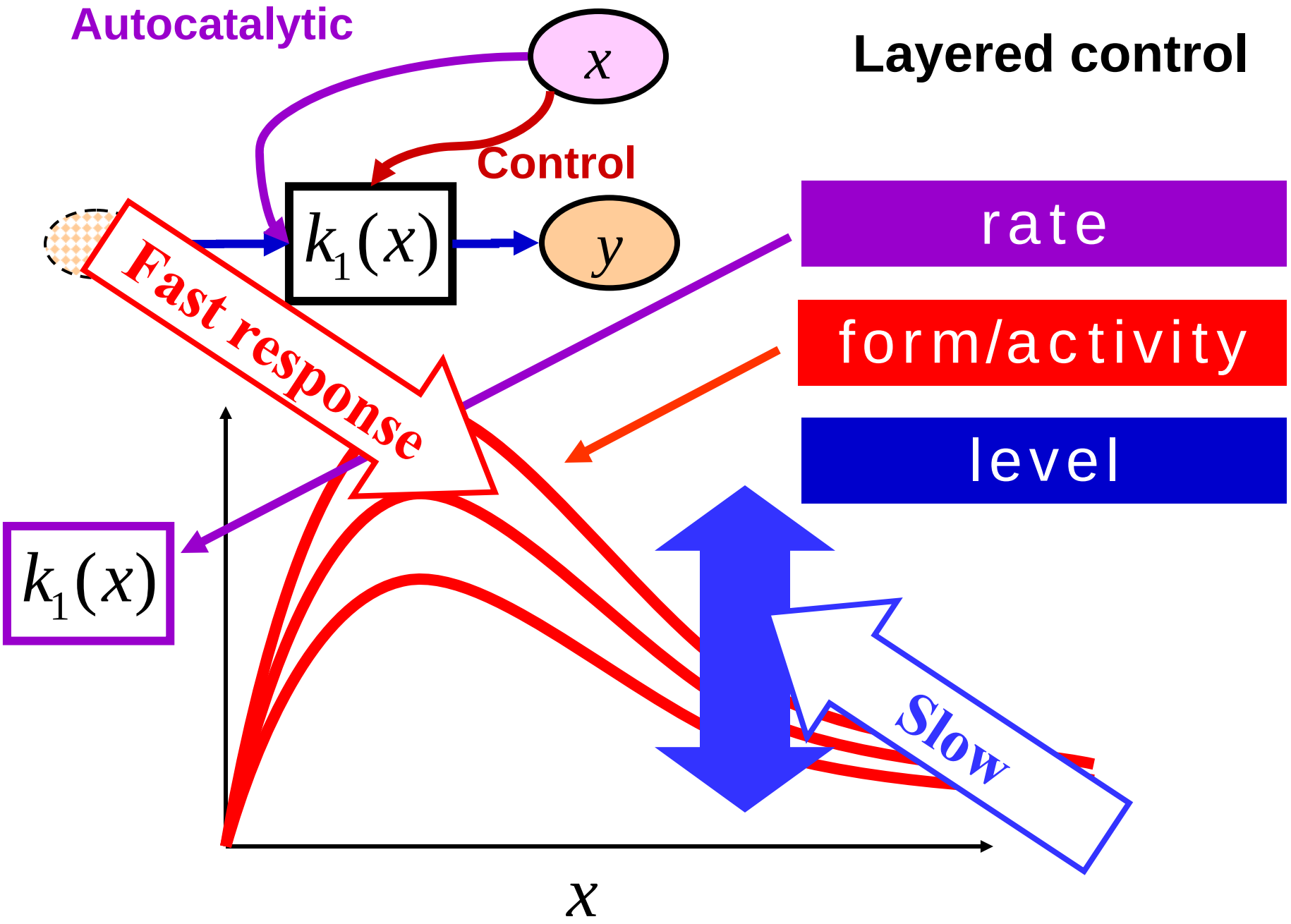


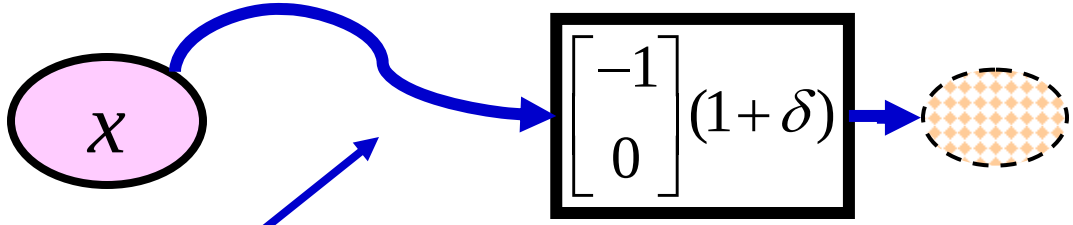



Autocatalytic
x
Control
$k_1(x)$
y
consumed
produced
$k_1(x)$
x


Autocatalytic
x
Control
$k_1(x)$
y
rate
form/activity
$k_1(x)$
x


Autocatalytic
x
Control
$k_1(x)$
y
Layered control
rate
form/activity
level
$k_1(x)$
x

