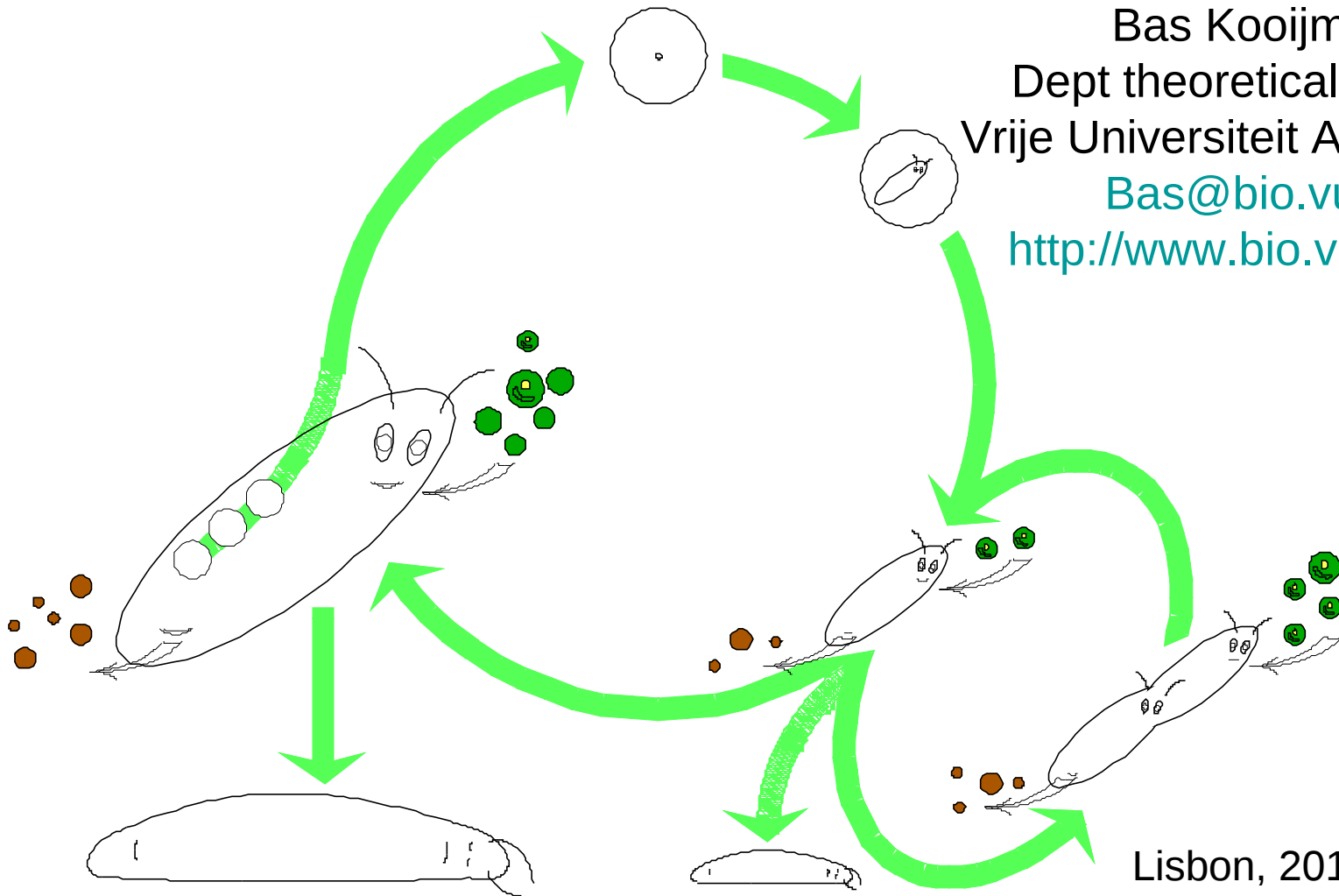# Metabolic dynamics
acceleration during the life cycle of an individual

Bas Kooijman
Dept theoretical biology
Vrije Universiteit Amsterdam
Bas@bio.vu.nl
http://www.bio.vu.nl/thb/

Lisbon, 2013/02/13

Metabolic dynamics
acceleration during the life cycle of an individual

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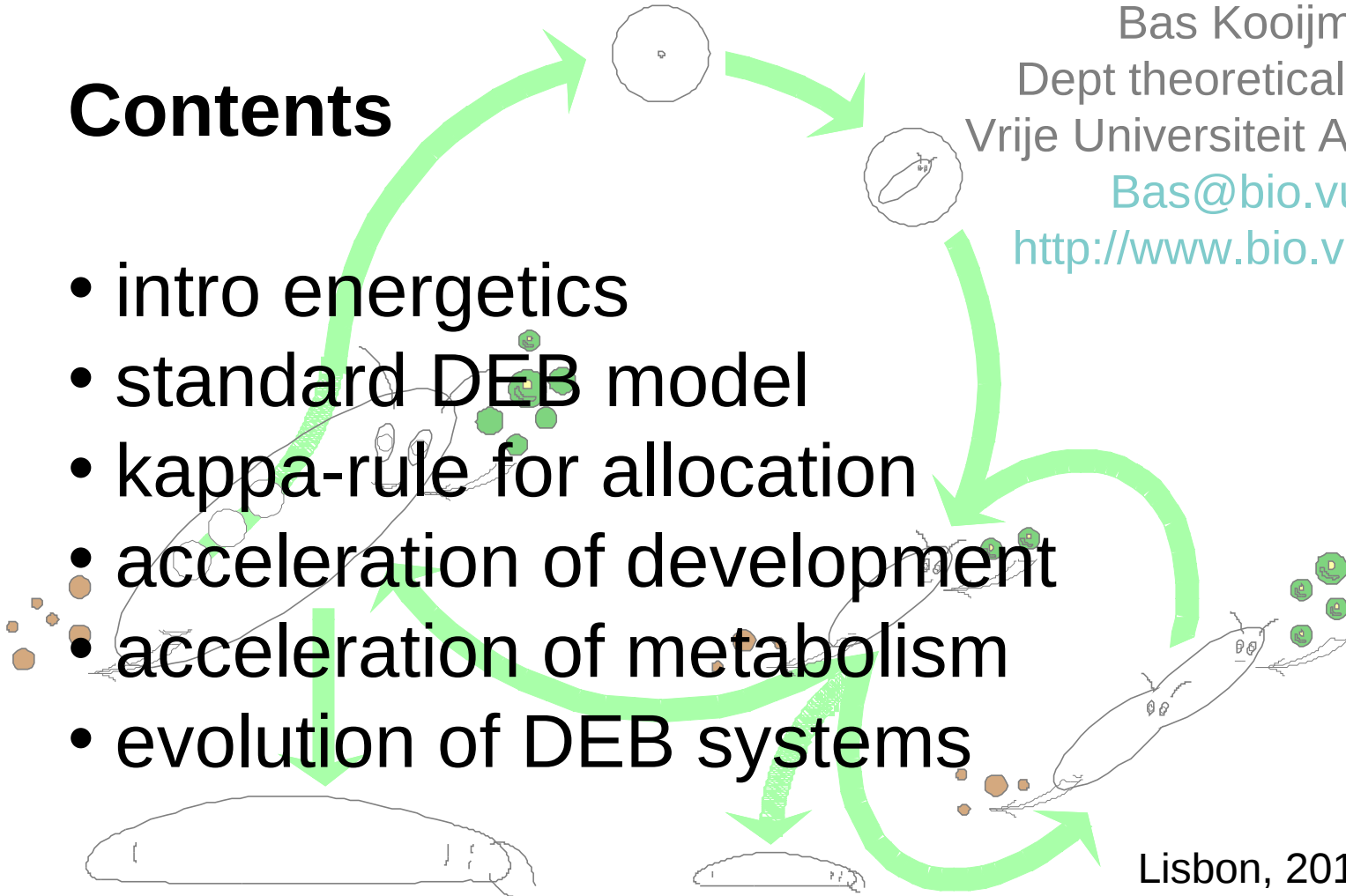Dept theoretical biology
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Contents

