Life: from molecules to system earth
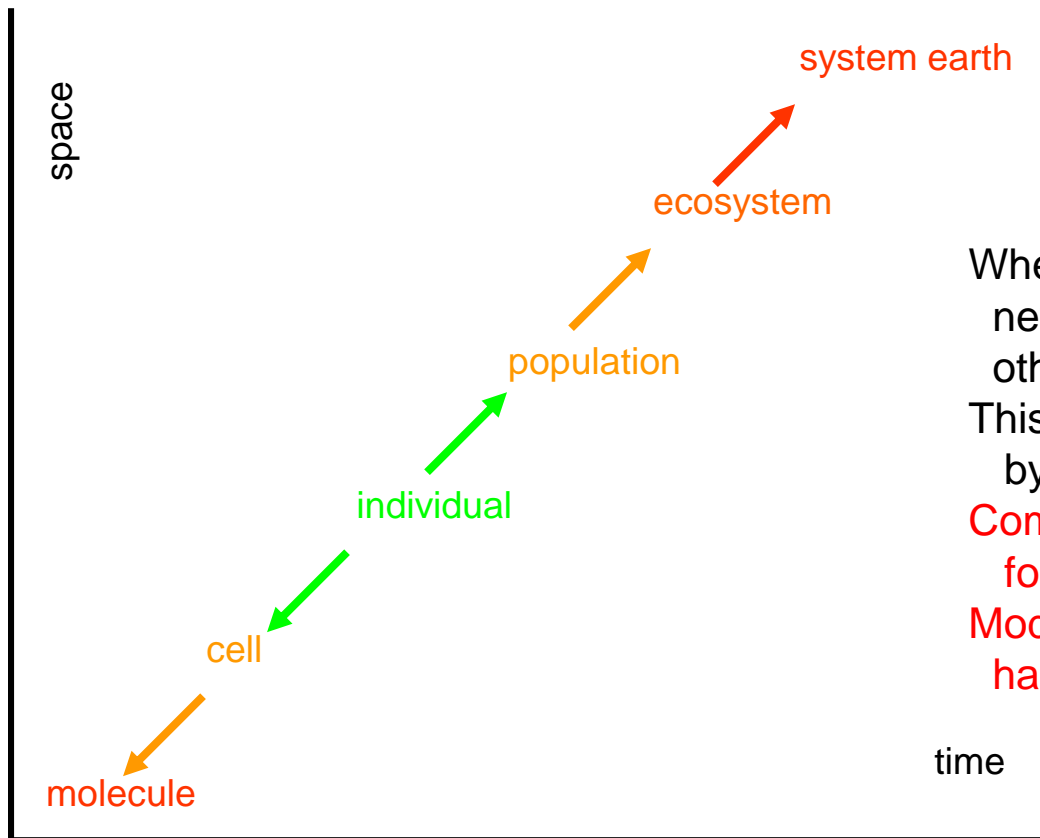
Bas Kooijman

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A-Life, VU University Amsterdam

DEB 2025

Space-time scales

Each process has its characteristic domain of space-time scales

When changing the space-time scale,
  new processes will become important
  other will become less important
This can be used to simplify models,
  by coupling space-time scales
Complex models are required
  for small time and big space scales and *vv*
Models with many variables & parameters
  hardly contribute to insight

Focus on individuals

- population dynamics is derived from
  properties of individuals + interactions between them

- evolution according to Darwin:
  variation between individuals + selection

- individuals are the survival machines of life

- material and energy balances:
  most easy for individuals
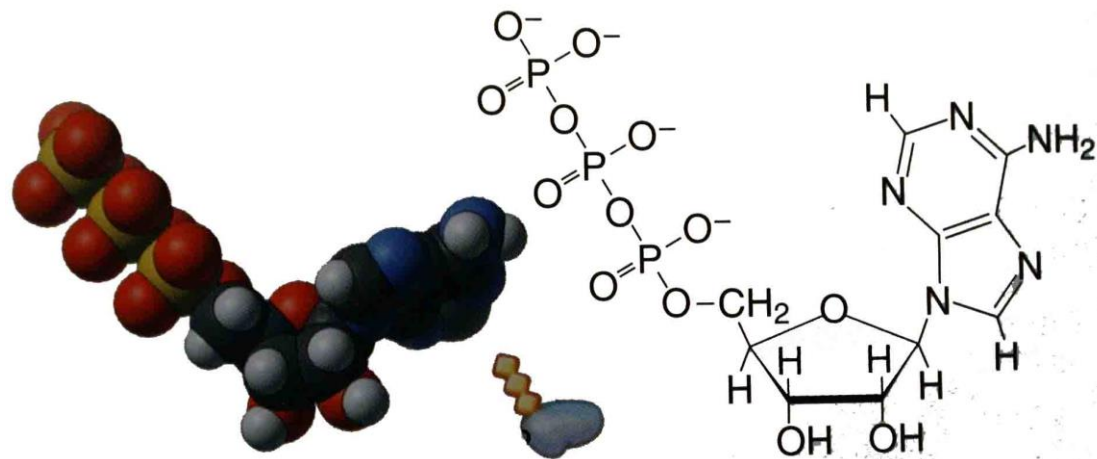
ATP generation & use

$5 \cdot 10^6$ ATP molecules in bacterial cell
  enough for 2 s of biosynthetic work

Only used if energy generating &
  energy demanding transformations
  are at different site/time

If ADP/ATP ratio varies, then
  rates of generation & use varies, but not
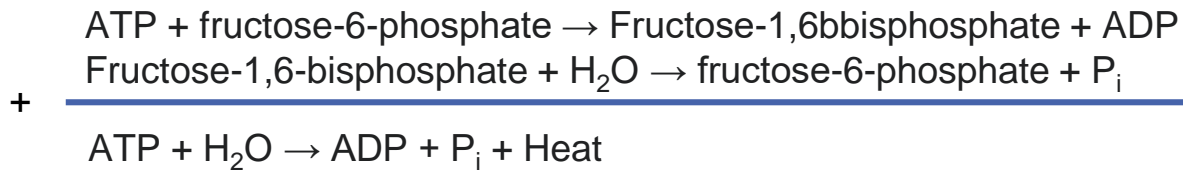 necessarily the rates of transformations they drive

Processes that are not much faster
  than cell cycle, should be linked
  to large slow pools of metabolites,
  not to small fast pools

DEB theory uses reserve as large slow
  pool for driving metabolism

Futile cycles

Example:

ATP + fructose-6-phosphate → Fructose-1,6bbisphosphate + ADP
Fructose-1,6-bisphosphate + H_2O → fructose-6-phosphate + P_i

+ _____

ATP + H_2O → ADP + P_i + Heat

Known since Steinberg 1963: all organisms have the required enzymes
Biochemists seem to agree that the destruction of ATP is its sole function
Puzzle: why first synthesize ATP at considerable cost and then destruct it?

DEB answer: in this way organisms can boost their growth and reproduction, due to the κ-rule
  Waste-to-Hurry (Kooijman 2013, *Oikos* **122**: 348–357)

Key: by increasing somatic maintenance, you can eat lot while keeping small
Especially attractive if resources are abundantly available temporarily only,
  but you need strategies for what to do between these peeks (torpor/migration)

Macrochemical reaction eq

Given substrates A, B and products C, D

    with chemical indices for element i: $n_{iA}, n_{iB}, n_{iC}, n_{iD}$

For $\dot{J}_{Ak}, \dot{J}_{Bk} < 0$ and $\dot{J}_{Ck}, \dot{J}_{Dk} > 0$

$$0 = n_{iA}\dot{J}_{Ak} + n_{iB}\dot{J}_{Bk} + n_{iC}\dot{J}_{Ck} + n_{iD}\dot{J}_{Dk}$$

$$0 = n_{iA}\dot{J}_{Ak}/\dot{J}_{Ck} + n_{iB}\dot{J}_{Bk}/\dot{J}_{Ck} + n_{iC}\dot{J}_{Ck}/\dot{J}_{Ck} + n_{iD}\dot{J}_{Dk}/\dot{J}_{Ck}$$

$$0 = n_{iA}Y_{AC}^{k} + n_{iB}Y_{BC}^{k} + n_{iC}Y_{CC}^{k} + n_{iD}Y_{DC}^{k}$$

$$-Y_{AC}^{k}A - Y_{BC}^{k}B \rightarrow C + Y_{DC}^{k}D$$

$\dot{J}_{Ck}$ is *the* rate of transformation k and $Y_{CC}^{k} \equiv 1$

Example: $CO_2 + H_2O \rightarrow CH_2O + O_2$

$\dot{J}_{jk}$	flux of compound j in transformation k in (C-)mole/time
Y_{ps}^{k}	yield of compound p on compound s in transformation k: $\dot{J}_{pk}/\dot{J}_{sk}$
n_{ij}	frequency of element i in compound j