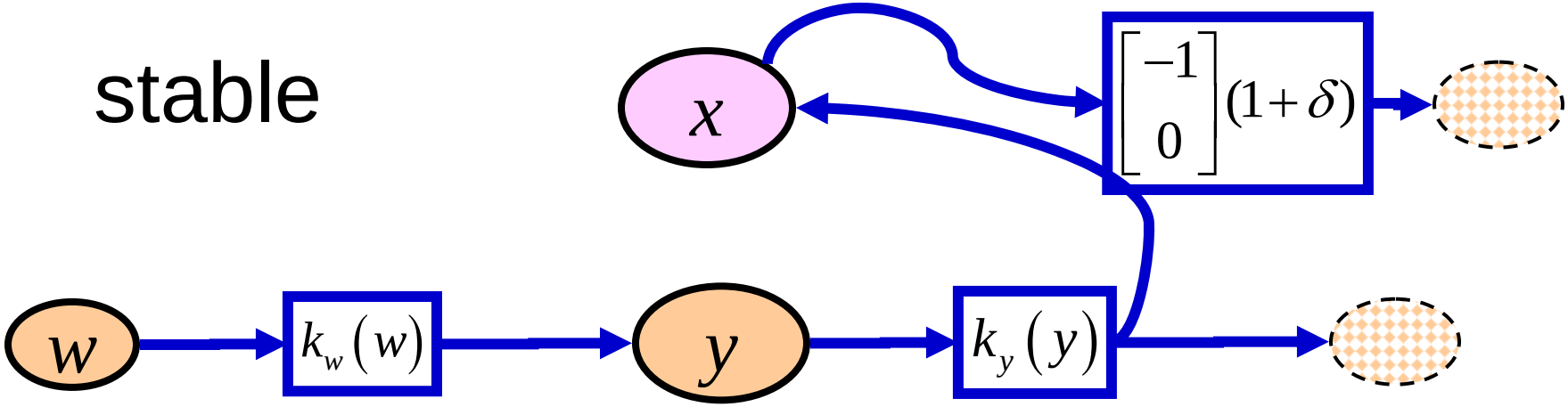

Autocatalytic
x
Control
$k_1(x)$
y
Layered control
rate
form/activity
level
Fast response
$k_1(x)$
Slow
x