- intro energetics
- standard DEB model
- kappa-rule for allocation
- acceleration of development
- acceleration of metabolism
- evolution of DEB systems

Lisbon, 2013/02/13

Energy Budgets

Basic processes	Life history events	Life stages

• Feeding
• Digestion
• Storing
• Growth
• Maturation
• Maintenance
• Reproduction
• Product formation
• Aging
	• zero:
	    start of development
	• birth:
	    start of feeding
	    start of acceleration
	• metamorphosis:
	    end of acceleration
	• puberty:
	    end of maturation
	    start of reproduction
		embryo
		
		juvenile
		
		adult

All have ecological implications
All interact during the life cycle

Quantitative Energetics

Biochemical approach: Chemically explicit

classify compounds in important and unimportant ones
model few import compounds
Problems:
mass & energy conservation is lost as modeling tool/check
time scales of transformations really short relative to life cycle
role of unimportant compounds might be important
spatial structure difficult to take into account

Balance approach: Pools of metabolites

partition biomass in a few metabolic pools
assume strong homeostasis for each pool: generalised compounds
assume weak homeostasis: constant pool ratios during growth at constant food
Problems:
homeostasis is not perfect
abstract, indirect testing

Model: more than formula where variables and parameters relate to physical or chemical quantities

Criteria for general energy models

- **Quantitative**
  Based on explicit assumptions that together specify all quantitative aspects to allow for mass and energy balancing

- **Consistency**
  Assumptions should be consistent in terms of internal logic, with physics and chemistry, as well as with empirical patterns

- **Simplicity**
  Implied model(s) should be simple (numbers of variables and parameters) enough to allow testing against data

- **Generality**
  The conditions species should fulfill to be captured by the model(s) must be explicit and make evolutionary sense

- **Explanatory**
  The more empirical patterns are explained, the better the model

From Sousa et al 2010
Phil. Trans. R. Soc. Lond. B **365**: 3413-3428

Empirical special cases of DEB 11.1

year	author	model	year	author	model
1780	Lavoisier	multiple regression of heat against mineral fluxes	1950	Emerson	cube root growth of bacterial colonies
1825	Gompertz	Survival probability for aging	1951	Huggett & Widdas	foetal growth
1889	Arrhenius	temperature dependence of physiological rates	1951	Weibull	survival probability for aging
1891	Huxley	allometric growth of body parts	1955	Best	diffusion limitation of uptake
1902	Henri	Michaelis--Menten kinetics	1957	Smith	embryonic respiration
1905	Blackman	bilinear functional response	1959	Leudeking & Piret	microbial product formation
1910	Hill	Cooperative binding	1959	Holling	hyperbolic functional response
1920	Pütter	von Bertalanffy growth of individuals	1962	Marr & Pirt	maintenance in yields of biomass
1927	Pearl	logistic population growth	1973	Droop	reserve (cell quota) dynamics
1928	Fisher & Tippit	Weibull aging	1974	Rahn & Ar	water loss in bird eggs
1932	Kleiber	respiration scales with body weight$^{3/4}$	1975	Hungate	digestion
1932	Mayneord	cube root growth of tumours	1977	Beer & Anderson	development of salmonid embryos

DEB theory is axiomatic, based on mechanisms not meant to glue empirical models

Since many empirical models turn out to be special cases of DEB theory the data behind these models support DEB theory

This makes DEB theory very well tested against data

Empirical patterns: stylised facts

Feeding

During starvation, organisms are able to reproduce, grow and survive for some time
At abundant food, the feeding rate is at some maximum, independent of food density

Growth

Many species continue to grow after reproduction has started
Growth of isomorphic organisms at abundant food is well described by the von Bertalanffy
For different constant food levels the inverse von Bertalanffy growth rate increases linearly with ultimate length
The von Bertalanffy growth rate of different species decreases almost linearly with the maximum body length
Fetuses increase in weight approximately proportional to cubed time

Reproduction

Reproduction increases with size intra-specifically, but decreases with size inter-specifically

Respiration

Animal eggs and plant seeds initially hardly use O_2
The use of O_2 increases with decreasing mass in embryos and increases with mass in juveniles and adults
The use of O_2 scales approximately with body weight raised to a power close to 0.75
Animals show a transient increase in metabolic rate after ingesting food (heat increment of feeding)

Stoichiometry

The chemical composition of organisms depends on the nutritional status (starved *vs* well-fed)
The chemical composition of organisms growing at constant food density becomes constant

Energy

Dissipating heat is a weighted sum of 3 mass flows: CO_2, O_2 and N-waste

Homeostasis 1.2

strong homeostasis

constant composition of pools (reserves/structures)
generalized compounds, stoichiometric constraints on synthesis

weak homeostasis

constant composition of biomass during growth in constant environments
determines reserve dynamics (in combination with strong homeostasis)

structural homeostasis

constant relative proportions during growth in constant environments
isomorphy .work load allocation

thermal homeostasis

ectothermy $\rightarrow$ homeothermy $\rightarrow$ endothermy

acquisition homeostasis

supply $\rightarrow$ demand systems

development of sensors, behavioural adaptations

Standard DEB scheme 2b

1 food type, 1 reserve, 1 structure, isomorph

food → *feeding* → *defecation* → faeces

assimilation

reserve

somatic maintenance κ *growth*

1-κ *maturity maintenance*

maturation reproduction

structure

maturity offspring
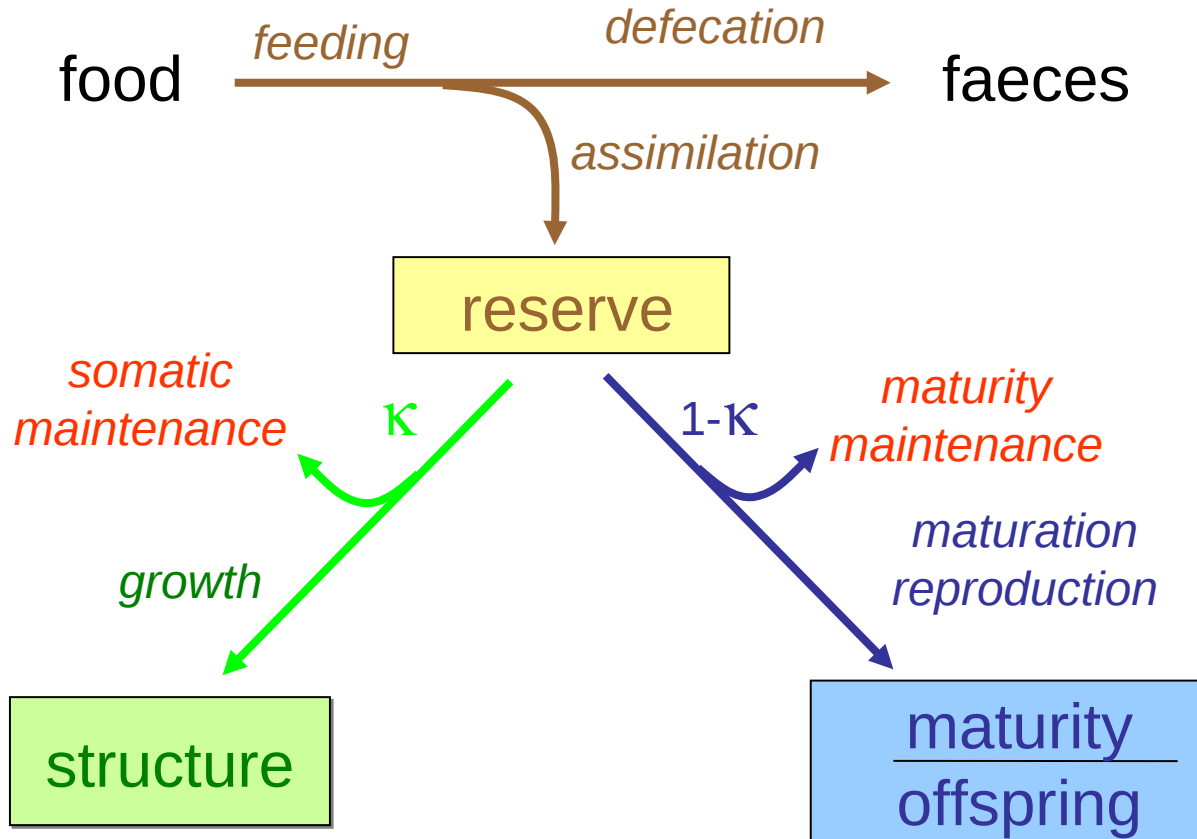
time: searching & handling
feeding ∝ surface area
weak & strong homeostasis
κ-rule for allocation to soma
maintenance has priority
   somatic maint ∝ structure
   maturity maint ∝ maturity
stage transition: maturation
   embryo: no feeding, reprod
   juvenile: no reproduction
   adult: no maturation
maternal effect: reserve density
   at birth equals that of mother
initially: zero structure, maturity