Macrochemical reaction eq

		substrate	$+Y_{OX}O$	$\rightarrow$	$Y_{PX}P$	$+Y_{EX}E$	$+Y_{VX}V$	$+Y_{CX}C$	$+Y_{HX}H$	$+Y_{NX}N$
$+$	**overall**	X	$+Y_{OX}O$	$\rightarrow$	$Y_{PX}P$	$+Y_{EX}E$	$+Y_{VX}V$	$+Y_{CX}C$	$+Y_{HX}H$	$+Y_{NX}N$
A	**assimilation**	X	$+Y_{OX}^{A}O$	$\rightarrow$	$Y_{PX}^{A}P$	$+Y_{EX}^{A}E$		$+Y_{CX}^{A}C$	$+Y_{HX}^{A}H$	$+Y_{NX}^{A}N$
A^c	catabolic	X	$+Y_{OX}^{A_c}O$	$\rightarrow$	$Y_{PX}^{A_c}P$			$+Y_{CX}^{A_c}C$	$+Y_{HX}^{A_c}H$	$+Y_{NX}^{A_c}N$
A^a	anabolic	X	$+Y_{OX}^{A_a}O$	$\rightarrow$		$Y_{EX}^{A_a}E$		$+Y_{CX}^{A_a}C$	$+Y_{HX}^{A_a}H$	$+Y_{NX}^{A_a}N$
D	**dissipation**	E	$+Y_{OE}^{D}O$	$\rightarrow$				$Y_{CE}^{D}C$	$+Y_{HE}^{D}H$	$+Y_{NE}^{D}N$
D^c	catabolic	E	$+Y_{OE}^{D_c}O$	$\rightarrow$				$Y_{CE}^{D_c}C$	$+Y_{HE}^{D_c}H$	$+Y_{NE}^{D_c}N$
D^a	anabolic	E $+Y_{VE}^{D_a}V$	$+Y_{OE}^{D_a}O$	$\rightarrow$			$-Y_{VE}^{D_a}V$	$+Y_{CE}^{D_a}C$	$+Y_{HE}^{D_a}H$	$+Y_{NE}^{D_a}N$
G	**growth**	E	$+Y_{OE}^{G}O$	$\rightarrow$			$Y_{VE}^{G}V$	$+Y_{CE}^{G}C$	$+Y_{HE}^{G}H$	$+Y_{NE}^{G}N$
G^c	catabolic	E	$+Y_{OE}^{G_c}O$	$\rightarrow$				$Y_{CE}^{G_c}C$	$+Y_{HE}^{G_c}H$	$+Y_{NE}^{G_c}N$
G^a	anabolic	E	$+Y_{OE}^{G_a}O$	$\rightarrow$			$Y_{VE}^{G_a}V$	$+Y_{HE}^{G_a}C$	$+Y_{HE}^{G_a}H$	$+Y_{NE}^{G_a}N$

Dissipation
- somatic maintenance
- maturity maintenance
- maturation
- reproduction overhead

X	food	C	carbon dioxide
E	reserve	H	water
V	structure	O	dioxygen
P	faeces	N	nitrigen waste

Synthesizing units

Generalized enzymes that process generalized substrates
and follow classic enzyme kinetics
$$E + S \leftrightarrow ES \leftrightarrow EP \leftrightarrow E + P$$
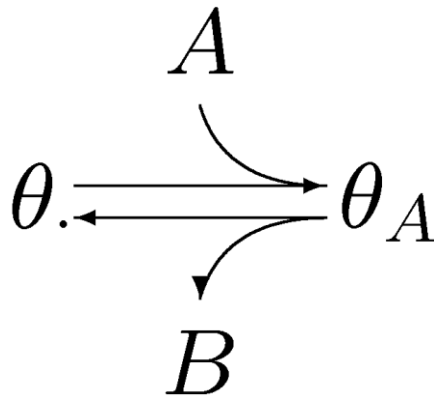with two modifications:
*   back flux is negligibly small (due to active transport of products)
    $$E + S \rightarrow ES \rightarrow EP \rightarrow E + P$$
*   specification of transformation is on the basis of
    arrival fluxes of substrates rather than concentrations
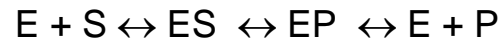
In spatially homogeneous environments:
arrival fluxes $\propto$ concentrations

Transformation A → B

$$\frac{d}{dt}\theta_. = \dot{k}_B\theta_A - \dot{b}_A X_A \theta_.$$

$$1 = \theta_. + \theta_A$$

$$\theta_.^* = \frac{\dot{k}_B}{\dot{k}_B + \dot{b}_A X_A}$$

$$\dot{j}_B = \dot{k}_B\theta_A^* = \frac{\dot{k}_B \dot{b}_A X_A}{\dot{k}_B + \dot{b}_A X_A}$$

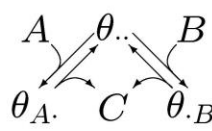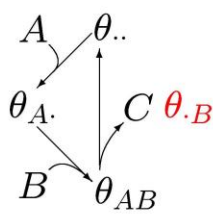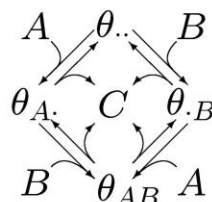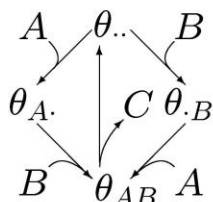Classification of behavioural modes:

 free & bound or searching & handling

Michealis-Menten (Henri 1902)
Holling type II (Holling 1957)

$\theta_.$	fraction of free SUs
θ_A	fraction of bound SUs
X_A	constantration of substrate A
$\dot{b}_A$	association rate of A to SU
$\dot{k}_B$	dissociation rtae of B from SU
$\dot{j}_B$	flux of produced B

Interactions of substrates

	substitutable $y_{CA}A \to C$; $y_{CB}B \to C$	complementary $y_{CA}A + y_{CB}B \to C$
sequential	$j_C = \dfrac{j''_A + j''_B}{1 + j'_A/\dot{k}_A + j'_B/\dot{k}_B}$ $j_A^+ = \dfrac{j'_A}{1 + j'_A/\dot{k}_A + j'_B/\dot{k}_B}$	$j_C = \dfrac{1}{\dot{k}^{-1} + j''_A{}^{-1} + j''_B{}^{-1}}$ $j_A^+ = y_{AC}j_C$
parallel	$j_C = \dfrac{y_{CA}}{\dot{k}_A^{-1} + j'_A{}^{-1}} + \dfrac{y_{CB}}{\dot{k}_B^{-1} + j'_B{}^{-1}}$ $j_A^+ = \dfrac{1}{\dot{k}_A^{-1} + j'_A{}^{-1}}$	$j_C = \dfrac{1}{\dot{k}^{-1} + j''_A{}^{-1} + j''_B{}^{-1} - (j''_A + j''_B)^{-1}}$ $j_A^+ = y_{AC}j_C$

$\dot{k}_*$	dissociation rate for $*$	j_*	spec. flux of compound $*$
j_*^+	spec. accepted flux	j_*^-	spec. rejected flux
j'_*	scaled flux: $\rho_* j_*$	j''_*	scaled flux: $y_{C*}j'_*$
ρ_*	binding probability	θ_*	fraction occupied by $*$

Modules of central metabolism

PP Pentose Phosphate cycle
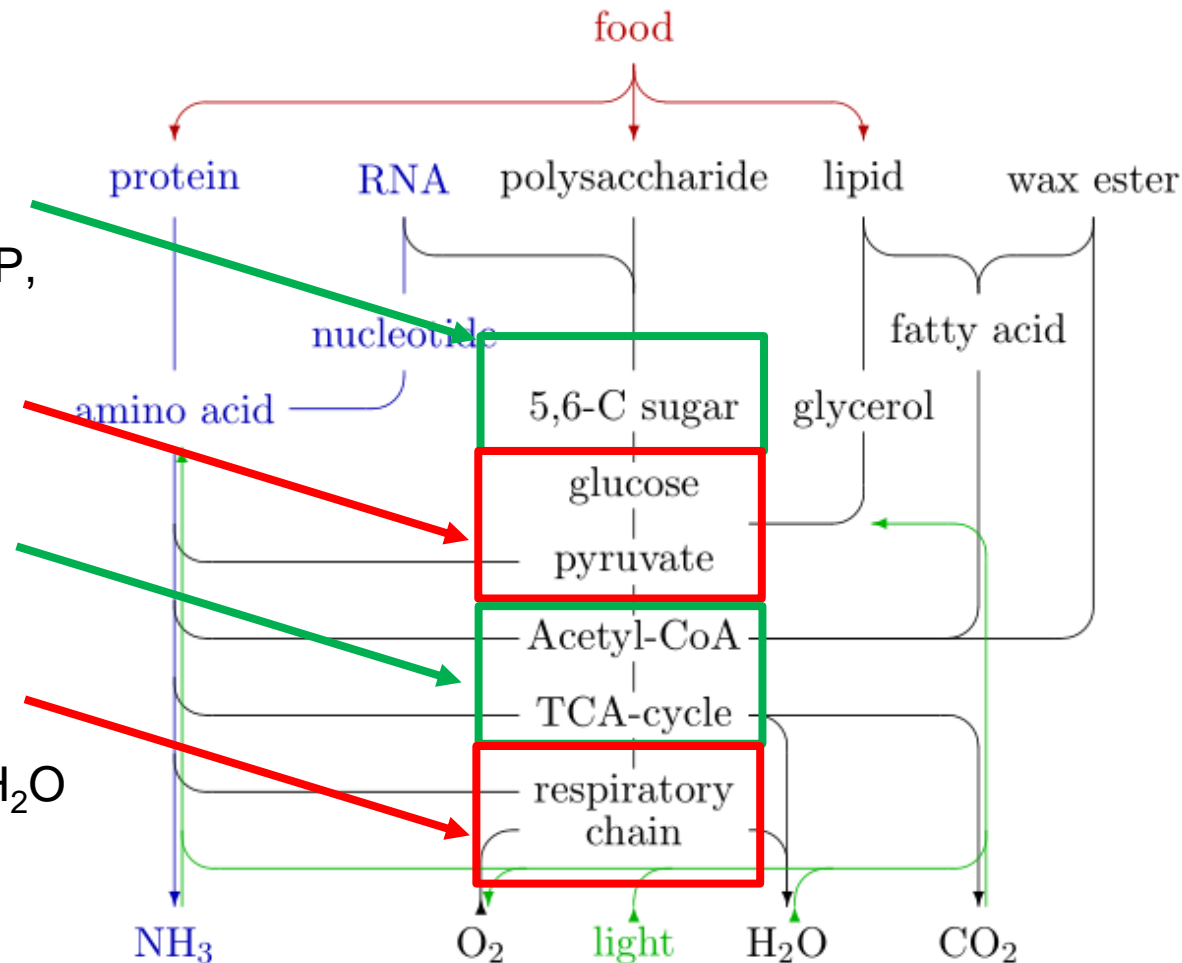glucose-6-P $\rightarrow$ ribulose-6-P,
NADP $\rightarrow$ NADPH

