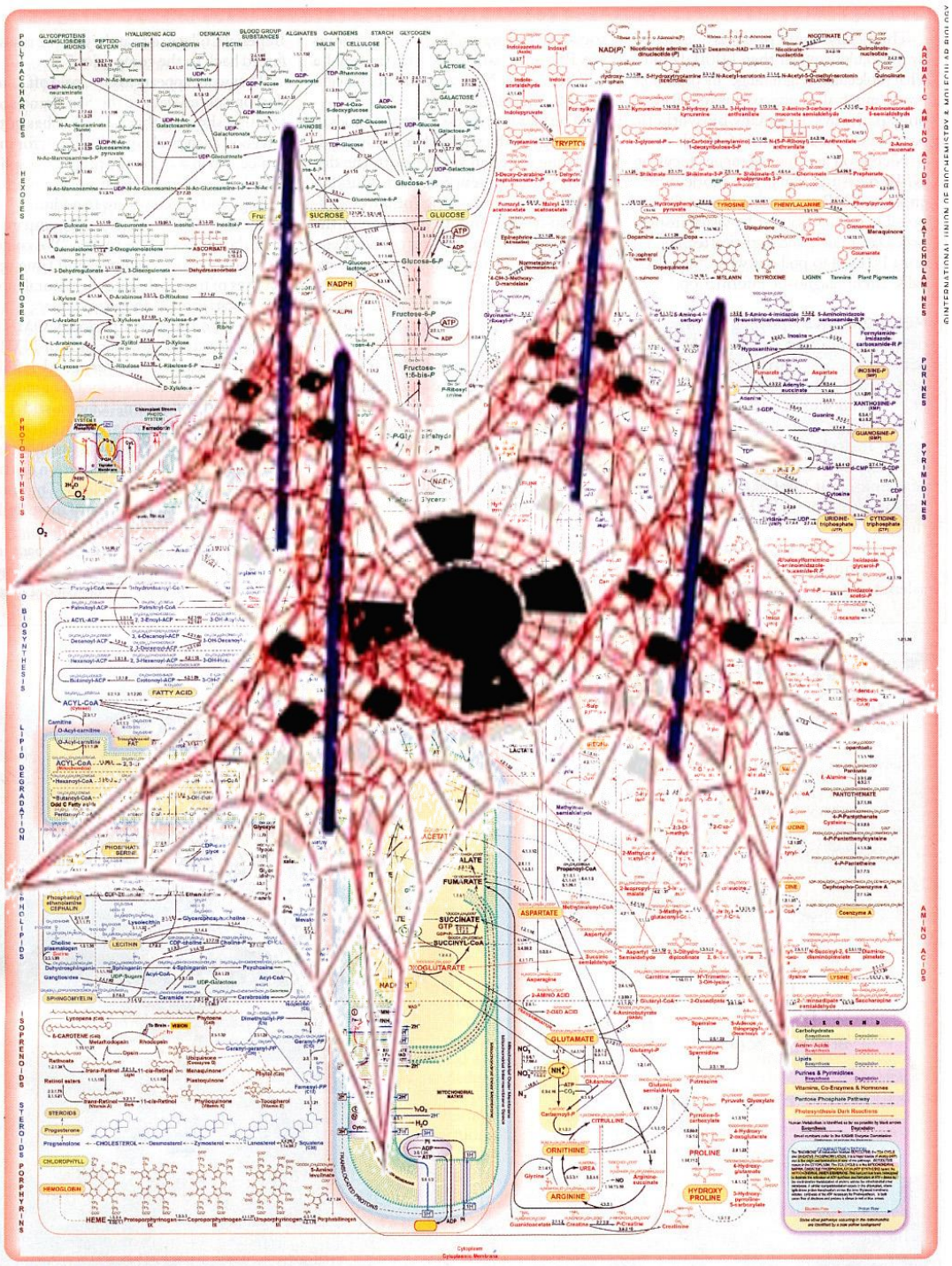
Sistemska biologija

O, kako lepo je biti zmodeliran!


POLYSACCHARIDES
HEXOSES
PENTOSES
PHOTOSYNTHESIS
LIPID BIOSYNTHESIS
LIPID DEGRADATION
PHOSPHOLIPIDS
ISOPRENOIDS
STEROIDS
PORPHYRINS
AROMATIC AMINO ACIDS
CATECHOLAMINES
PURINES
PYRIMIDINES
AMINO ACIDS
INTERMEDIATE METABOLISM & MULTIFUNCTIONAL ENZYMES
GLUCOSE
SUCROSE
NADPH
ATP
ADP
TRYPTOPHAN
TYROSINE
PHENYLALANINE
FATTY ACID
ACYL-CoA
ACETYL-CoA
ALANINE
FUMARATE
SUCCINATE
SUCCINYL-CoA
ASPARTATE
OXOGLUTARATE
GLUTAMATE
ORNITHINE
CITRULLINE
ARGININE
PROLINE
HYDROXY PROLINE
LEGEND

Systems biology is the coordinated study of biological systems by:

(1) investigating the components of cellular networks and their interactions,

(2) applying experimental high-throughput and whole-genome techniques, and

(3) integrating computational methods with experimental efforts.

Systems biology is modeling.

Klipp et al. (2005) *Systems Biology in Practice*. Wiley

The aim of **systems biology** is **predictive (quantitative) understanding.**

Szallasi, Stelling & Periwal (2006) *System Modeling in Cellular Biology*. MIT Press

Systems biology...is about putting together rather than taking apart, integration rather than reduction. It requires that we develop ways of thinking about integration that are as rigorous as our reductionist programmes, but different....It means changing our philosophy, in the full sense of the term.

Denis Noble

Systems biology can be considered from a number of different aspects:

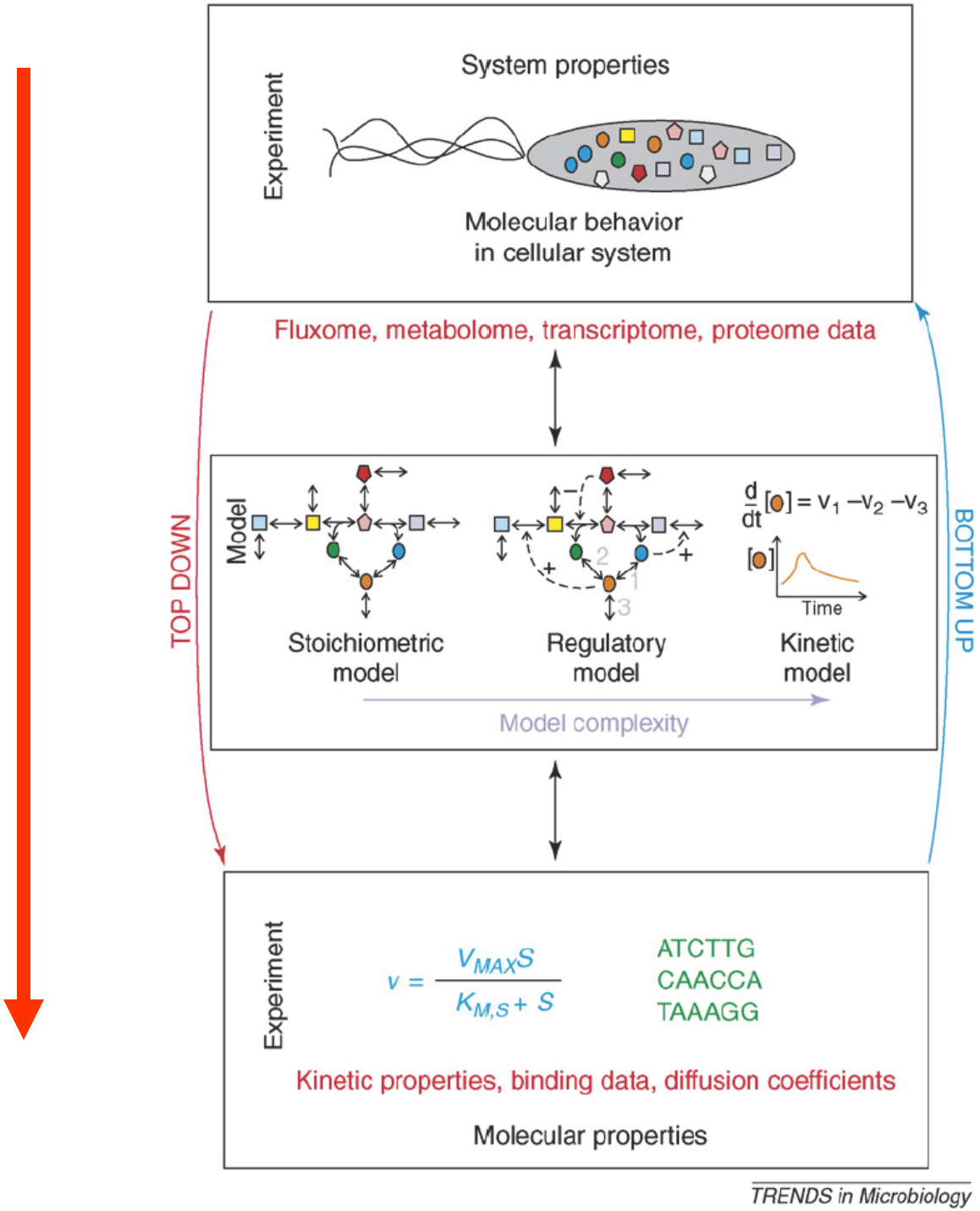
Some sources discuss systems biology as a **field of study** ...,

Other sources consider systems biology as a **paradigm** ...,

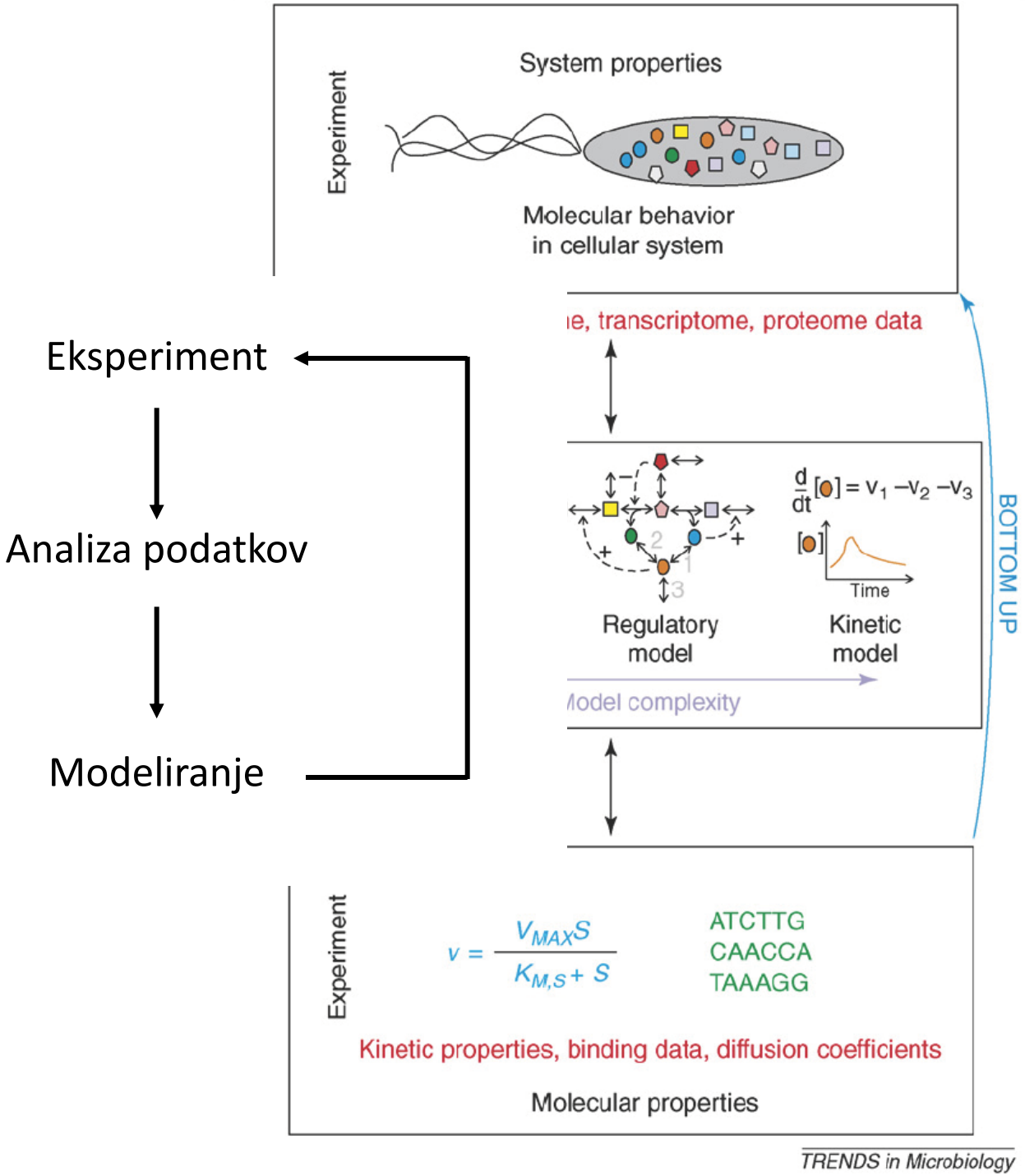
Still other sources view systems biology in terms of the **operational protocols used for performing research** ...,

Finally, some sources see it as a **socioscientific phenomenon** ...