Change in body shape 4.2.2

Isomorph:
surface area $\propto$ volume$^{2/3}$
volumetric length = volume$^{1/3}$
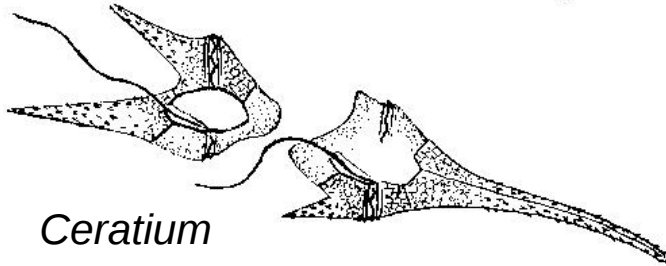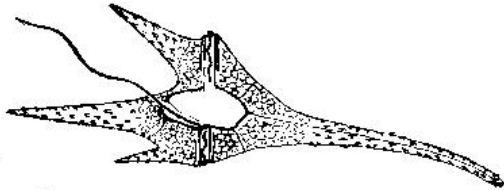
Mucor

Ceratium
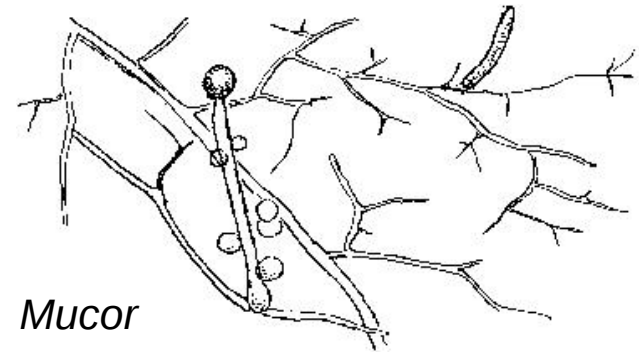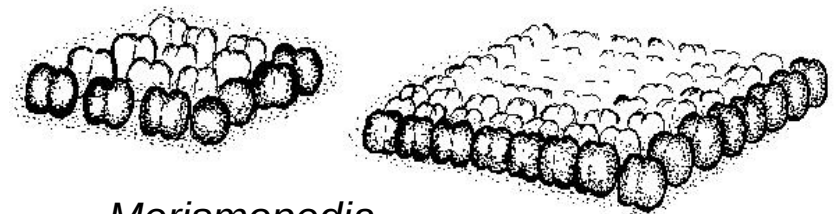
Merismopedia

V0-morph:
surface area $\propto$ volume^0

V1-morph:
surface area $\propto$ volume^1

Change in body shape 4.2.2
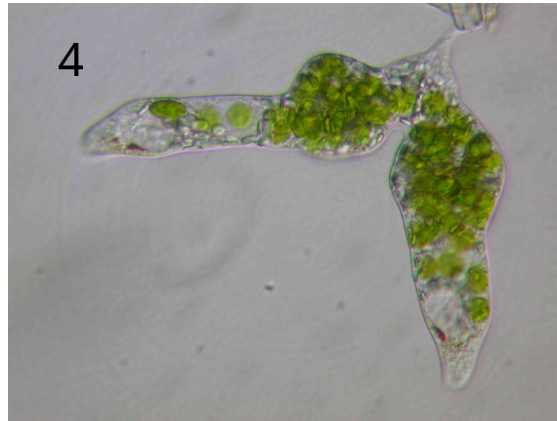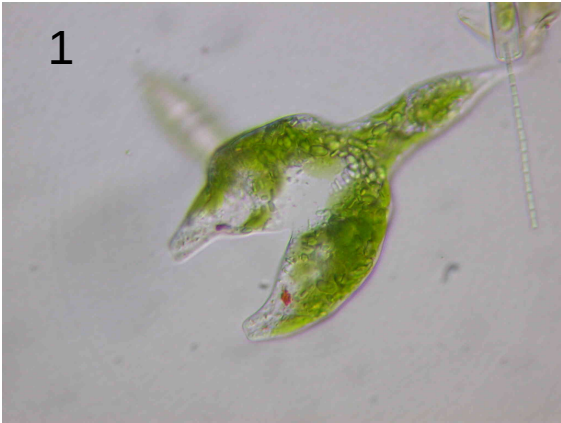
Euglena

surface area ∝ radius
volume ∝ radius^2

V½-morph:
   surface area ∝ volume$^{1/2}$

Reserve residence time

$$t_E = \frac{E}{\dot{p}_C} = \frac{1 + f/g}{\dot{v}/L + \dot{k}_M(1 + L_T/L)}$$

$$t_{Em} = (\dot{k}_M g)^{-1} \quad \text{for } f = 1; L = L_m; L_T = 0$$

$$t_{Em} = L_m/\dot{v}$$

enzymes in E loose their activity (first order)

within individual: t_E increases with L

individual looses metabolic performance with L

inter-species: $t_{Em} \propto L_m$, $E_m \propto L_m^4$

active enzyme density independent of L_m

f	scaled functional response
E	reserve
$\dot{p}_C$	mobilisation power
$\dot{v}$	engergy conductance
g	energy investment ratio
$\dot{k}_M$	somatic maint. rate coeff.
L	structural length
L_m	maximum length
L_T	heating length