Gly Glycolysis
glucose-6-P $\rightarrow$ pyruvate
ADP + P $\rightarrow$ ATP

TCA TriCarboxcyl Acid cycle
pyruvate $\rightarrow$ CO_2
NADP $\rightarrow$ NADPH

RC Respiratory chain
NADPH + O_2 $\rightarrow$ NADP + H_2O
ADP + P $\rightarrow$ ATP

Evolution of central metabolism

in prokaryotes (= bacteria)

3.8 Ga   2.7 Ga
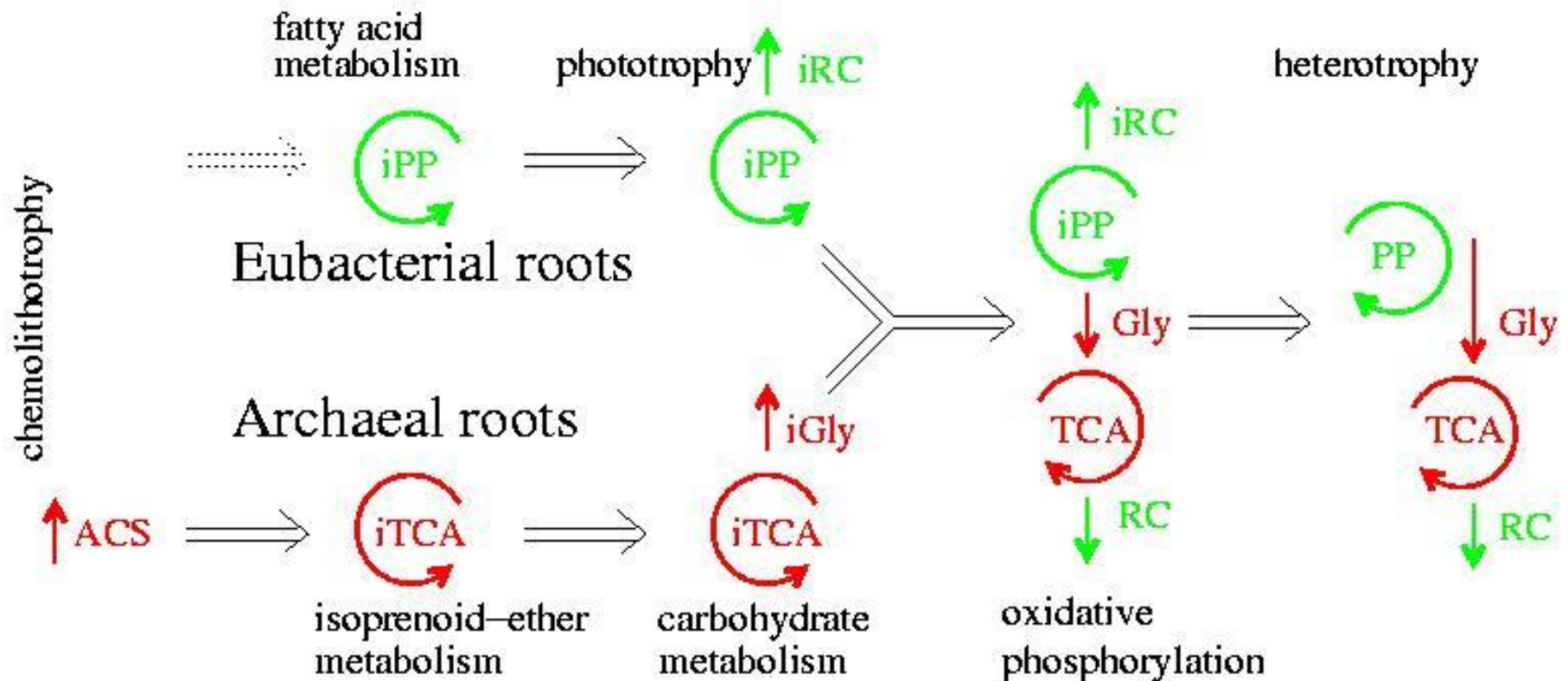
i = inverse

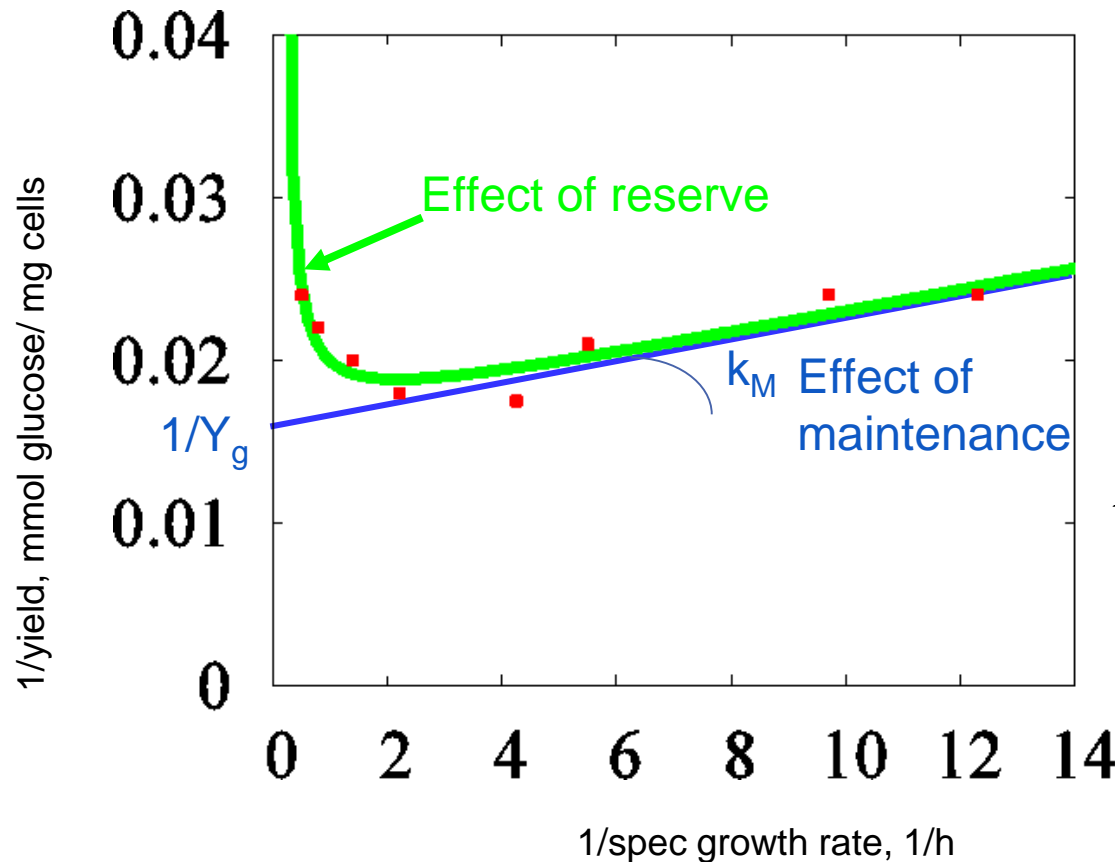ACS = acetyl-CoA Synthase pathway   RC = Respiratory Chain
PP = Pentose Phosphate cycle   Gly = Glycolysis
TCA = TriCarboxylic Acid cycle

Kooijman & Hengeveld 2005
Kooiman & Troost 2007

Structure vs Reserve

Streptococcus bovis, Russell & Baldwin (1979)

Effect of reserve

Marr-Pirt
(no reserve)