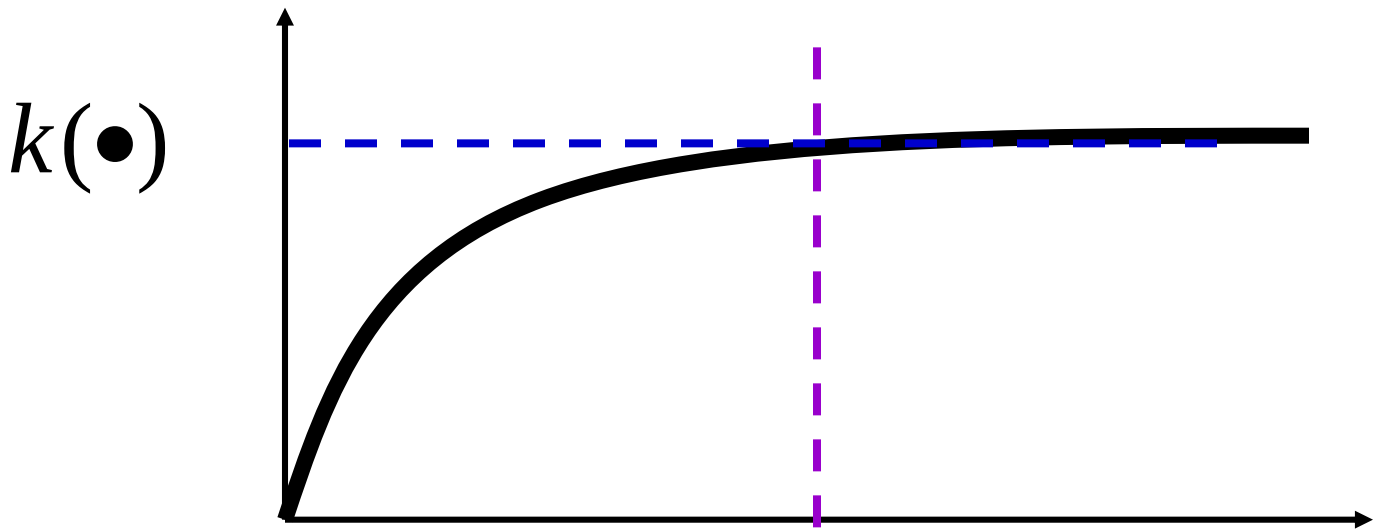


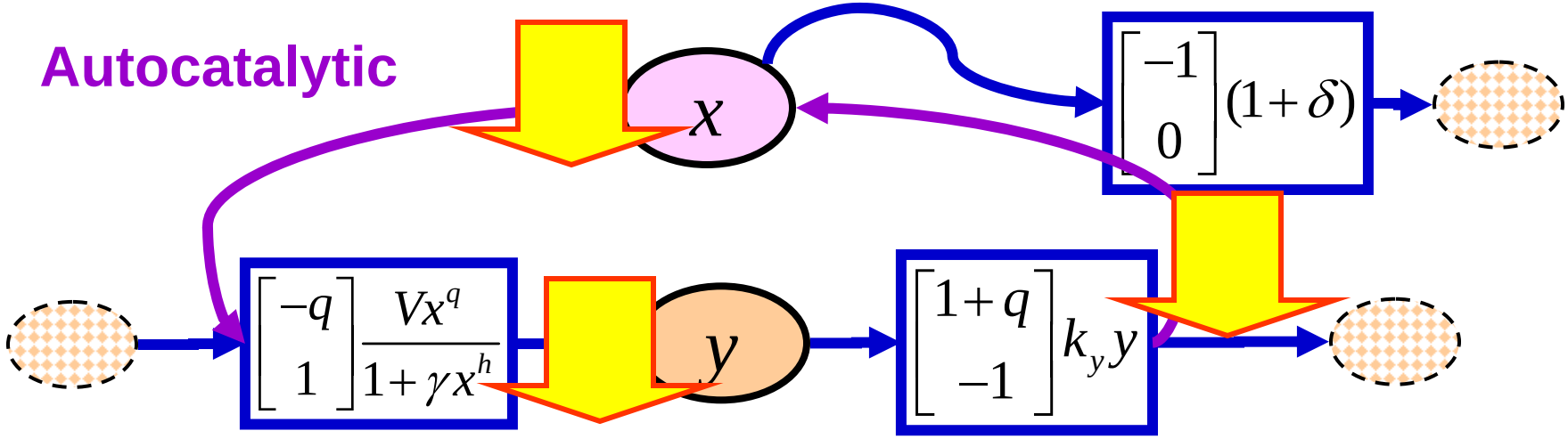
consumed

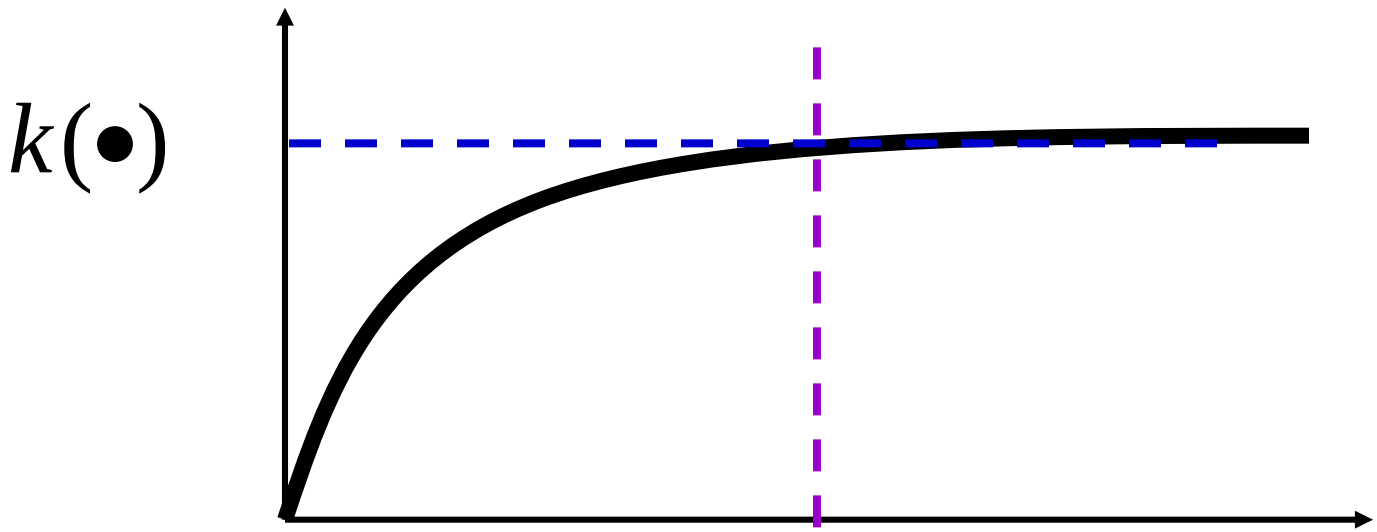
$$\begin{bmatrix} \dot{x} \\ \dot{y} \end{bmatrix} = \begin{bmatrix} -q \\ 1 \end{bmatrix} k_x(x) + \begin{bmatrix} 1+q \\ -1 \end{bmatrix} ky + \boxed{\begin{bmatrix} -1 \\ 0 \end{bmatrix}(1+\delta)}$$