κ-rule for allocation 2.4

Respiration $\propto$
$$vL^2 + k_M L^3$$

O$_2$ consumption, µg/h

Length, mm

Ingestion $\propto$
$$fL^2$$

Ingestion rate, 10^3 cells/h

Length, mm

Reproduction $\propto$
$$vL^2 + k_M L^3 - (1 + g/f)k_M L_p^3$$

Cum # of young

Age, d

Growth:
$$\frac{d}{dt}L = r_B(L_\infty - L)$$

Von Bertalanffy

Length, mm

Age, d
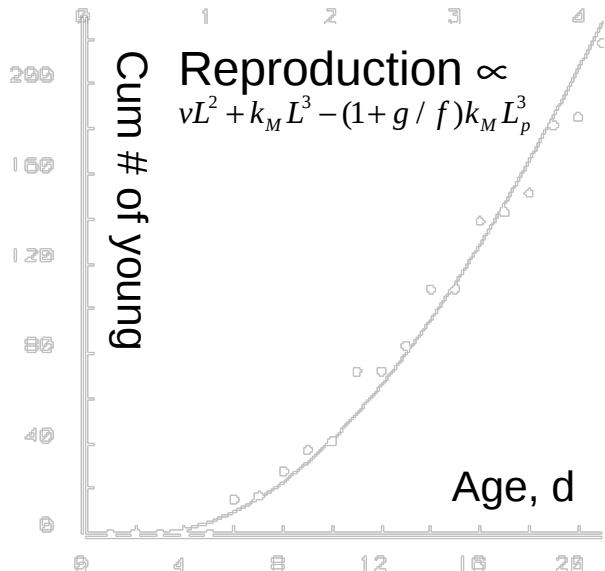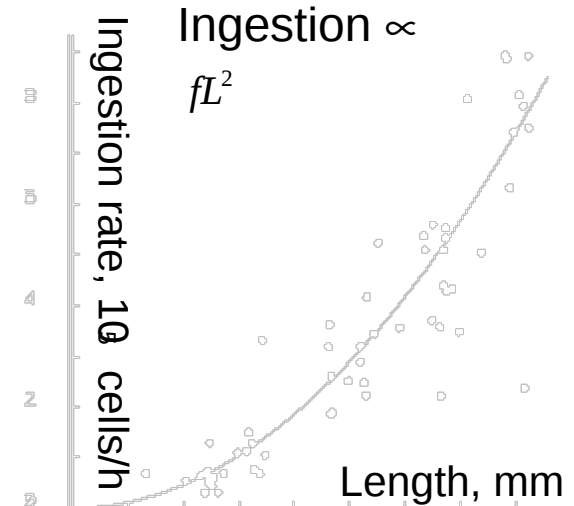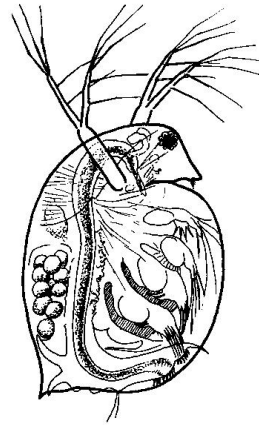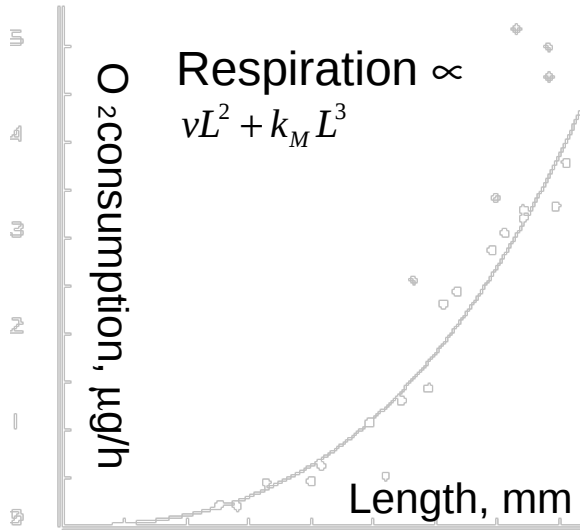
- large part of adult budget is allocated to reproduction in *Daphnia magna*
- puberty at 2.5 mm
- no change in ingest., resp., or growth
- where do resources for reprod. come from? Or:
- what is fate of resources in juveniles?
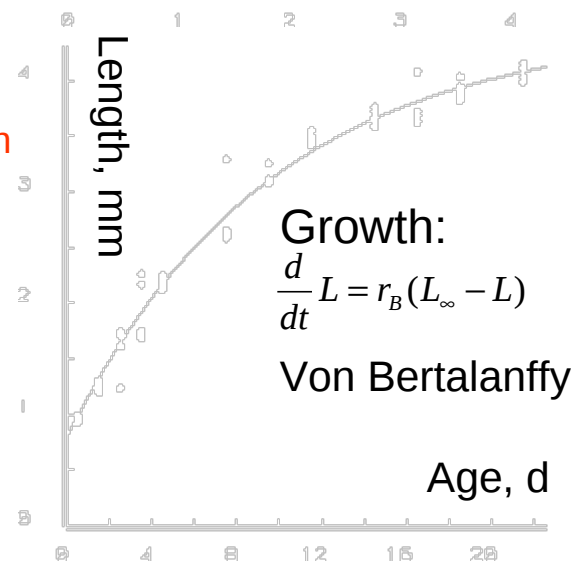
Topological alternatives
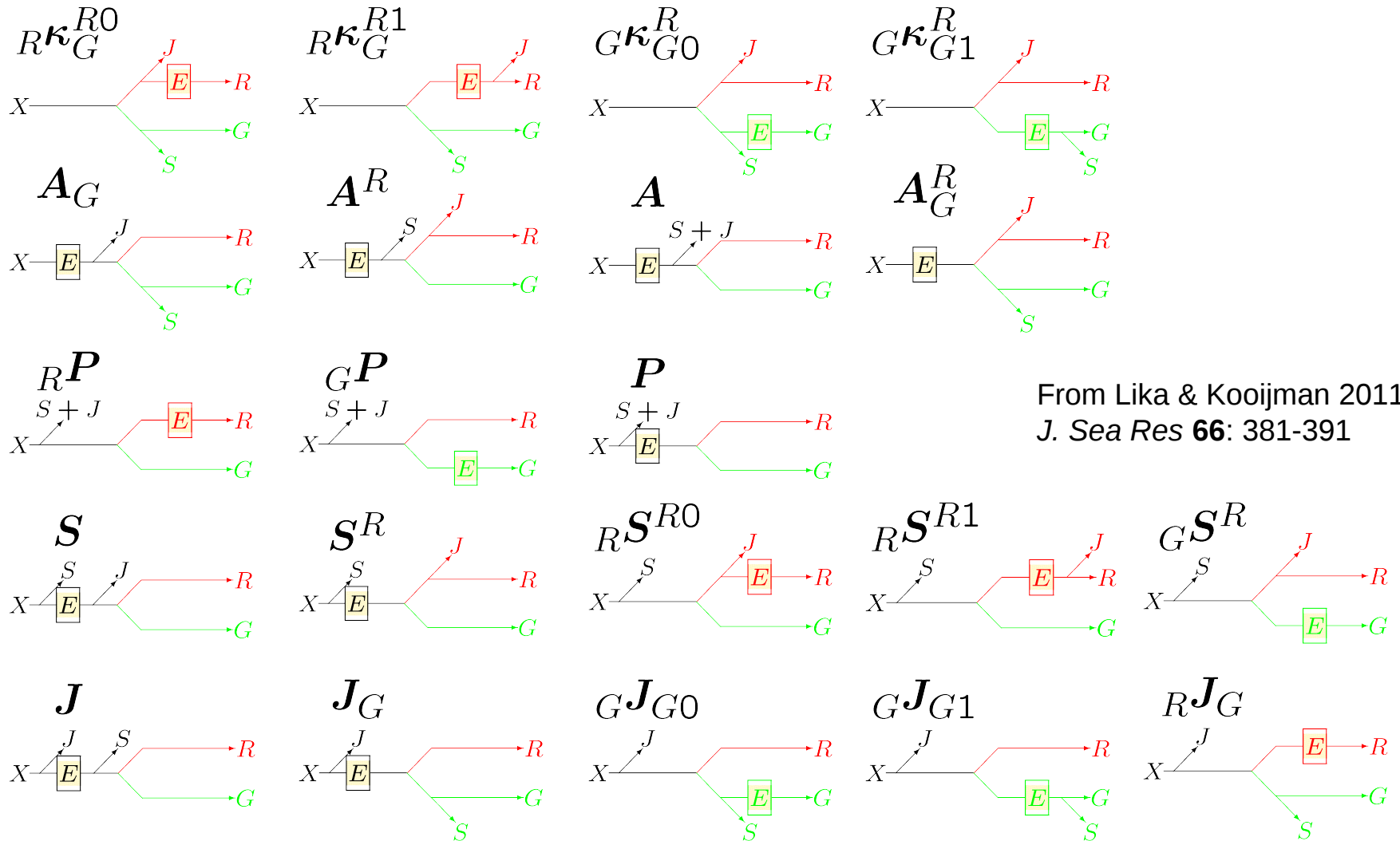
From Lika & Kooijman 2011
J. Sea Res **66**: 381-391