DEB
(reserve)

k_M Effect of maintenance

$1/Y_g$

1/yield, mmol glucose/ mg cells

1/spec growth rate, 1/h

$$r = k_E \frac{f - l_d}{f + g} \quad \text{spec growth rate}$$

$$Y = Y_g \frac{f}{g} \frac{f - l_d}{f + g} \quad \text{yield}$$

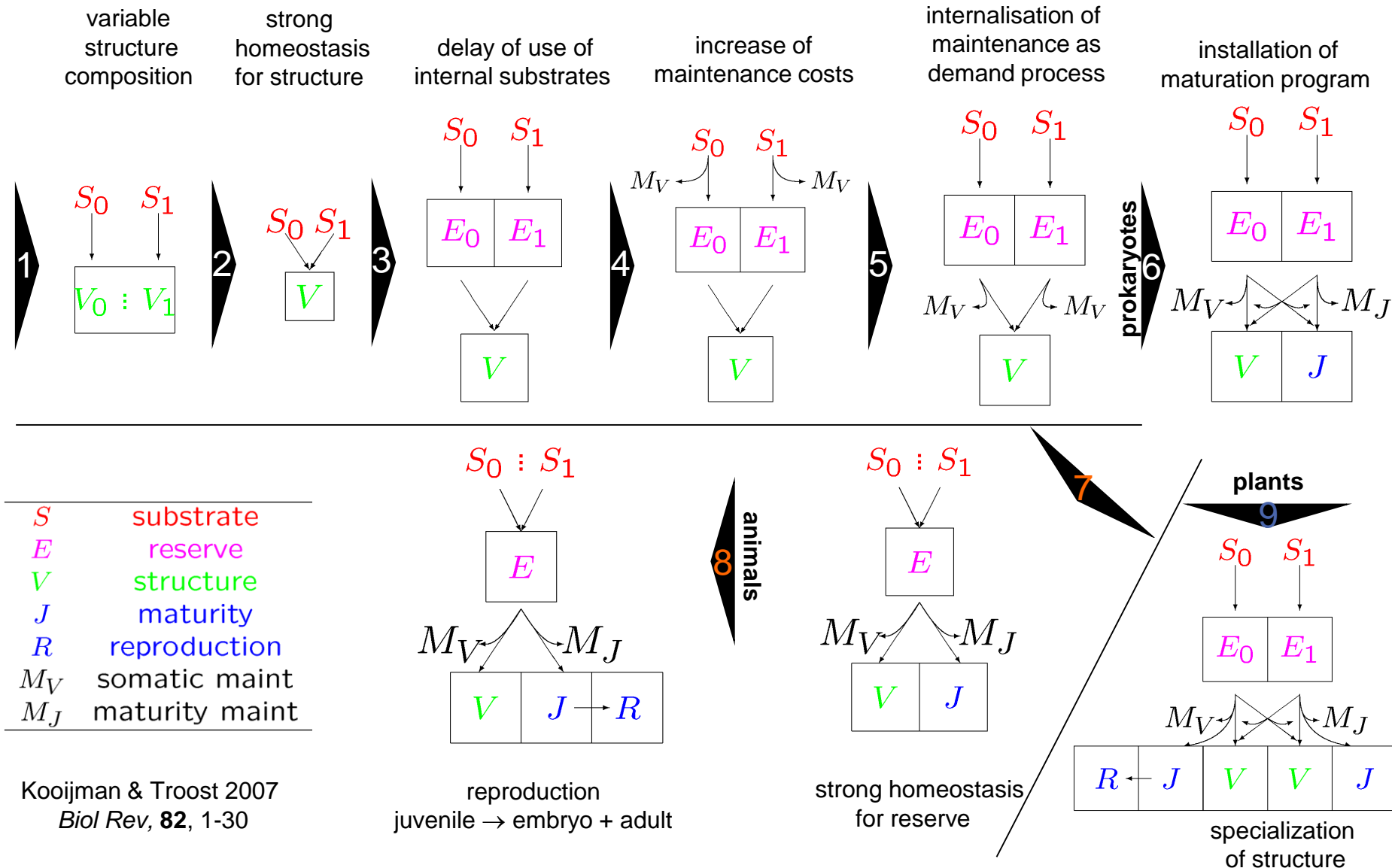$$= Y_g \frac{1 - r/k_E}{1 + k_M/r}$$

l_d scaled length: $g k_M / k_E$
k_M maintenance rate coefficient
k_E reserve turnover rate
g energy investment ratio
f scaled functional response
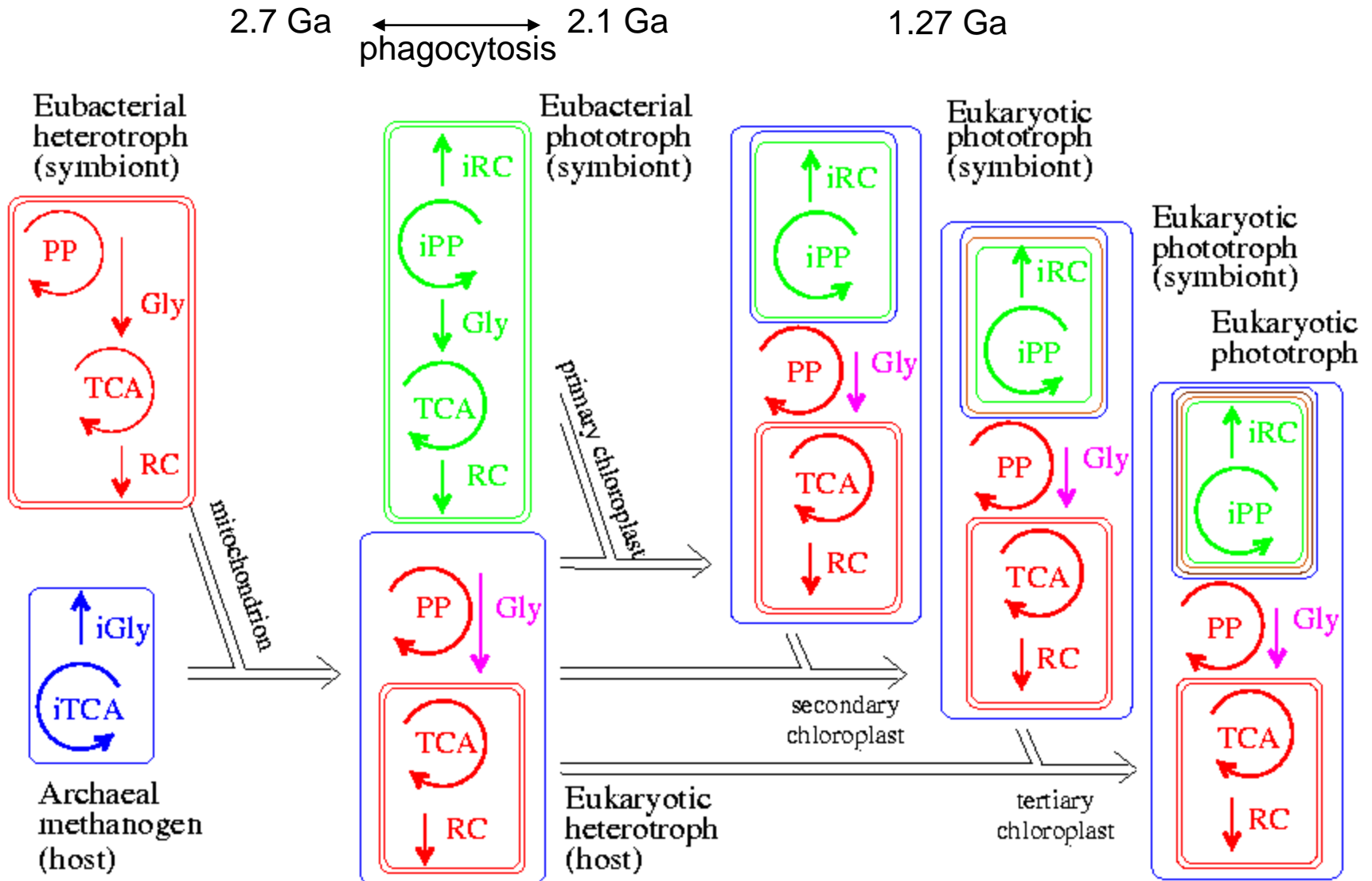Y_g true yield

Russell & Cook (1995): this is evidence for down-regulation of maintenance at high growth rates
DEB theory: high reserve density gives high growth rates structure requires maintenance, reserves do not

Evolution of reserves & structures

variable structure composition

strong homeostasis for structure

delay of use of internal substrates

increase of maintenance costs

internalisation of maintenance as demand process

installation of maturation program

prokaryotes

plants

animals

S substrate
E reserve
V structure
J maturity
R reproduction
M_V somatic maint
M_J maturity maint

Kooijman & Troost 2007
Biol Rev, **82**, 1-30

reproduction
juvenile $\rightarrow$ embryo + adult

strong homeostasis
for reserve

specialization
of structure

Symbiogenesis

individuals → populations

Steady state: Euler-Lotka equation in constant environments

$$1 = \int_{a=0}^{\infty} S(a)R(a)e^{-ra}\,da$$

specified by model   *specific growth rate*

S survival probability ⎱ end-points at pop level
R reproduction rate ⎰ depend on food density

Conversion efficiency

Individual: Consider a young dog and an adult (fully grown) one
  we daily give them both some food, which they eat all happily
  efficiency of conversion food $\rightarrow$ dog > 0 for young; = 0 for adult
  dog's physiology controls efficiency

Population: Consider a manager of a carp pond who daily orders 1 lorry grain for his carps
  if he does not harvest fish: efficiency of conversion grain $\rightarrow$ fish = 0 at steady state
  if he takes 1 fish per day: efficiency of conversion grain $\rightarrow$ fish = very low at steady state
  if he takes 100 fish per day: efficiency of conversion grain $\rightarrow$ fish = higher at steady state
  manager controls efficiency, fish physiology only sets constraints for maximum efficiency