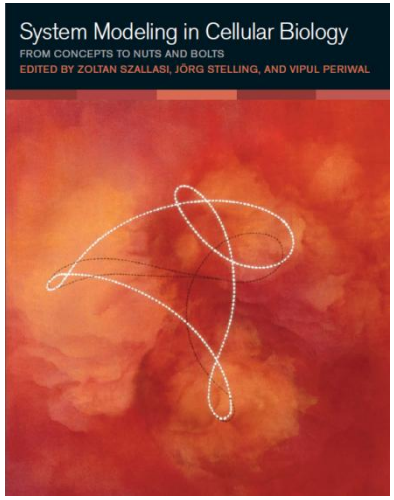
http://en.wikipedia.org/wiki/Systems_biology

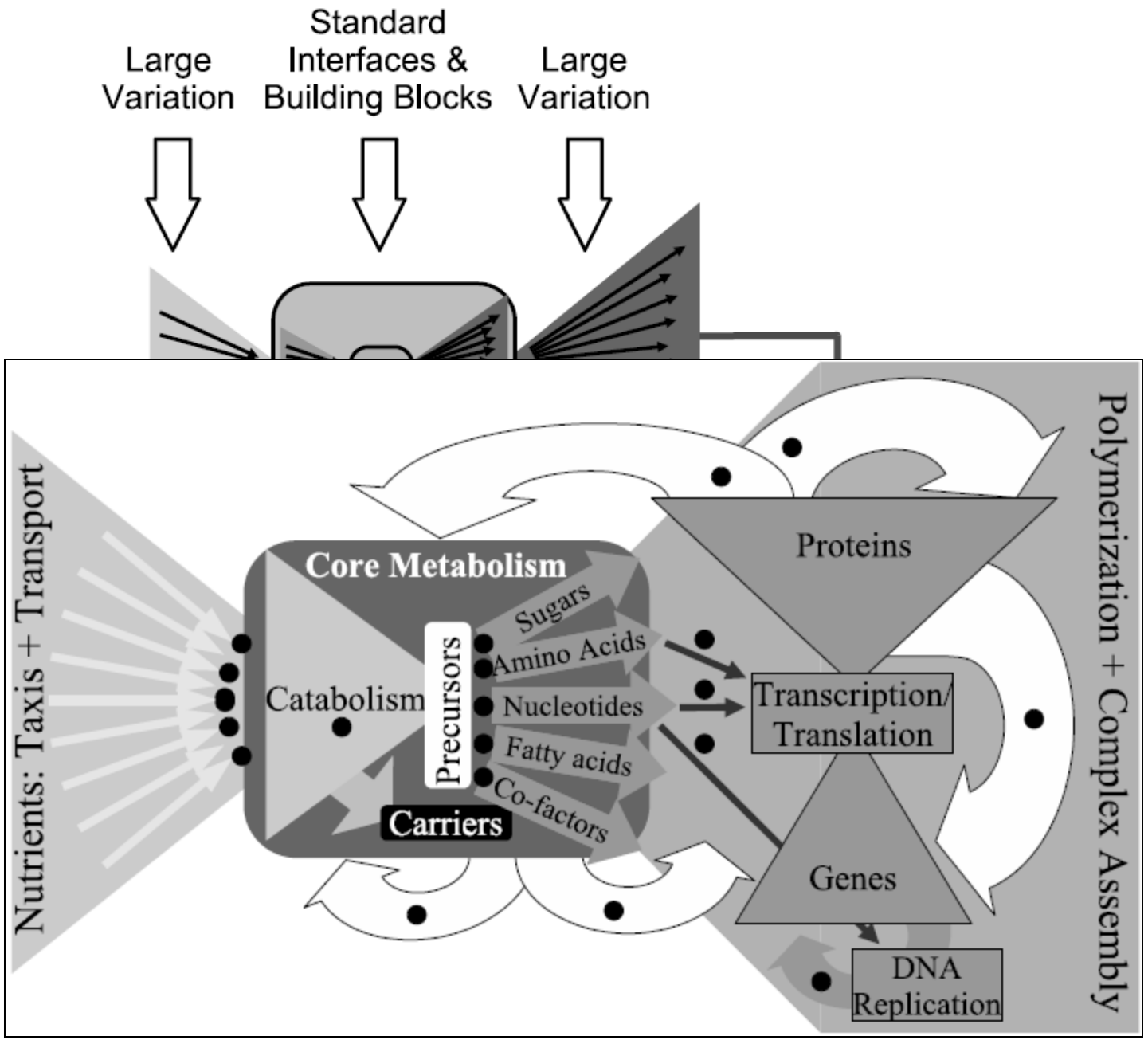


Trends in Microbiology
(2007) 15:45



Trends in Microbiology
(2007) 15:45





Szallasi, Stelling & Periwal (2006) *System Modeling in Cellular Biology*. MIT Press