Test of properties 11.1d

model	F2	G2	R2	R4	S1	E2
$_R\kappa_G^{R0}$	−	−/−	+	+	+/−	−
$_R\kappa_G^{R1}$	−	−/−	+	+	+/−	−
$_G\kappa_{G0}^{R}$	+	+/−	+	+	+/−	+
$_G\kappa_{G1}^{R}$	+	+/−	+	+	+/−	−
A_G	+	−/−	+	+	+/+	+
A^R	+	+/+	−	+	+/+	+
A	+	?/?	−	−	+/+	+
A_G^R	+	+/−	+	+	+/+	+
$_RP$	−	−/−	−	−	+/−	−
$_GP$	+	−/−	−	+	+/−	+
P	+	?/?	−	−	+/+	−
S	+	?/?	−	−	+/+	−
S^R	+	+/+	−	+	+/+	−
$_RS^{R0}$	−	−/−	−	−	+/−	−
$_RS^{R1}$	−	−/−	−	−	+/−	−
$_GS^R$	+	+/+	−	+	+/−	+
J	+	?/?	−	−	+/+	−
J_G	+	−/−	+	+	+/+	−
$_GJ_{G0}$	+	−/−	+	+	+/−	+
$_GJ_{G1}$	+	−/−	+	+	+/−	−
$_RJ_G$	−	−/−	+	+	+/−	−

Empirical pattern

F2 During starvation, organisms are able to reproduce, grow and survive
G2 The inverse von Bertalanffy growth rate increases linearly with ultimate length
   both intra-specifically (or different constant food levels) and inter-specifically
R2 Reproduction increases with size intra-specifically,
   but decreases with size inter-specifically
R4 Growth can be simultaneous with reproduction,
   but growth can also cease long before reproduction is initiated.
S1 The chemical composition of organisms depends on the nutritional status
E2 Dissipating heat is a weighted sum of three mass flows:
   carbon dioxide, dioxygen and nitrogenous waste

From Lika & Kooijman 2011
J. Sea Res, **66**: 381-391

+	empirical pattern is matched
−	empirical pattern is not matched
?	result depends on numerical analysis
∗/∗	fixed/variable κ

Allocation to soma 10.5.2
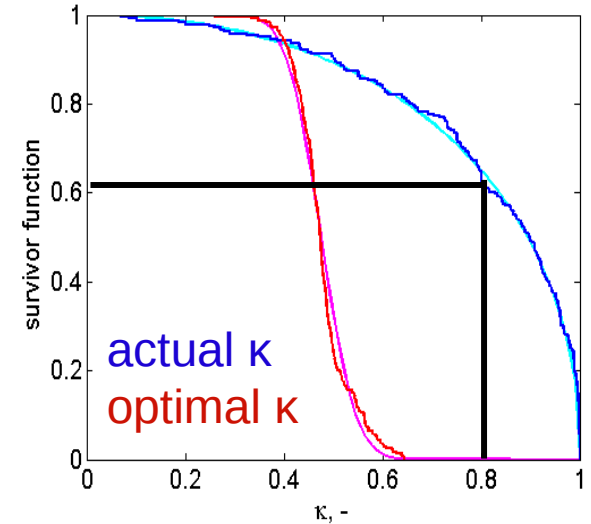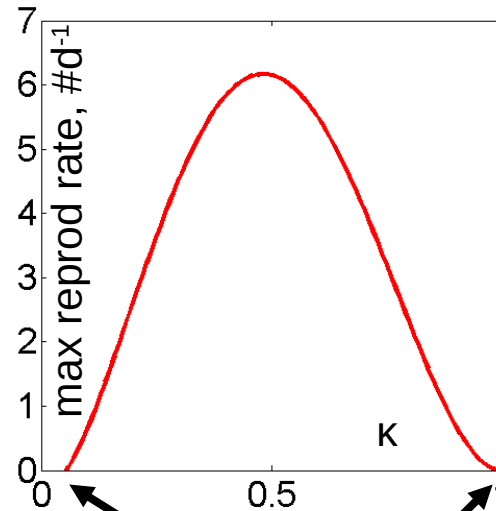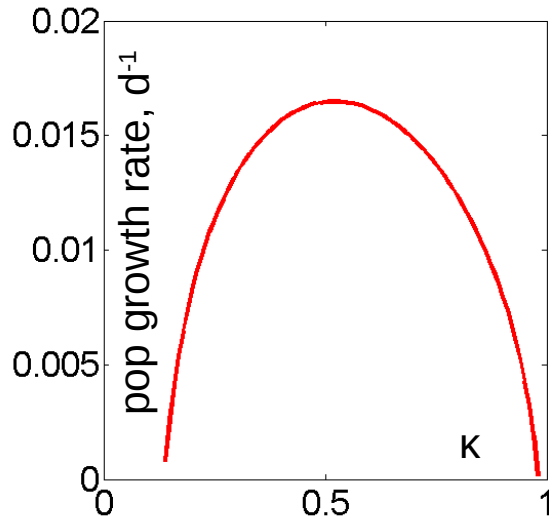
$$\kappa^2(1 - \kappa) = \frac{\dot{k}_J E_H^p [\dot{p}_M]^2}{f^3 \{\dot{p}_{Am}\}^3}$$

$L_m = 1 \, \text{cm}$ $f = 1$
$\dot{v} = 0.02 \, \text{cm} \, \text{d}^{-1}$ $\kappa_R = 0.95$
$[\dot{p}_M] = 18 \, \text{J} \, \text{d}^{-1} \text{cm}^{-3}$ $\dot{k}_J = 0.002 \, \text{d}^{-1}$
$\{\dot{p}_T\} = 0 \, \text{J} \, \text{d}^{-1} \text{cm}^{-2}$ $[E_G] = 2800 \, \text{J} \, \text{cm}^{-3}$
$E_H^b = 0.275 \, \text{J}$ $E_H^p = 50 \, \text{J}$
$\ddot{h}_a = 10^{-6} \, \text{d}^{-2}$ $s_G = 0.01$

Frequency distribution of κ
among species in the
add_my_pet collection:
Mean κ = 0.81,
but optimum is κ = 0.5