Conclusion: Control of conversion efficiency is sensitive to level of organisation

Intra-specific competition: juvenile-driven cycles

Surface area-linked assimilation & volume-linked maintenance
  causes out-competition of older cohorts in isomorphs (not realistic)

Partial repairs:
  1) thinning: hazard such that increase of feeding by growth in a cohort of neonates
     is exactly balanced by a reduction in numbers (no extra parameters)

  2) parameters scatter between individuals (reduces synchronization)
      problem: large scatter is required, lots of computation time

  3) neonates need higher food quality, compared to adults
      two types of food are required, adults can live of both types, juveniles not

  4) temporal and spatial heterogeneity
      problem: there are many ways to structure time and space

Juvenile-driven cycles:

Juveniles outcompete adults and synchronize in homogenous environments (not realistic)

food dynamics in stirred fed-batch reactor

$$\frac{d}{dt}X = \frac{\dot{j}_X^I}{V_X} - \dot{h}_X X - \frac{X\{\dot{j}_{XAm}\}}{K + X}\sum_i L_i^2$$

initial condition:
X(0) = 0; 1 neonate

par-setting: *Daphnia magna* at 20 C
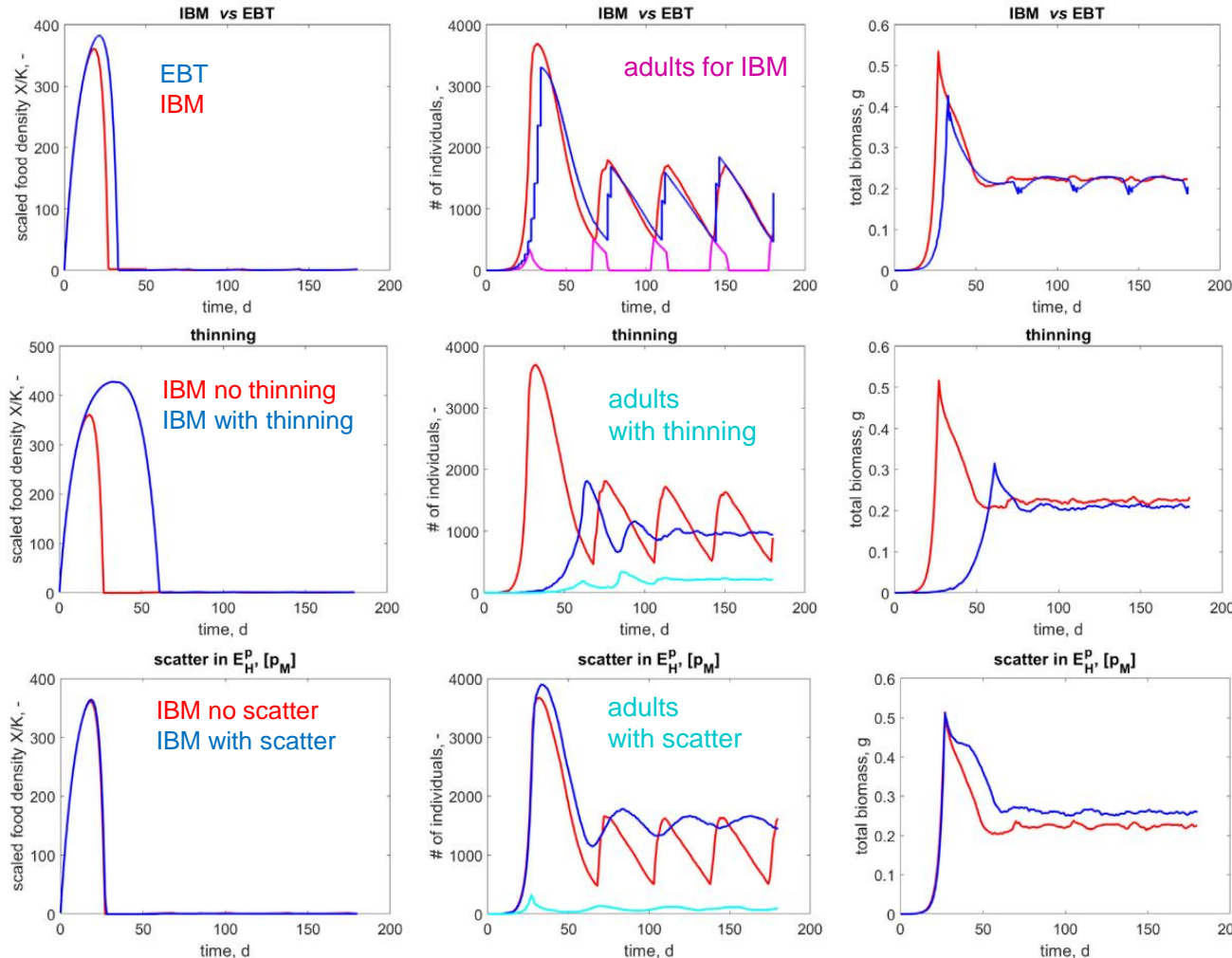
symbol	description
t	time
X	food density
K	half-saturation constant
V_X	reactor volume
$\dot{h}_X$	hazard rate for food
$\dot{j}_X^I$	food input
$\{\dot{j}_{XAm}\}$	spec feeding rate
L_i	struc length for ind i

Kooijman 2024
Ecol Mod **490** 110649
SI for Kooy2024 has code on GitHub

19

Inter-specific competition:

Gause's law: # of competing species < # of resources

Also known as the competitive exclusion principle (not realistic)

It is difficult to preserve biodiversity in community models:
No more recompeting species than resources
if feeding is a monotonous function of resource density

Repairs:

1) temporal and spatial heterogeneity
problem: there are many ways to structure time and space

2) exploit concept of syntrophy

3) more details in nutrition

4) make feeding also a function of population density: social inhibition

Social inhibition of $X \rightarrow E$

sequential
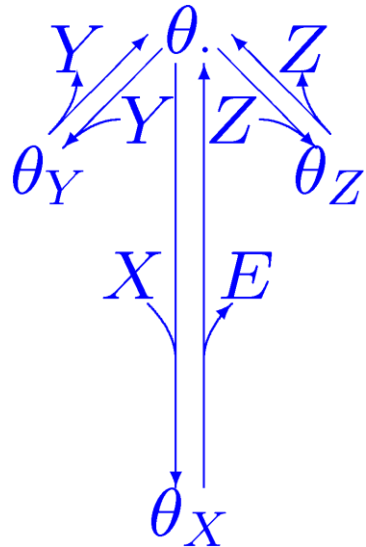
parallel
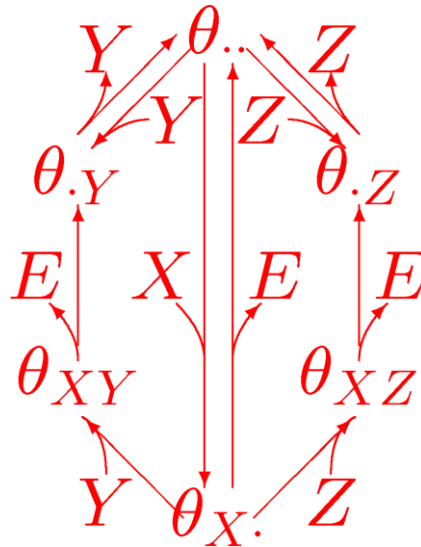
substrate conc.
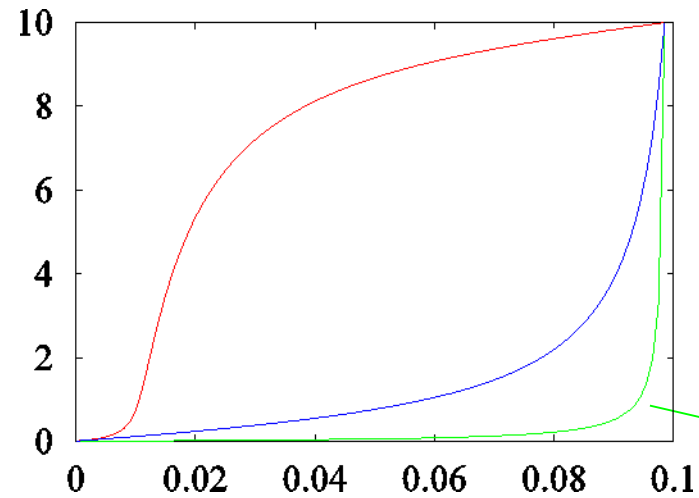
biomass conc.
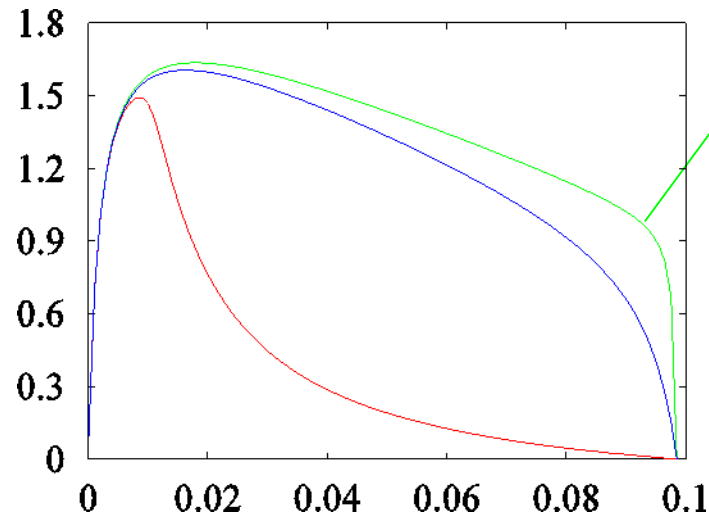
dilution rate