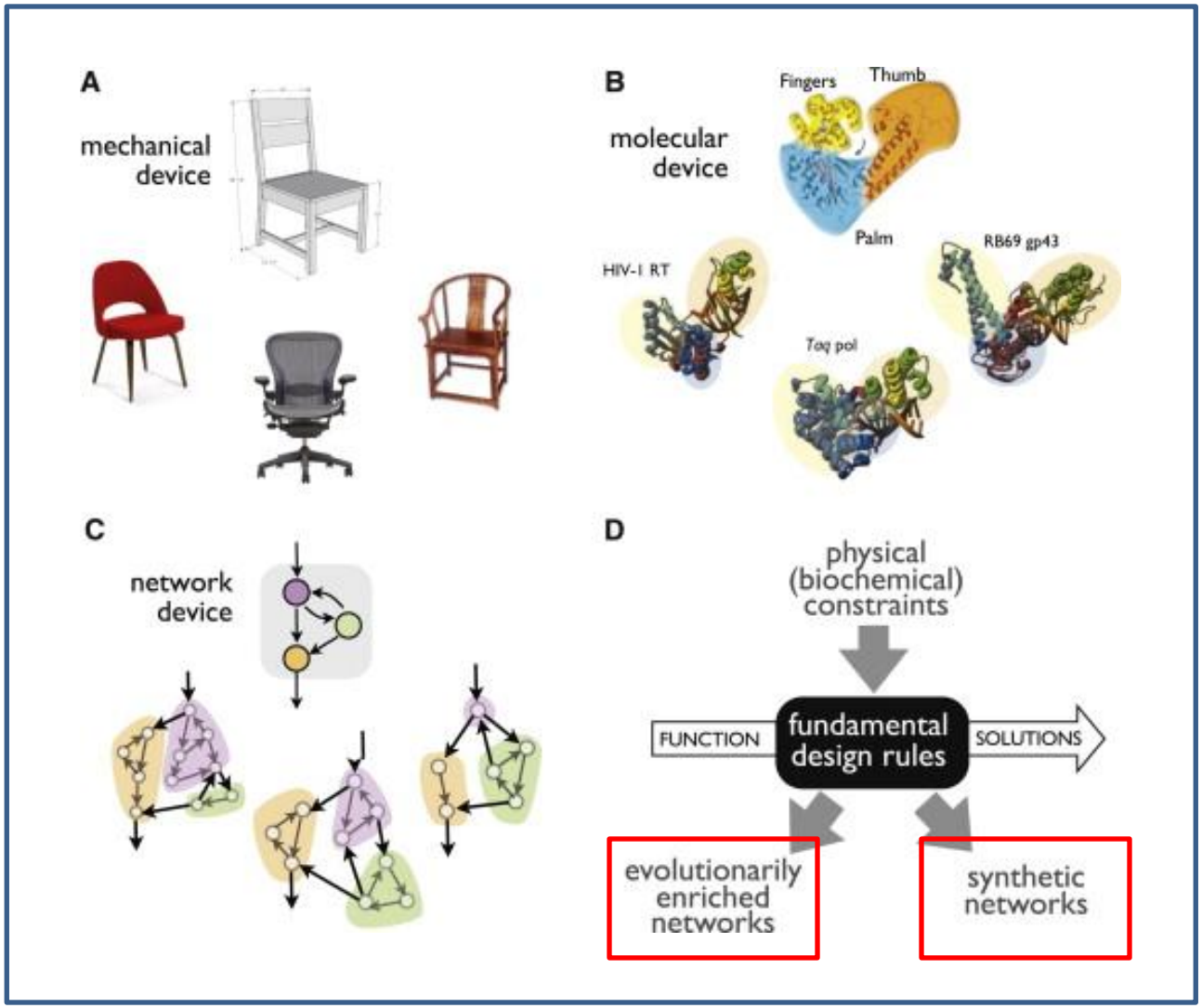
Viri perturbacij bioloških sistemov

- zunanje perturbacije (vplivi okolja)

- notranje perturbacije (mutacije)

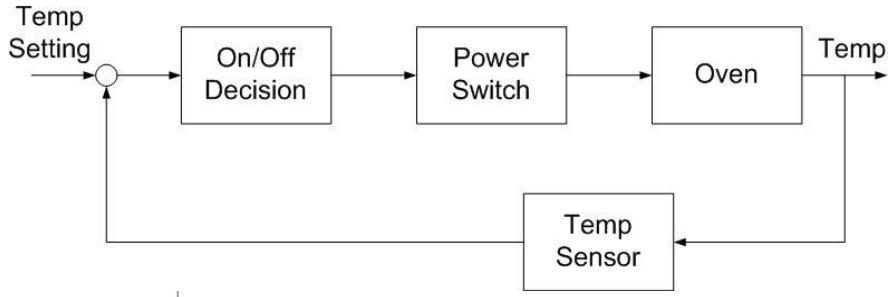
- intrinzični šum (posledica majhnega števila celičnih komponent (npr. nizke koncentracije molekul))