Lika *et al* 2011 , 2013
J. Sea Res, **22**: 278-288

Selection for reproduction

Gallus gallus:
Red Jungle fowl
White Leghorn
Indian River broiler
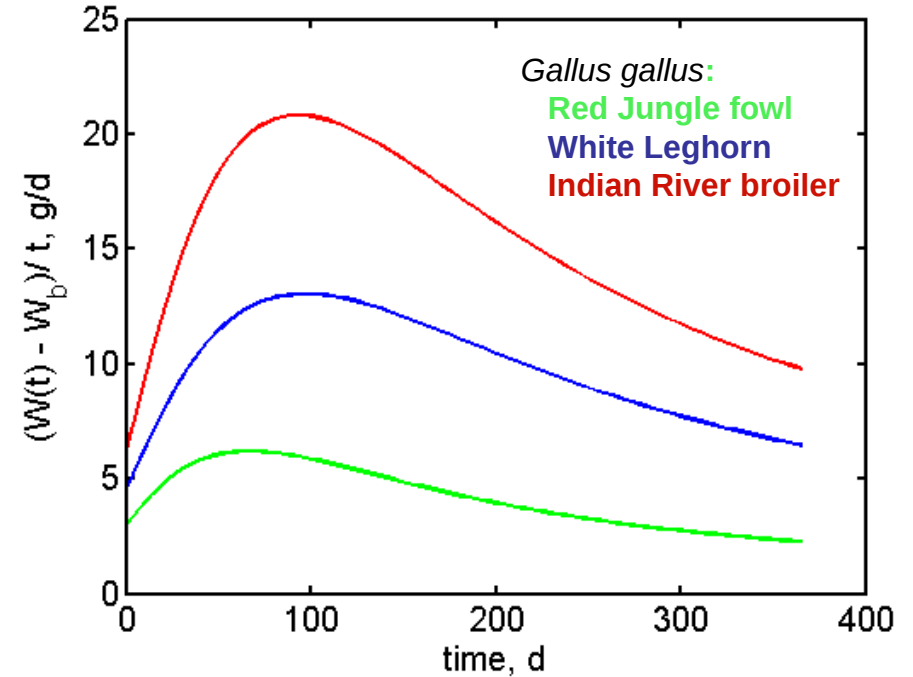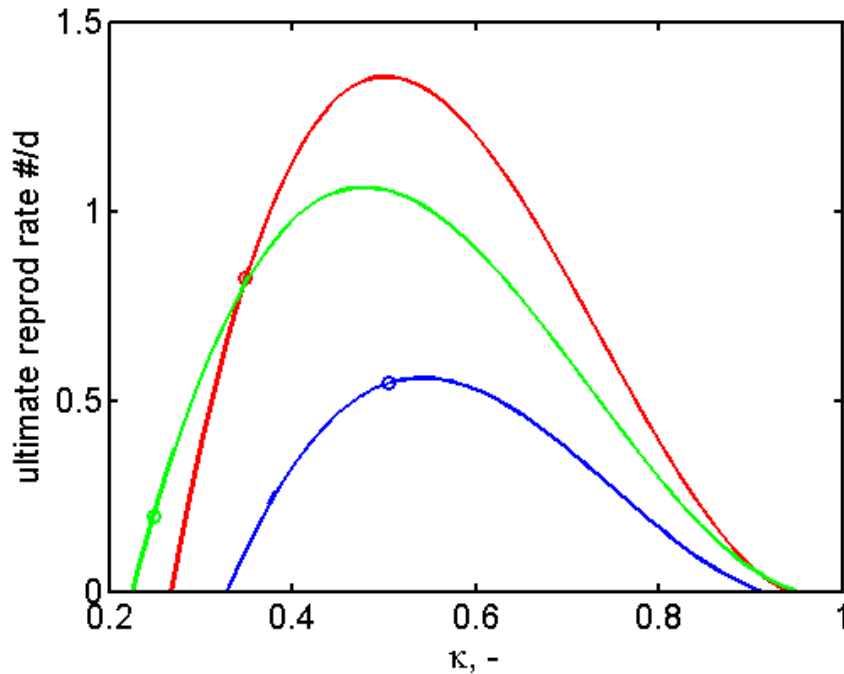
parameter at 20 °C	symbol	unit	RJ, f	RJ, m	WL, f	WL, m	IR, f	IR, m
spec. assimilation rate	$\{\dot{p}_{Am}\}$	J/d.cm^2	427	372	270	301	435	178
energy conductance	$\dot{v}$	cm/d	0.0083	0.0090	0.0113	0.0111	0.00965	0.0155
fraction to soma	κ	-	0.2486	0.4317	0.5051	0.4306	0.3492	0.6734
spec som. maint. cost	$[\dot{p}_M]$	J/cm^3	21.38	26.82	15.79	14.39	18.09	9.739
mat. maint. rate coeff.	$\dot{k}_J$	1/d	0.0025	0.0039	0.0020	0.0020	0.0020	0.0011
spec. cost structure	$[E_G]$	J/cm^3	9918	9864	9948	9947	7709	10600
maturity at birth	E_H^b	J	8.99e4	4.61e4	8.14e4	9.72e4	9.12e4	7.43e4
maturity at puberty	E_H^p	J	2.67e6	1.65e6	2.87e6	3.68e6	6.53e6	2.69e6
aging acceleration	$\ddot{h}_a$	1/d^2	2.72e-49	1.32e-45	2.32e-22	1.41e-21	5.24e-21	8.69e-22

Max reprod vs optimal max reprod
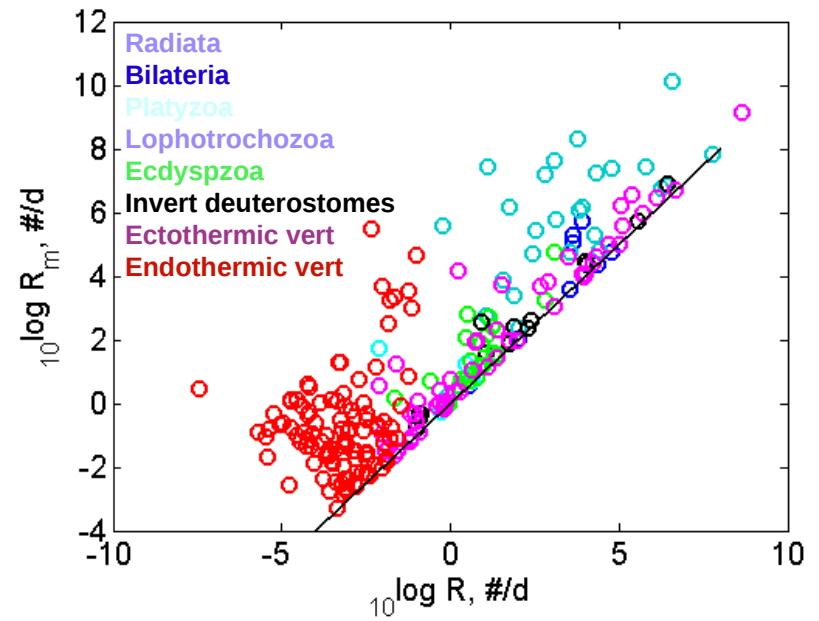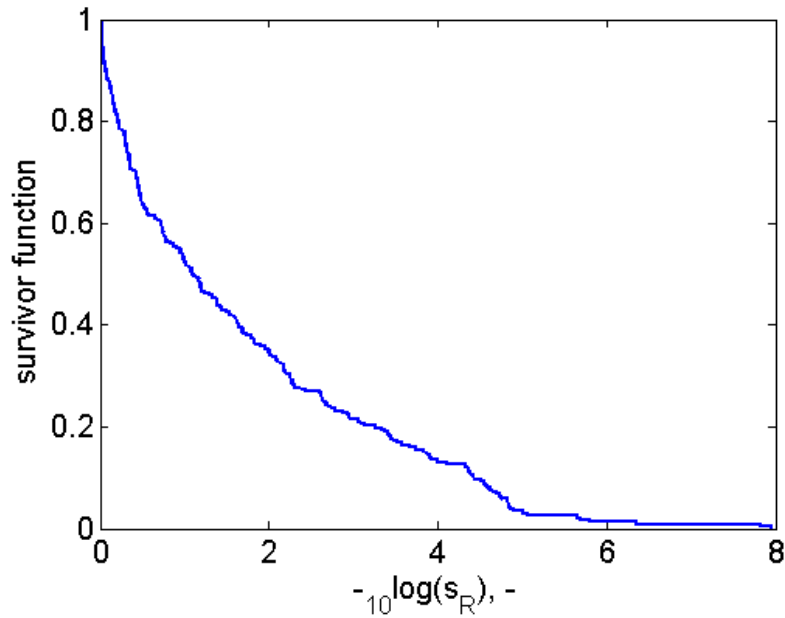
$\dot{R}$	max product rate
$\dot{R}_m$	optimized $\dot{R}$
s_R	$\dot{R}/\dot{R}_m$