No socialization

Implications:
  stable co-existence of
    competing species

X substrate
E reserve
Y species 1
Z species 2

absence of paradox of enrichment

Paradox of enrichment 1

Deterministic model in closed homogeneous system

$$m_N = N/P - n_{NC}C/P - n_{NP}$$

$$\frac{d}{dt}P = P(\dot{r}_P - C_s j_{Pm}/K)$$

$$\dot{r}_P = \frac{\dot{k}_N m_N}{y_{NP} + m_N}$$

$$\frac{d}{dt}C_s = C_h \dot{k} - C_s(\dot{h}_C + P\dot{k}/K)$$

$$Y_{CP} = \left(y_{CP}^{-1} + y_{CN}^{-1}m_N^{-1} - (y_{CP} + y_{CN}m_N)^{-1}\right)^{-1}$$

$$\frac{d}{dt}C_h = C_s P \delta_t \dot{k}/K - C_h(\dot{h}_C + \dot{k})$$

$$\delta_t = 1 + Y_{CP}/y_{CP}^{\epsilon}; \quad y_{CP}^{\epsilon} = j_{Pm}/\dot{k}$$

Stochastic model

event type i	F feeding	S searching	D_s dying of C_s	D_h dying of C_h	G growing
intensity $\dot{\lambda}_i$	$\dot{k}\frac{PC_s}{KC_\epsilon}$	$\dot{k}\frac{C_h}{C_\epsilon}$	$\dot{h}_C\frac{C_s}{C_\epsilon}$	$\dot{h}_C\frac{C_h}{C_\epsilon}$	$\dot{r}_P\frac{P}{P_\epsilon}$
change dP	$-P_\epsilon$	0	0	0	P_ϵ
dC_s	$-C_\epsilon$	C_ϵ	$-C_\epsilon$	0	0
dC_h	$\underline{\delta_t}C_\epsilon$	$-C_\epsilon$	0	$-C_\epsilon$	0

symbol	dim	interpretation
t	t	time
N	mol l^{-3}	total nutrient in the system
P, P_ϵ	mol l^{-3}	producer density, increment -
C, C_s, C_h, C_ϵ	mol l^{-3}	consumer density , searching -, handling -, increment -
m_N	mol mol^{-1}	nutrient-reserve density of producer

Rosenzweig1971
AAAS **171**: 385–387.
Kooijman *et al* 2007
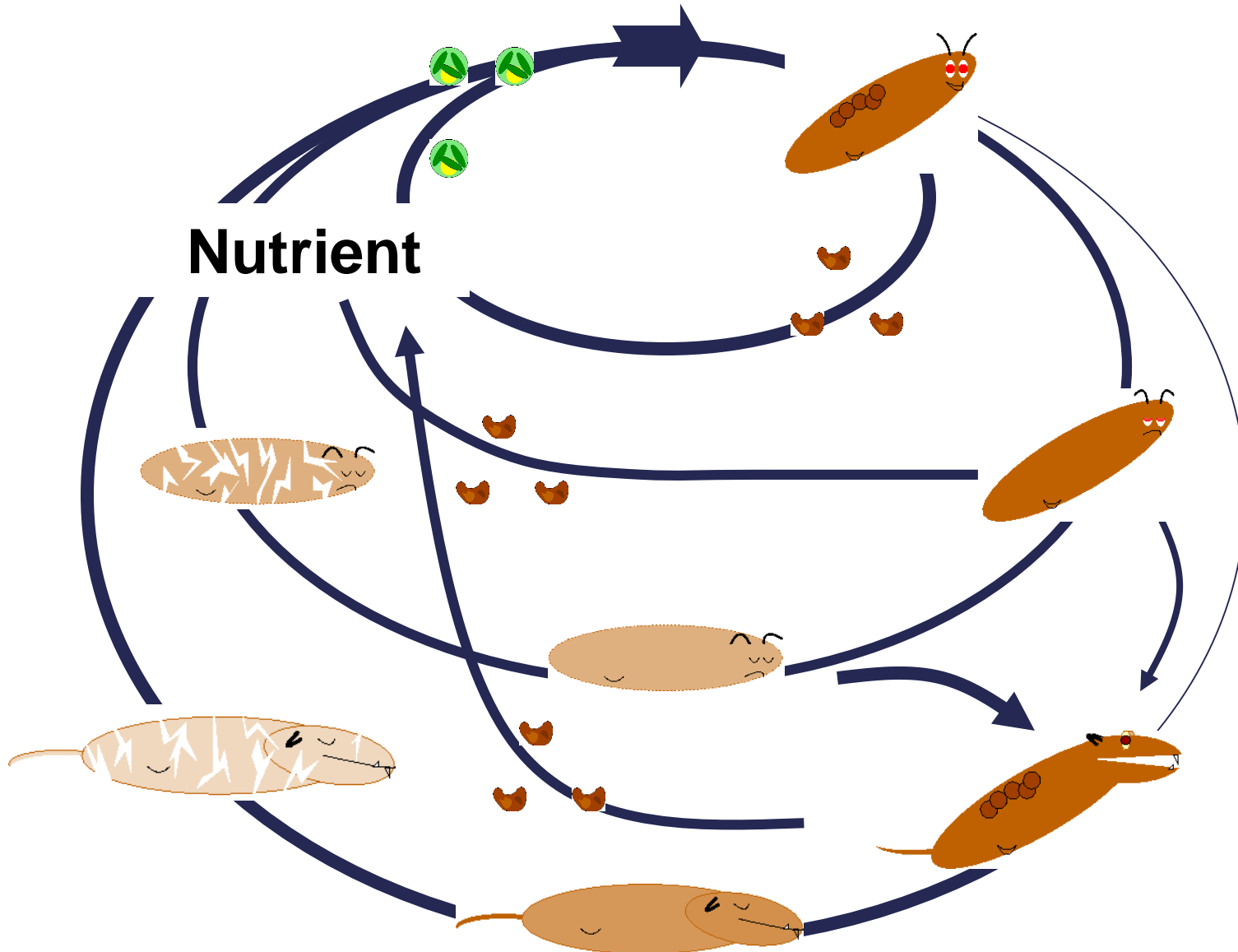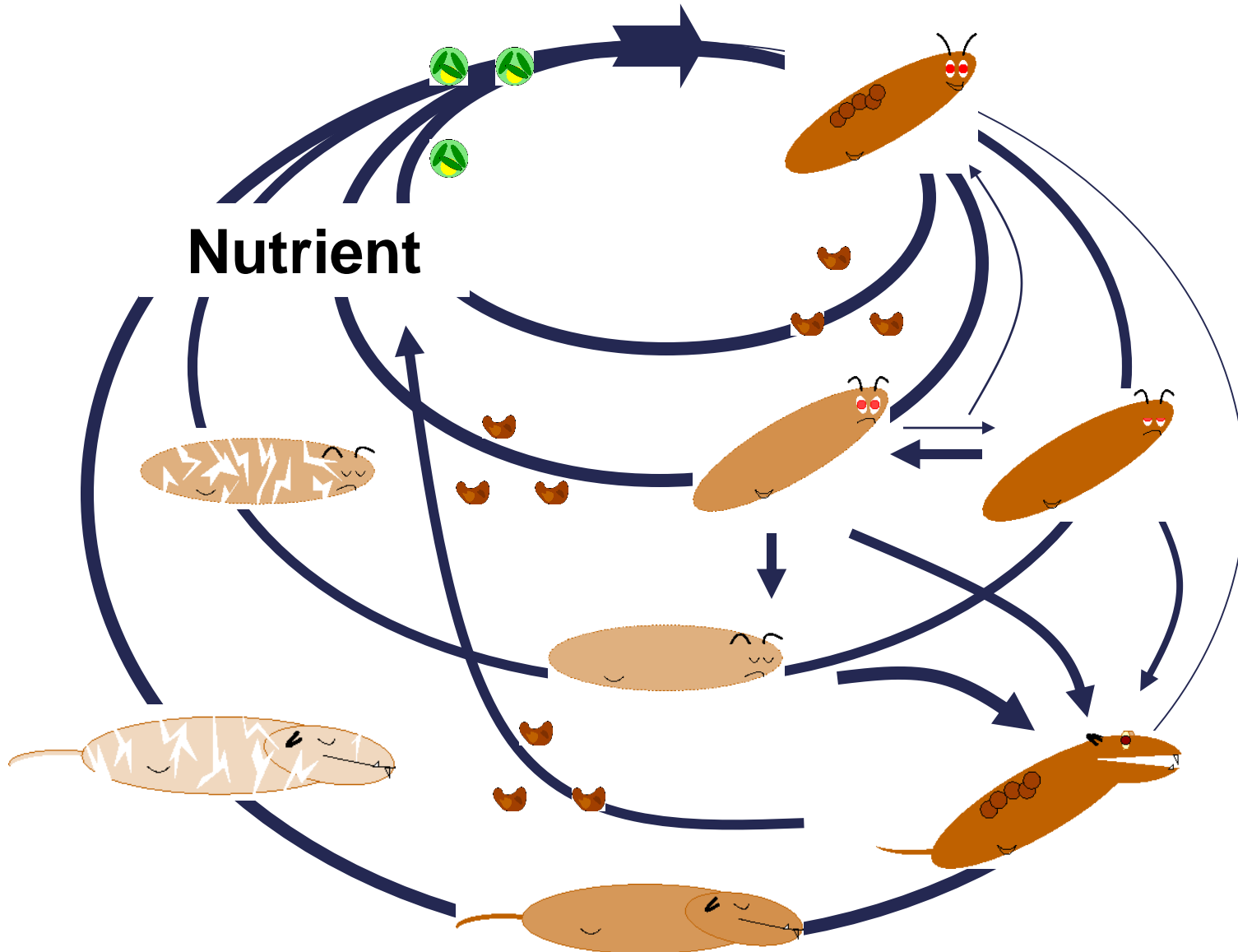*Math Biosci,* **210**, 378-394
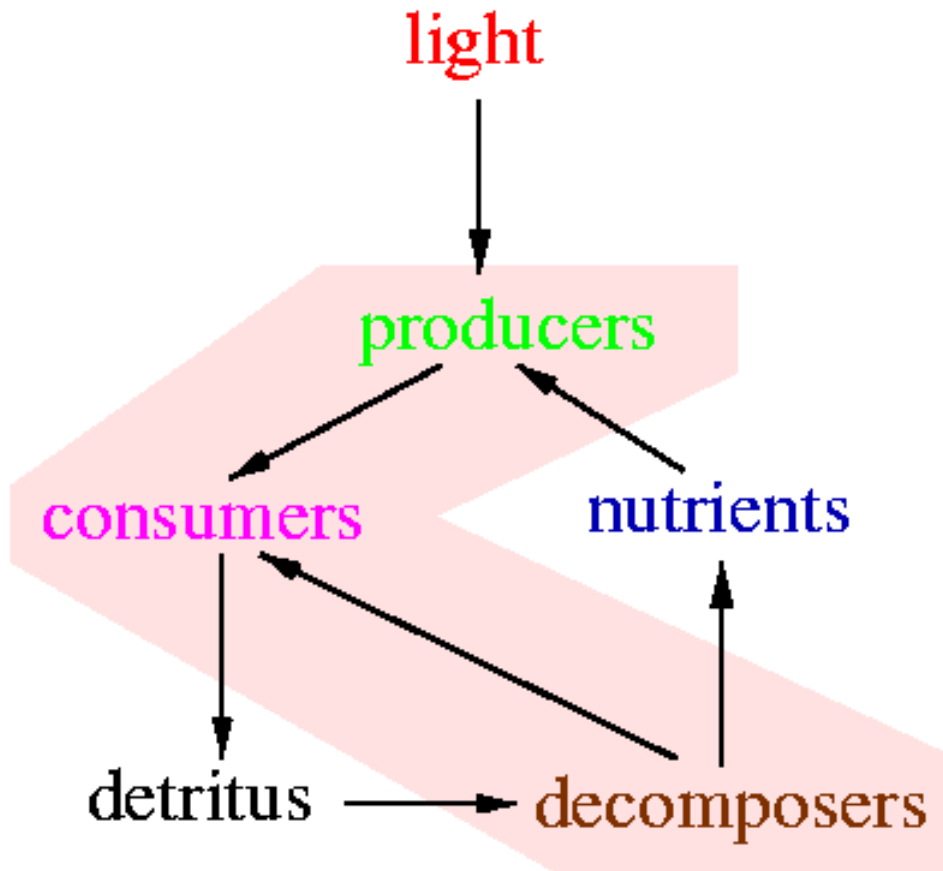
Paradox of enrichment 2