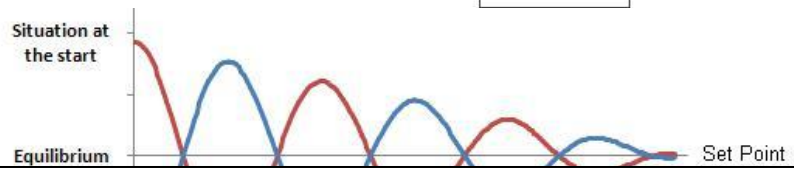
Princip izgradnje regulatornih mrež

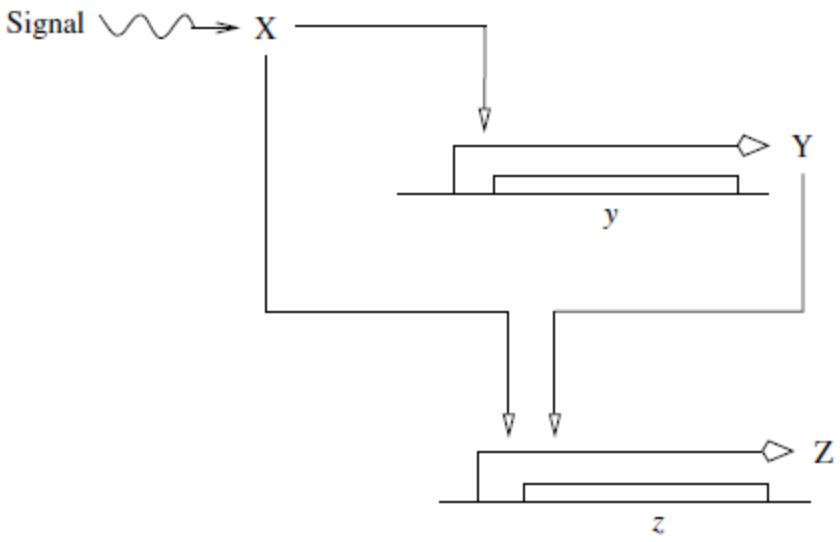


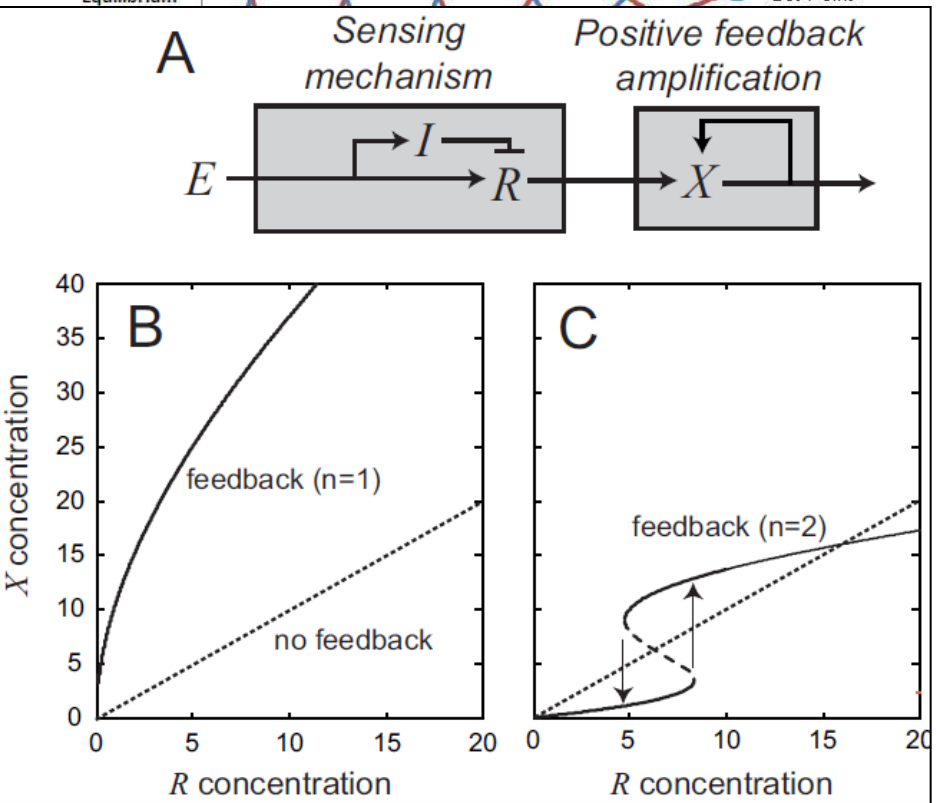
Molecular Cell (2013) *49:202*

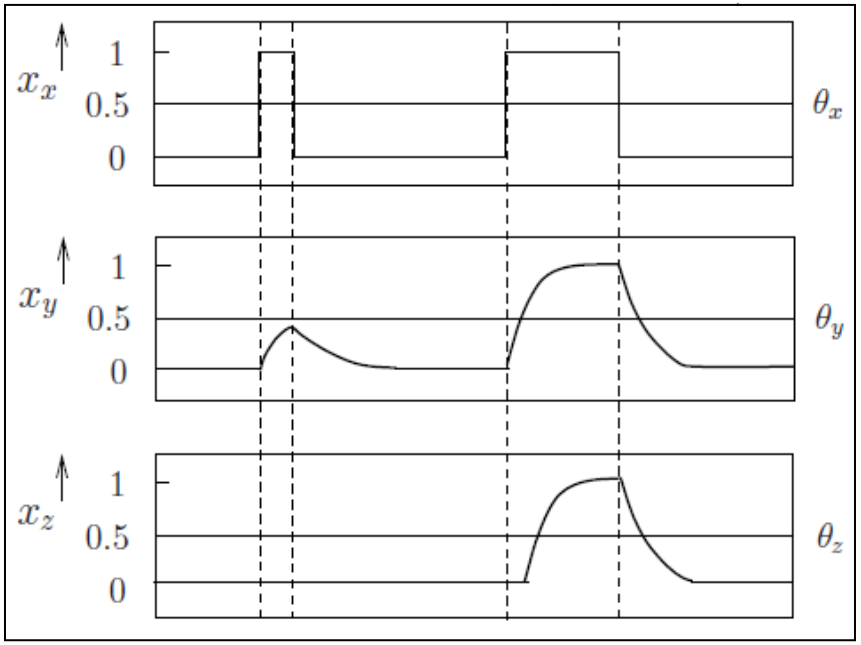
Povratne in vnaprejšnje zanke



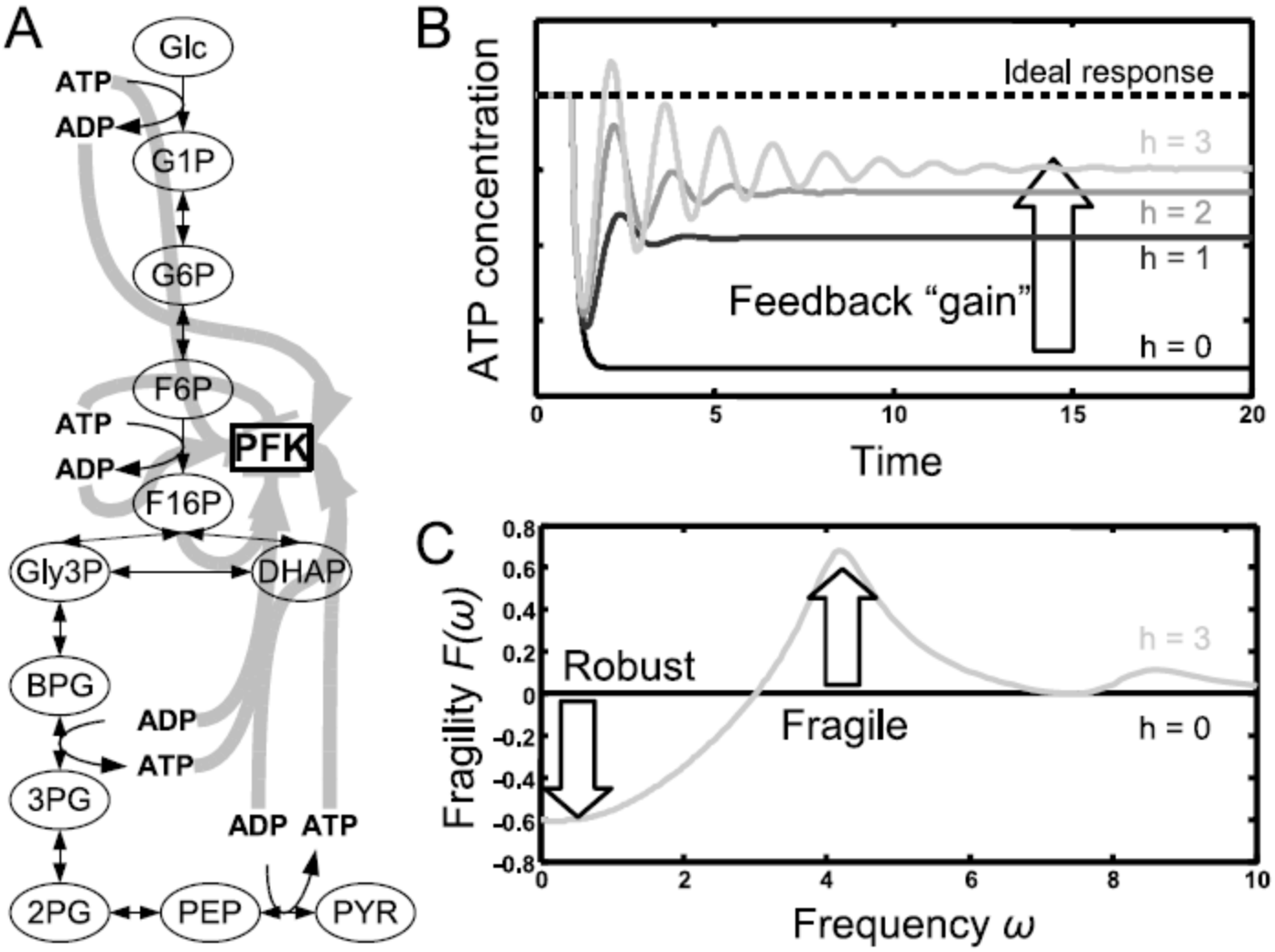






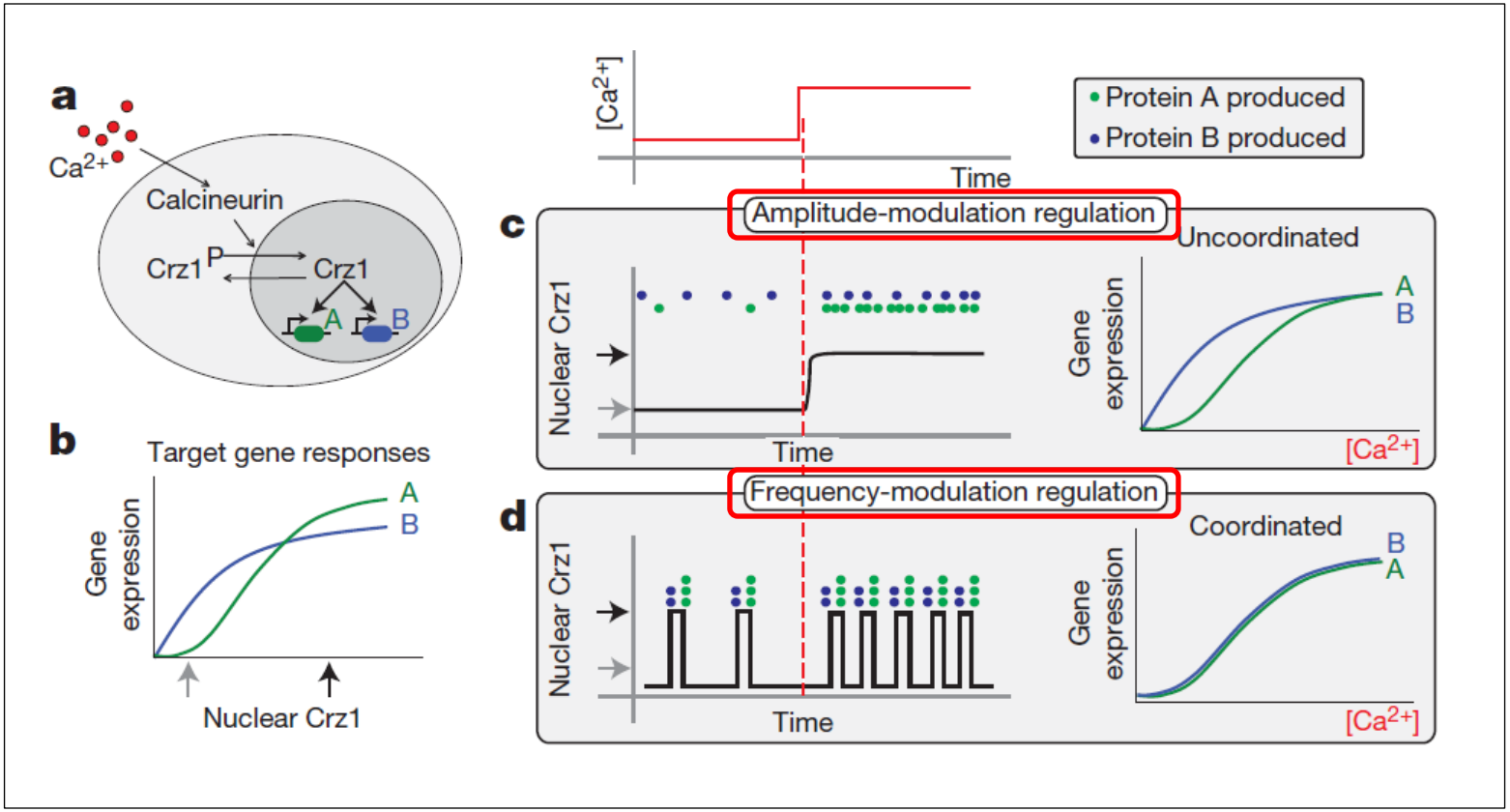