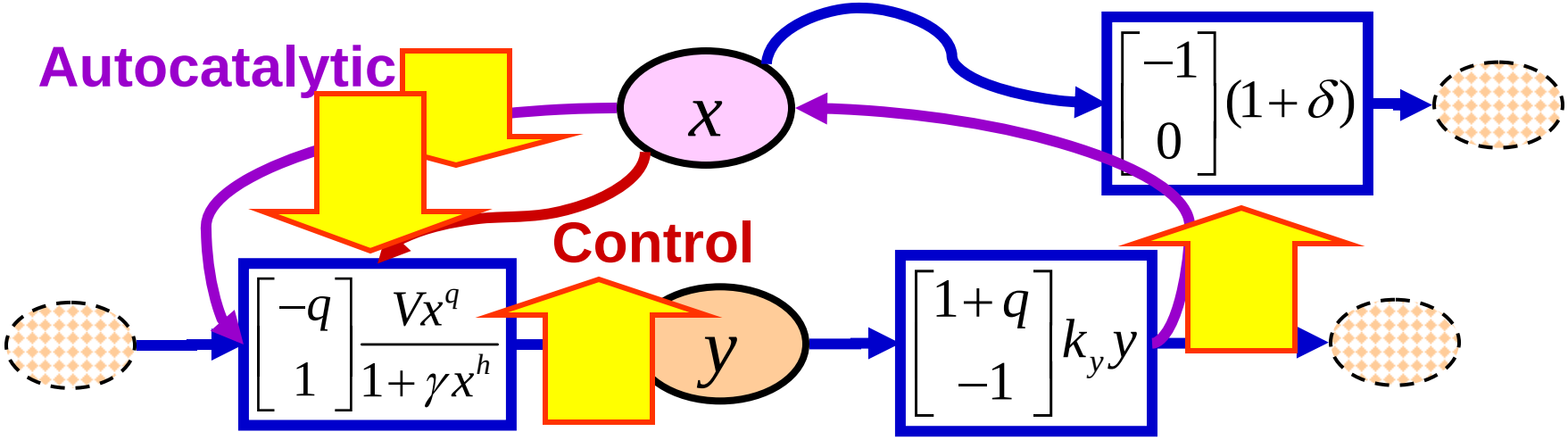
stable

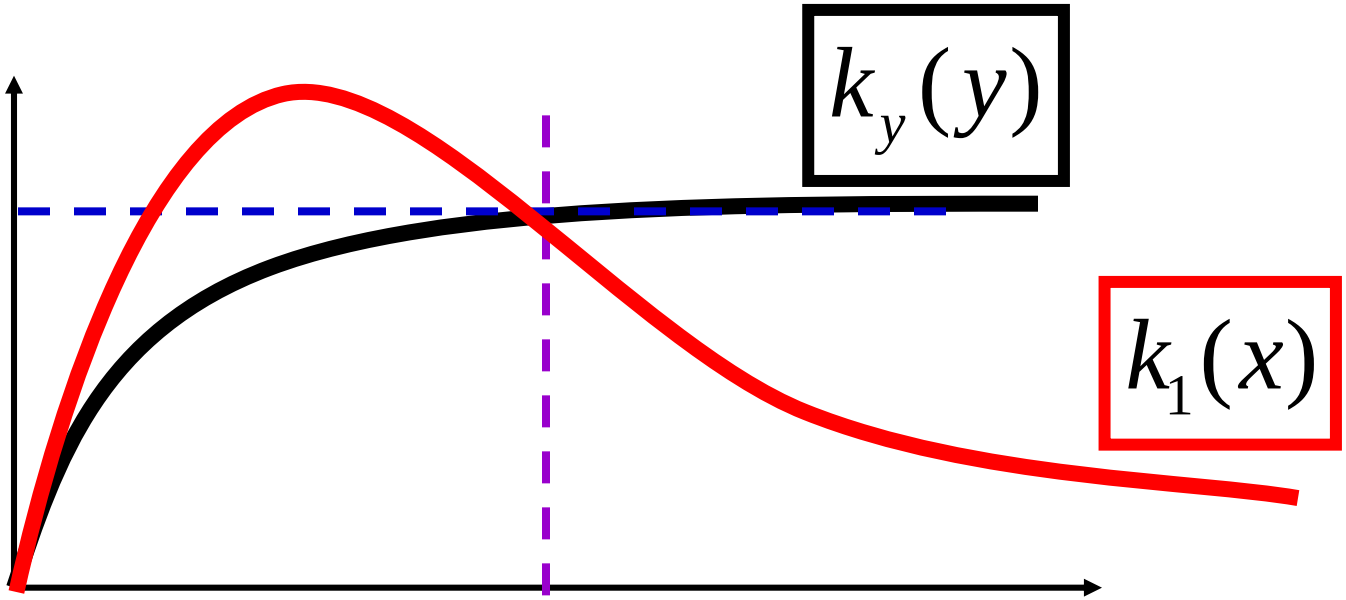


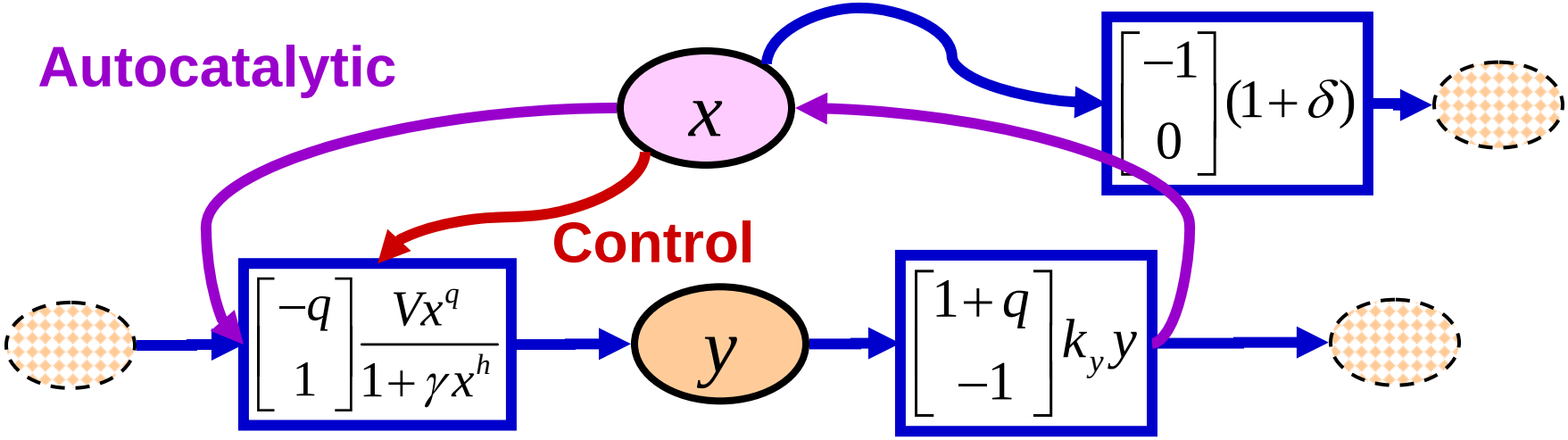



Autocatalytic
x
$\begin{bmatrix} -1 \\ 0 \end{bmatrix}(1+\delta)$
$\begin{bmatrix} -q \\ 1 \end{bmatrix}\frac{Vx^q}{1+\gamma x^h}$
y
$\begin{bmatrix} 1+q \\ -1 \end{bmatrix}k_y y$


$k(\bullet)$


Autocatalytic
x
$\begin{bmatrix} -1 \\ 0 \end{bmatrix}(1+\delta)$
Control
$\begin{bmatrix} -q \\ 1 \end{bmatrix}\frac{Vx^q}{1+\gamma x^h}$
y
$\begin{bmatrix} 1+q \\ -1 \end{bmatrix}k_y y$


$k_y(y)$
$k_1(x)$



Robust	Yet Fragile
Strong inhibition	Enzyme complexity, Oscillations
Low autocatalysis	Inefficiency, metabolic load
High reaction rates	