Bifurcation diagram

consumers

tangent
focus

Hopf

nutrient

1.0

1.15

1.23

1.53

2.8

1.75

2.3

2.4

2.5

2.7

3.0

isoclines

Resource dynamics
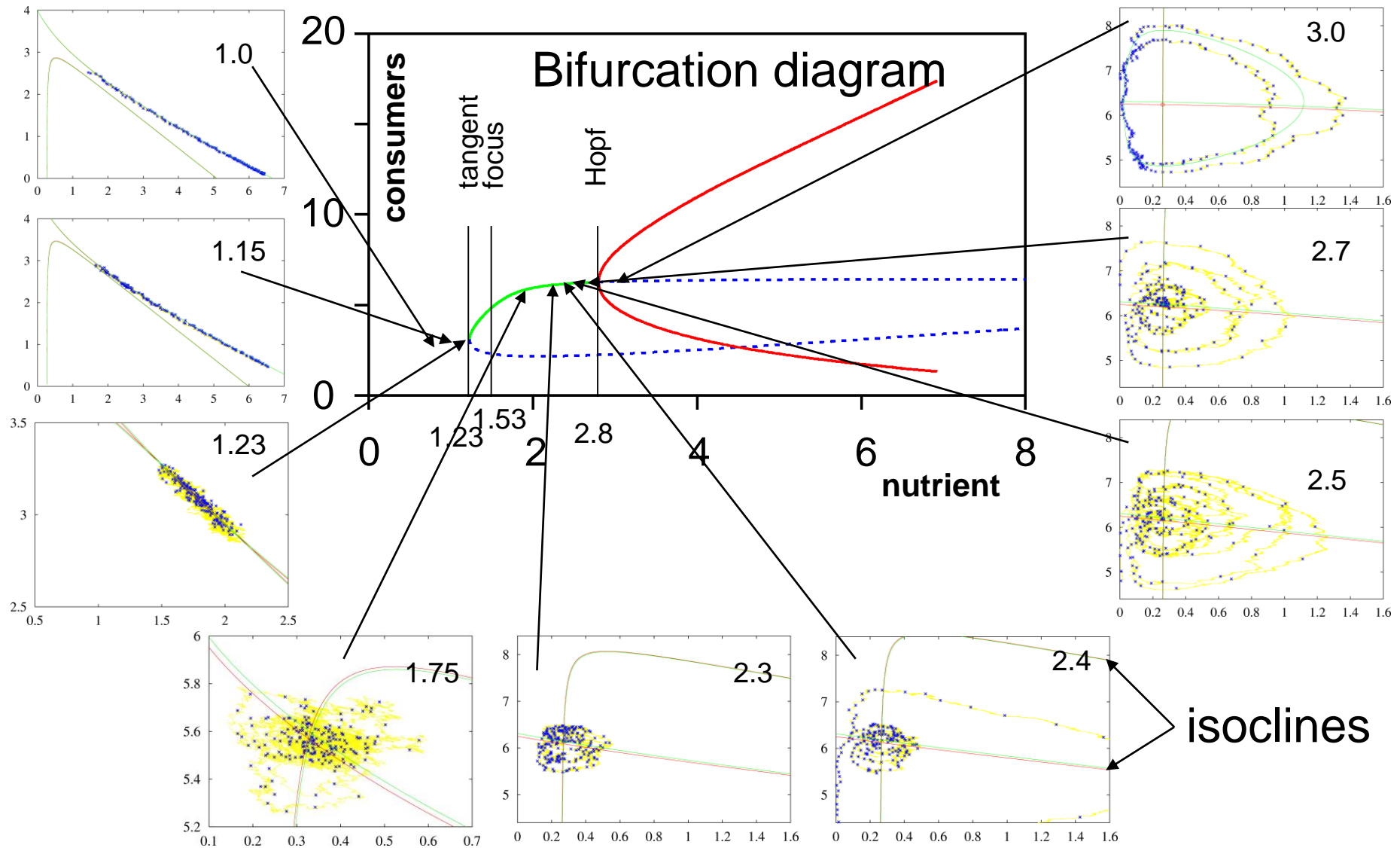
Nutrient
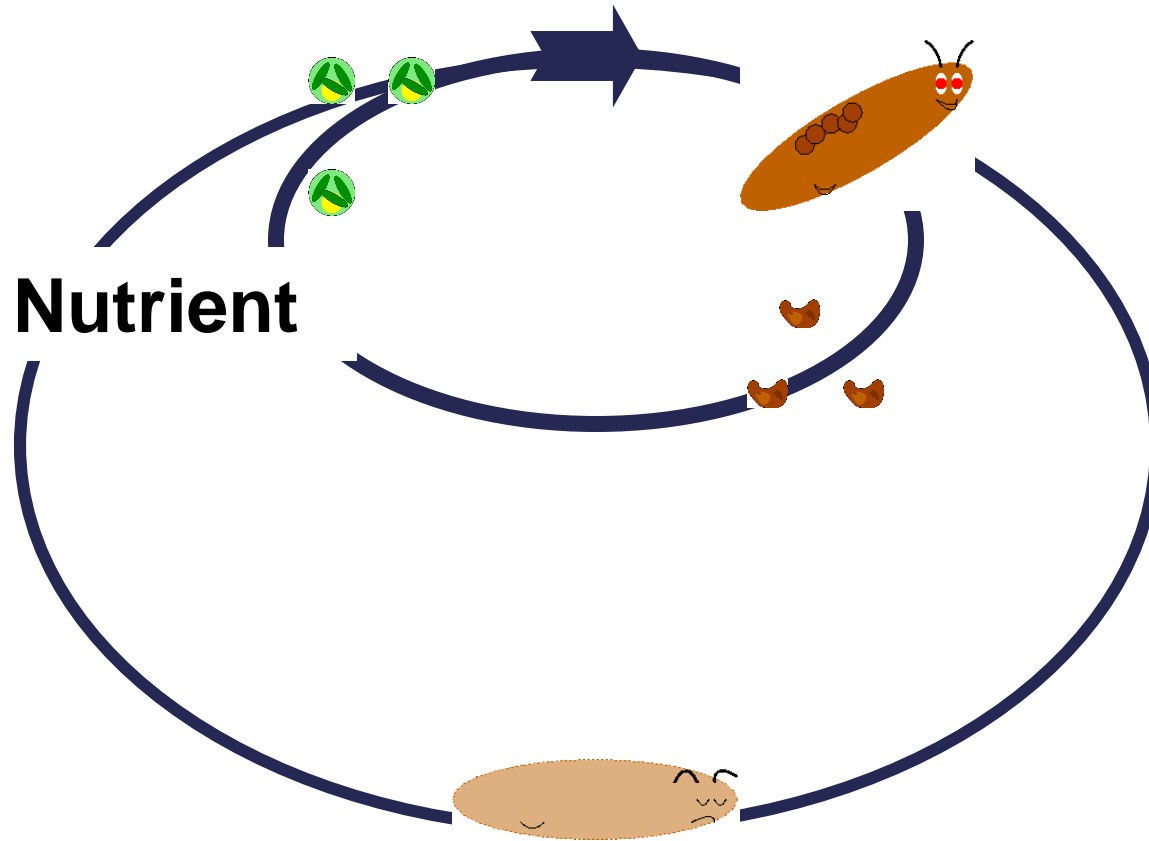
Resource dynamics