Specific somatic maintenance 10.5.3

$20\,^\circ\text{C}$
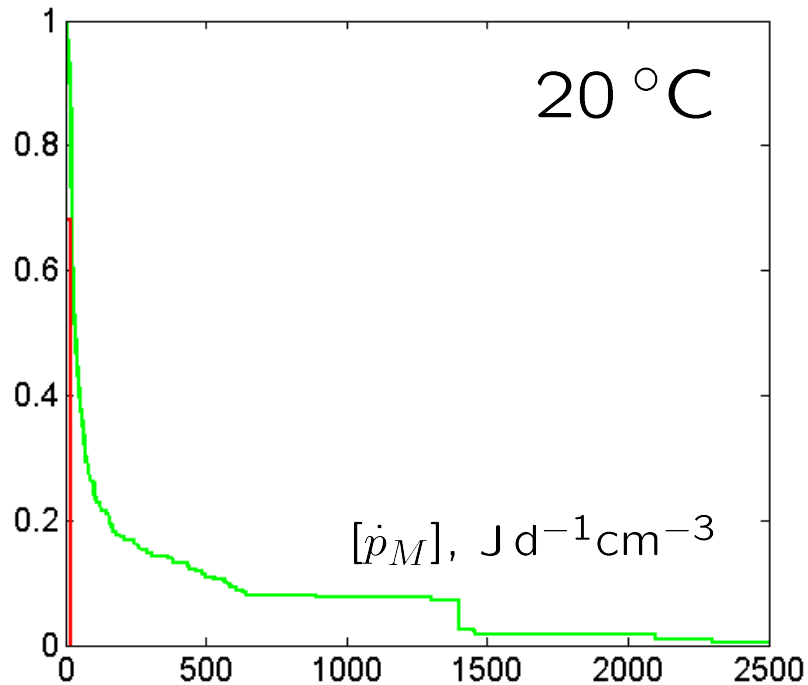
$[\dot{p}_M]$, $\text{J}\,\text{d}^{-1}\text{cm}^{-3}$

Typical value at $20\,^\circ\text{C}$:
$[\dot{p}_M] = 18\,\text{J}\,\text{d}^{-1}\text{cm}^{-3}$

Low: < 10 J/d.cm³   High: > 1000 J/d.cm³

3 Eunectus	1300 Oikopleura
4 Boa	1400 daphnids, copepods
5 Andrias	1450 Caenorhaditis
7 Callorhinus	2100 Bosmina
8 Esox	2300 Oikopleura
10 Acipenser	8100 Thalia

Rather high: > 200 , < 1000 J/d.cm³

205 Crinia	490 Geocrinia,
260 Dendrobaena	490 Pseudophryne
307 Lymnaea	500 Danio
370 Crinia	560 Folsomia
380 Leptodora	580 Asplanchna
480 Brachionus	610 Gammarus
480 Macropus	890 Chydorus

Thalia
8 kJ/d.cm³

Kooijman 2013,
Waste to hurry.
Oikos, to appear

Primary parameters standard DEB model 8.2.1

assimilation	$\{\dot{p}_{Am}\}$	22.5	$\mathrm{J\,d^{-1}cm^{-2}}$	max spec assimiation rate
feeding	$\{\dot{F}_m\}$	6.5	$\mathrm{l\,d^{-1}cm^{-2}}$	max spec searching rate
digestion	κ_X	0.8	$-$	digestion effiency
growth	$[E_G]$	2800	$\mathrm{J\,cm^{-3}}$	spec cost for structure
mobilisation	$\dot{v}$	0.02	$\mathrm{cm\,d^{-1}}$	energy conductance
heating, osmosis	$\{\dot{p}_T\}$	0	$\mathrm{J\,d^{-1}cm^{-2}}$	spec somatic maintenance costs
turnover, activity	$[\dot{p}_M]$	18	$\mathrm{J\,d^{-1}cm^{-3}}$	spec somatic maintenance costs
regulation, defence	$\dot{k}_J$	0.002	$\mathrm{d^{-1}}$	maturity maintenance rate coeff
allocation	κ	0.8	$-$	allocation fraction to soma
reproduction	κ_R	0.95	$-$	reproduction efficiency
life cycle	E_H^b	0.285	J	maturity at birth
life cycle	E_H^p	166	J	maturity at puberty
ageing	$\ddot{h}_a$	10^{-6}	$\mathrm{d^{-2}}$	ageing acceleration
ageing	s_G	0	$-$	Gompertz stress coefficient
temperature	T_A	8000	K	Arrhenius temperature

For zoom factor $z = 1$ at $T_{\mathrm{ref}} = 293\,\mathrm{K}$
For other z values, multiply
$\{\dot{p}_{Am}\}$ and $\ddot{h}_a$ with z
E_H^b, E_H^p with z^3

$z = L_m / L_m^{\mathrm{ref}}$
$L_m = \kappa\{\dot{p}_{Am}\}/[\dot{p}_M]$
$L_m^{\mathrm{ref}} = 1\,\mathrm{cm}$

Reproduction rate & investment

Radiata
Bilateria
Platyzoa
Lophotrochozoa
Ecdyspzoa
Invert deuterostomes
Ectothermic vert
Endothermic vert
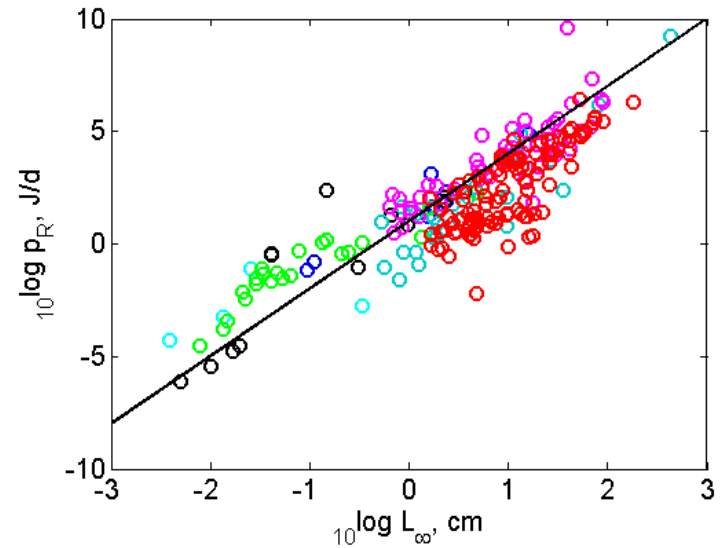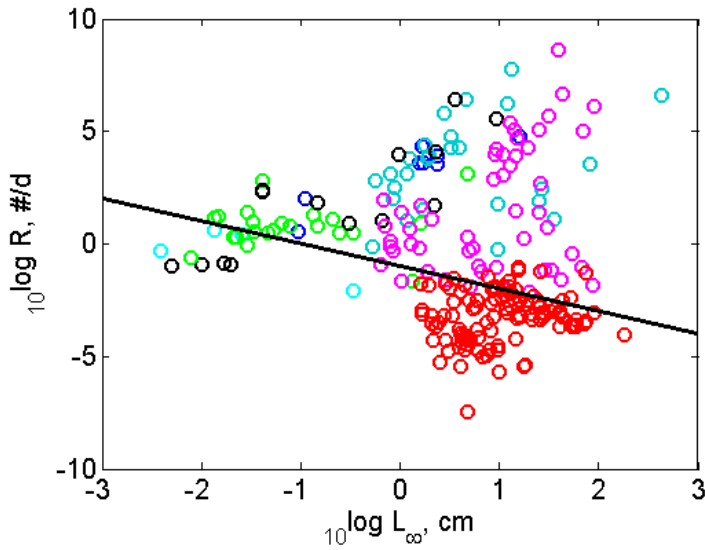
$\dot{R}$	max product rate
$\dot{R}_m$	optimized $\dot{R}$
s_R	$\dot{R}/\dot{R}_m$