Robustnost vs. krhkost



Napovedljivost vs. šum

Viri šuma:
- majhno število molekul
- nizka frekvenca interakcij
- podobnost proteinskih domen
- pozicija nukleosomov



Nature (2010) 467:167

Bayesove metode / Bayesova inferenca

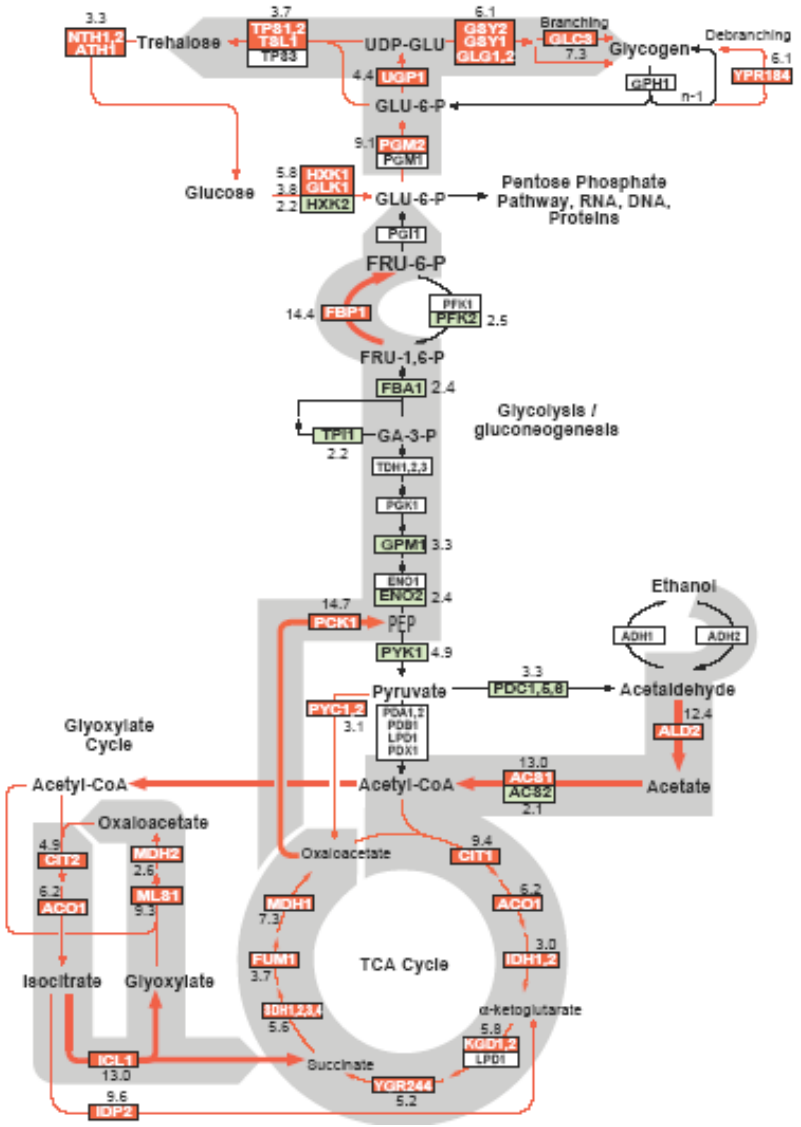
Uporaba v biologiji zaradi nepopolnih podatkov