Nutrient

Resource dynamics

Nutrient

Canonical community

Short time scale:
Mass recycling
in a community
  closed for mass
  open for energy

Long time scale:
Nutrients leaks and influxes

Memory is controlled by
  life span (links to body size)
Spatial coherence is controlled by
  transport (links to body size)

Marine plankton affects climate

- organic carbon pump

  transport of atmospheric CO_2 to deep ocean (1000 year memory)
  linked to nutrient cycling, terrestrial ecosystems

- calcification (inorganic carbon pump)

  precipitation of CO_2 in $CaCO_3$ → burial by plate tectonics

- albedo

  emission of DMS → cloud formation, effects on radiation

Half rules:
Half of evaporation is from land (plants compensate land/sea difference)
Half of present primary production is from marine plankton
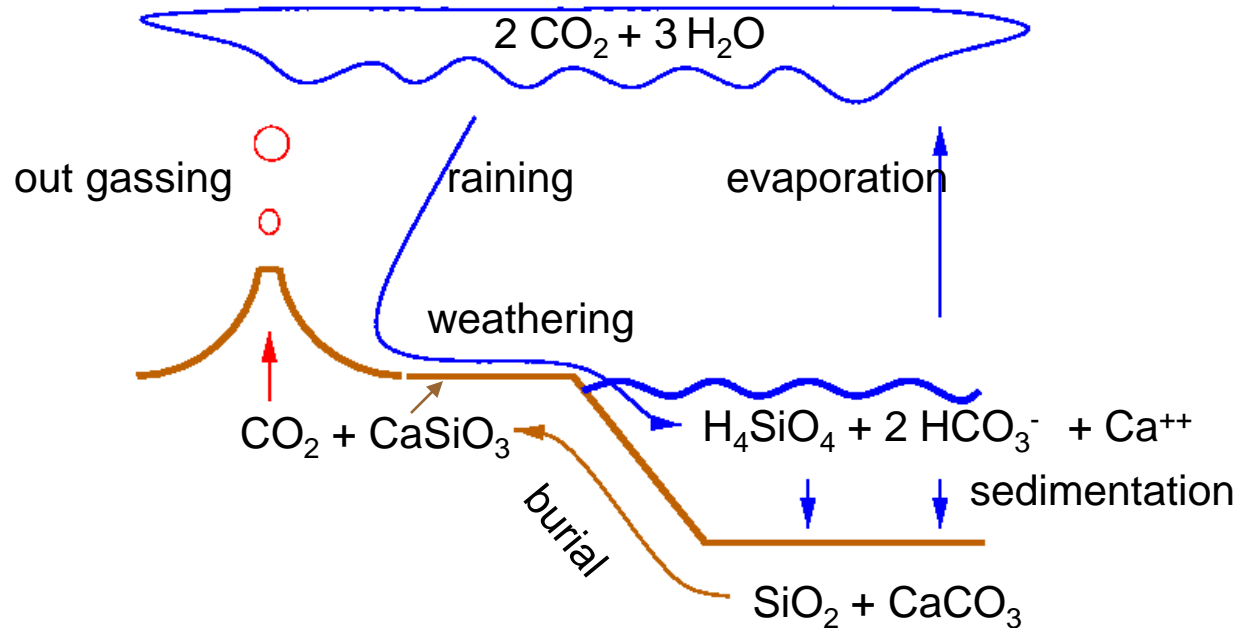Half of carbonate precipitation is by reefs (corals),
  the rest by plankton (forams and coccolithophores)

Kooijman 2004. On the coevolution of life and its environment.
In: Schneider et al, Scientists Debate Gaia; the next century, 343–351.
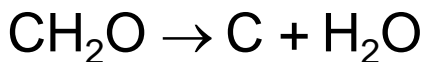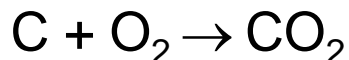MIT Press, Cambridge, Mass

Rock cycle

$2\,CO_2 + 3\,H_2O$

out gassing

raining

evaporation

weathering

$CO_2 + CaSiO_3$

burial

$H_4SiO_4 + 2\,HCO_3^- + Ca^{++}$

sedimentation

$SiO_2 + CaCO_3$

Photosynthesis: $H_2O + CO_2 + light \rightarrow CH_2O + O_2$

Fossilisation: $CH_2O \rightarrow C + H_2O$

Burning: $C + O_2 \rightarrow CO_2$

Calcification: $2HCO_3^- + Ca^{++} \rightarrow CaCO_3 + CO_2 + H_2O$

Silification: $H_4SiO_4 \rightarrow SiO_2 + 2H_2O$

pH of seawater = 8.3

98 % DIC = HCO_3^-

not available to most org.

After Peter Westbroek

Nutrients: rocks → plankton
by plants + micro's

HISTORICAL EVIDENCES

During the Silurian, plants began to colonize land.

By the Devonian, the land is almost entirely covered in vegetation.
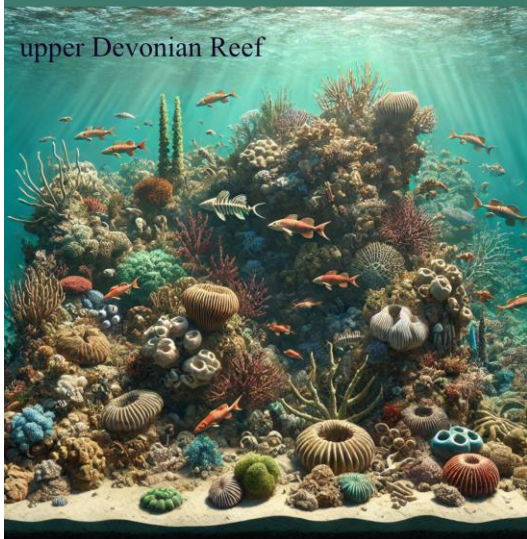
Filter-feeding reefs thrived in both the Silurian and Devonian.

Pangaea formed during the Permian

lower Devonian Landscape

upper Devonian Reef

HYPOTHESIS

Plants released nutrients from the lithosphere, which rivers transported to oceans.

Plankton used these nutrients, and reefs fed on the plankton, growing during the Silurian and Devonian.

The formation of Pangaea reduced this nutrient input, leading to reef extinction

Organic carbon pump
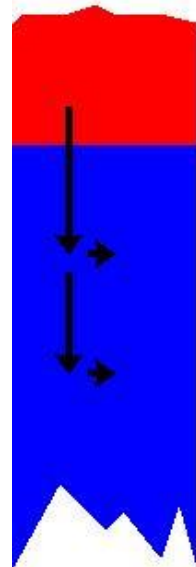

Wind: weak   moderate   strong
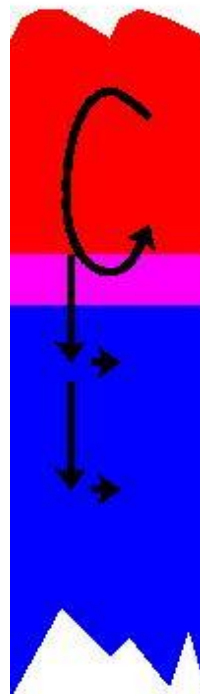
light + CO_2

"warm"
no nutrients

cold
nutrients
no light

recovery of
nutrients to
photo-zone
controls pump

no growth   growth ←—— poor growth
bloom

producers
bind CO_2
from atmosphere
and transport
organic carbon
to deep ocean

readily degradable

poorly degradable

Final slide

Thank you for your attention

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Questions/remarks are very welcome

Also later during breaks