p(podatki|hipoteza) : p(hipoteza|podatki)

Occamovo rezilo (“Če slišiš kopita, pomisli na konje, ne na zebre.”)

Kako vemo, kaj “pomeni” nabor genov?

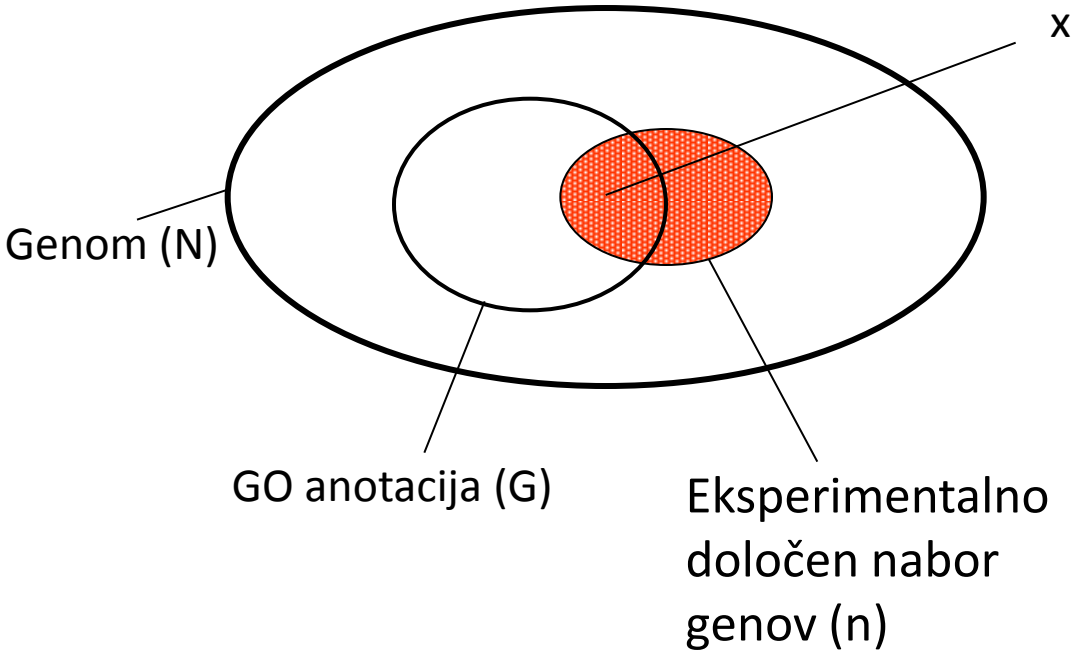
Mapiranje genov na metabolne (signalne) poti



Science (1997) 278:680

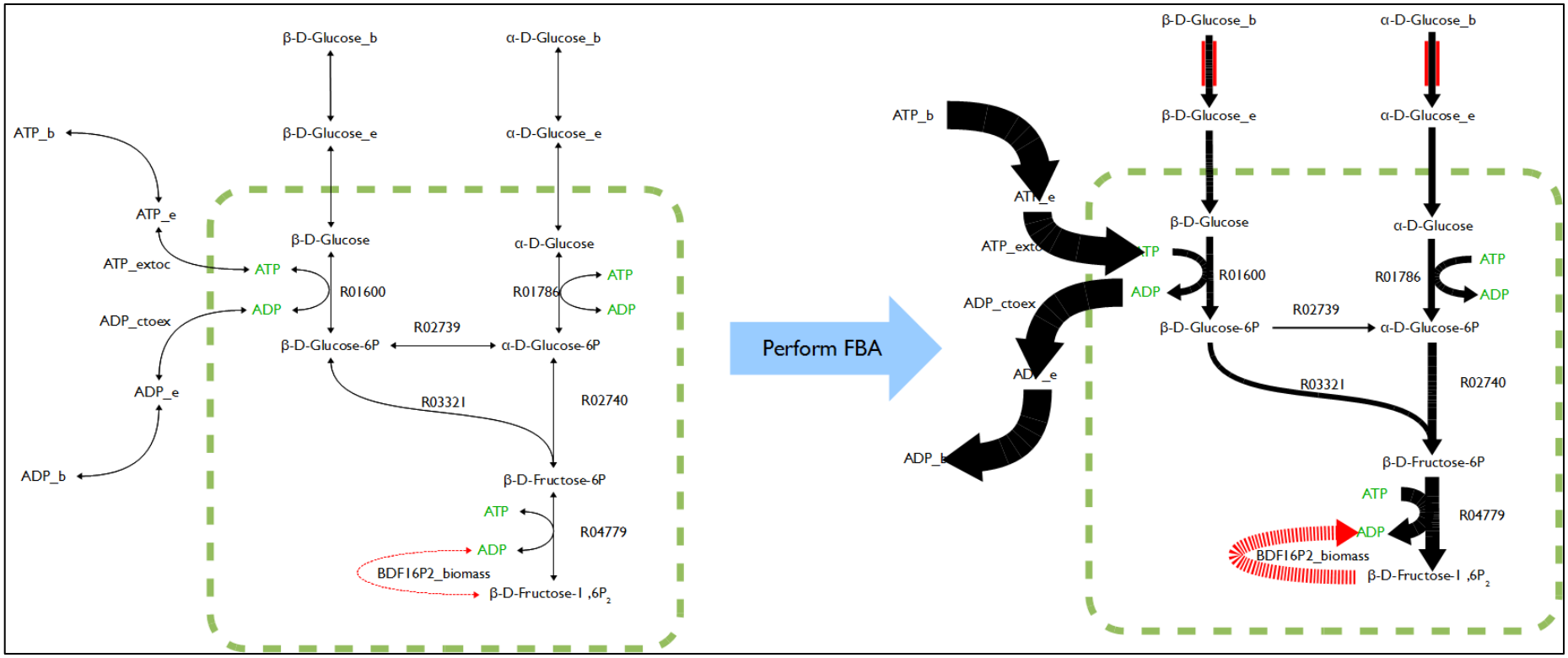
Kako vemo, kaj “pomeni” nabor genov?

Tehnika analize obogatenosti genskih skupin (npr. GO Term Finder)



p = verjetnost, da je dogodek naključen

FBA & MCA

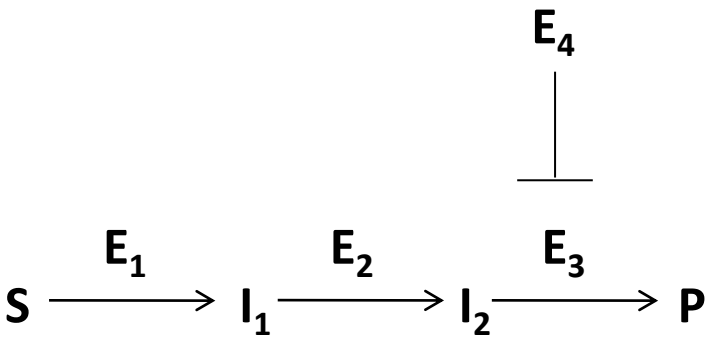


Flux Balance Analysis

Metabolic Control Analysis

Flux Control Coefficient

$$C_{Ei,J} = \frac{\delta J/J}{\delta E_i/E_i}$$

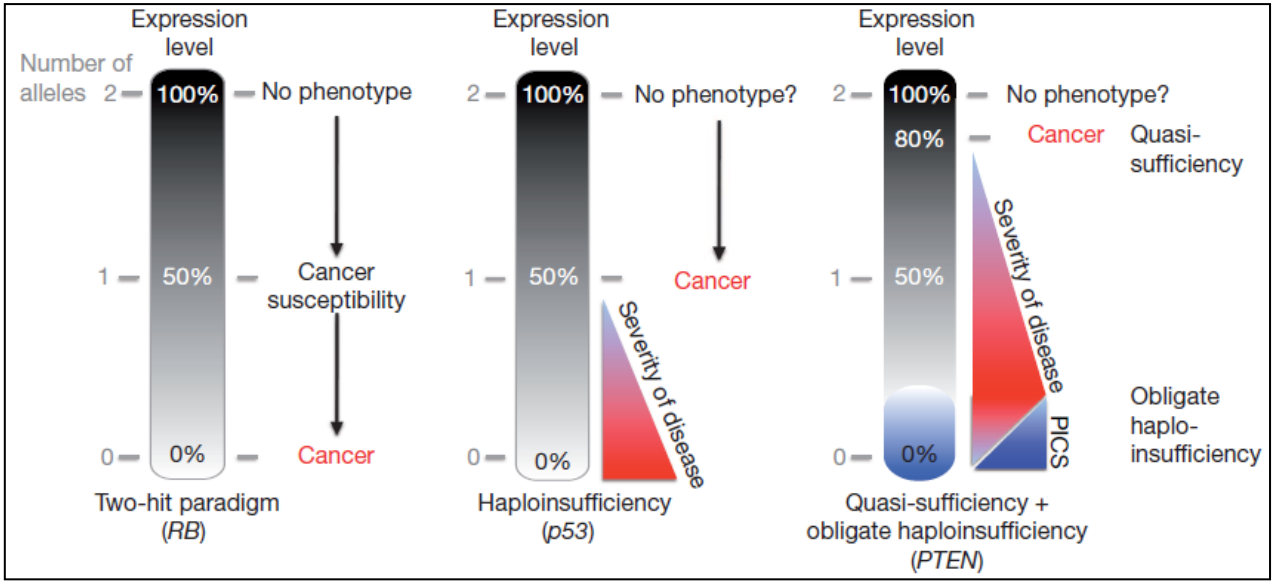


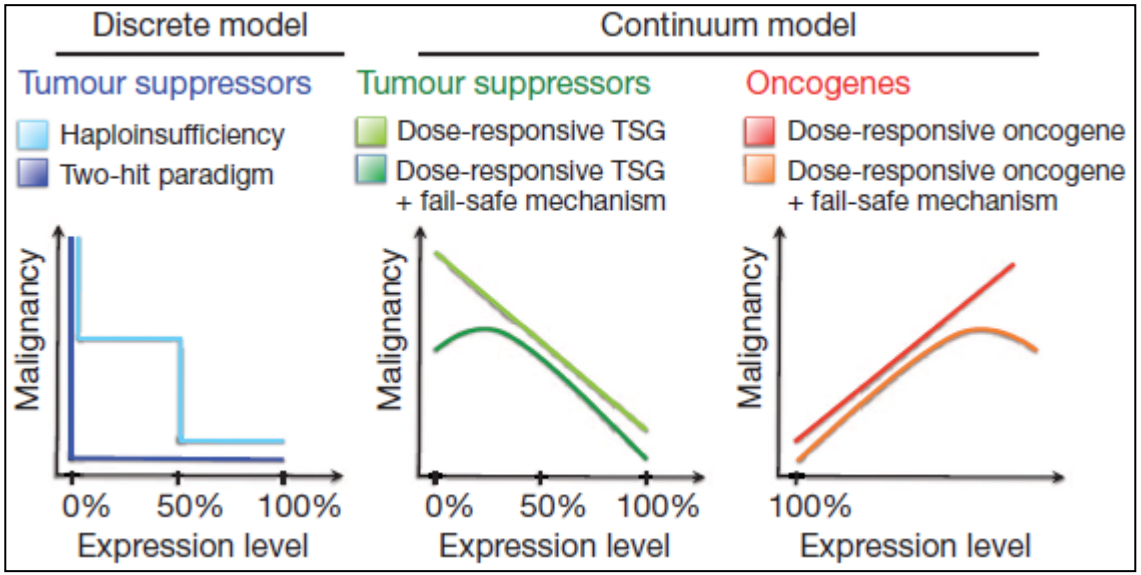
The Summation Theorem

$$\sum_{i=1}^{N} C_{Ei,J} = 1$$

$E_{1\text{-}3}$: C > 0
E_4: C < 0

(Ne)monotonost dinamike bioloških sistemov





Nature (2011) 476:162