Scaling of respiration 8.2.2d

Respiration: contributions from growth and maintenance
Weight: contributions from structure and reserve

	intra-species	inter-species
maintenance	$\propto L_T L^2 + L^3$	$\propto L_T L^2 + L^3$
growth	$\propto L_g L^2 - L^3$	0
$\dfrac{\text{reserve}}{\text{structure}}$	$\propto L^0$	$\propto L$
$\dfrac{\text{respiration}}{\text{weight}}$	$\propto \dfrac{L_s L^2 + L^3}{d_V L^3 + d_E L^3}$	$\propto \dfrac{L_T L^2 + L^3}{d_V L^3 + d'_E L^4}$

L	structural length	L_T	heating length
L_g	constant	L_s	constant
d_V	spec density of structure	d_E	spec density of reserve

Metabolic rate 8.2.2e

2 curves fitted:

$0.0226 \, L^2 + 0.0185 \, L^3$

$0.0516 \, L^{2.44}$

O $_2$consumption, μl/h

Length, cm

slope = 1

endotherms

ectotherms

unicellulars

slope = 2/3

Log metabolic rate, w

Log weight, g
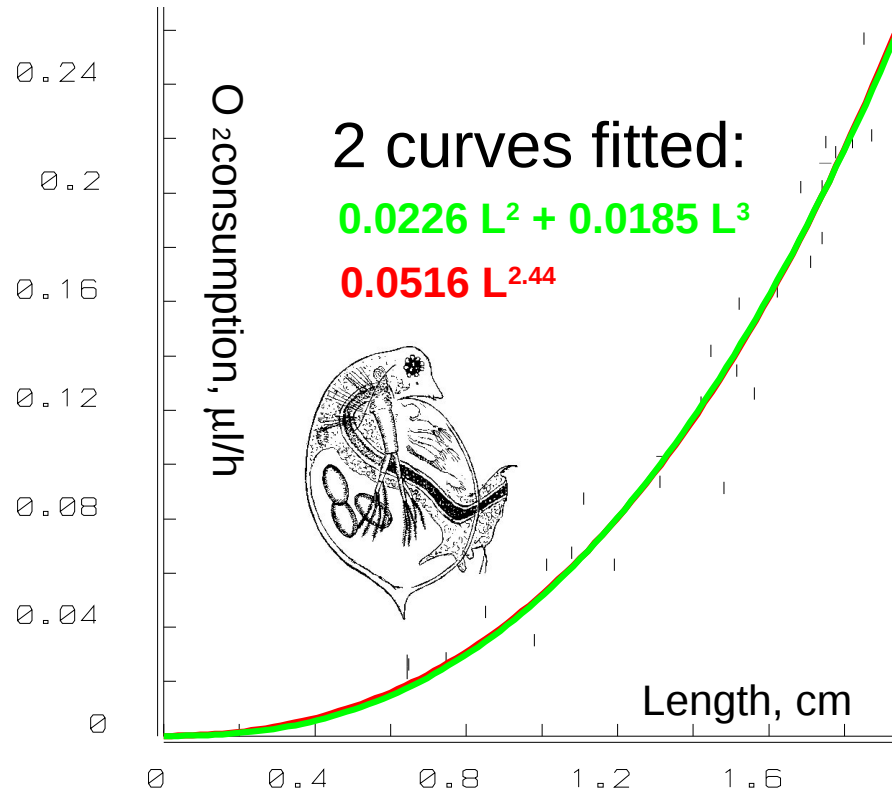
Intra-species
(Daphnia pulex)

Inter-species

Data: Richman 1958; curve fitted from DEB theory
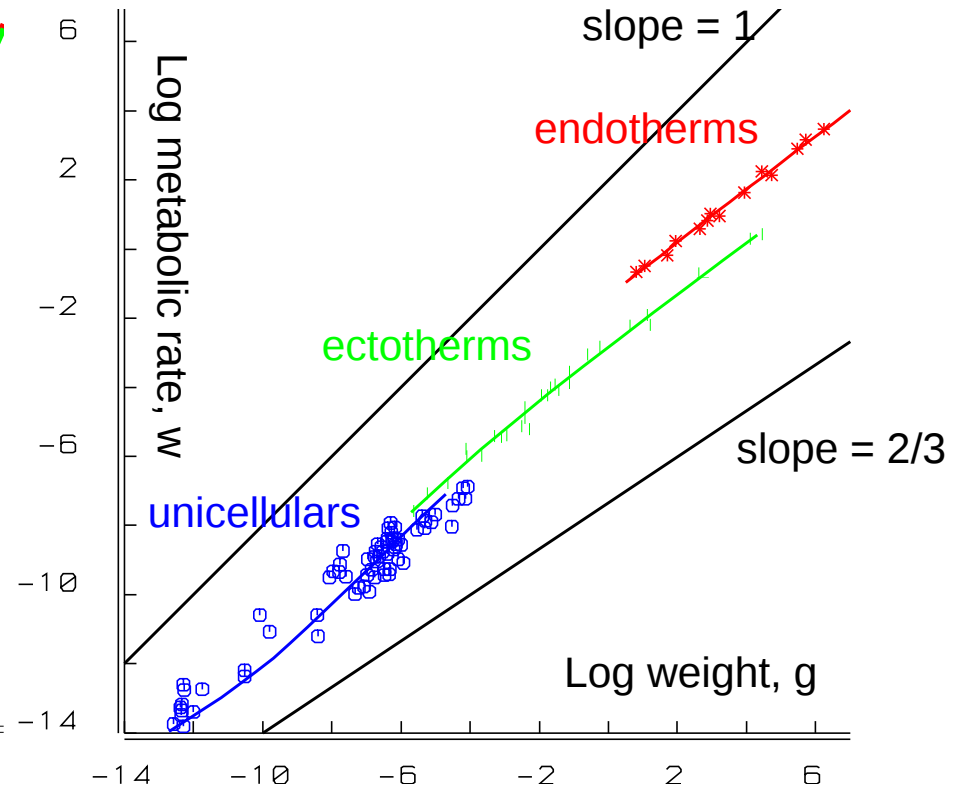
Data: Hemmingson 1969; curve fitted from DEB theory

Embryonic development

Crocodylus johnstoni,
Data: Whitehead 1987

embryo

yolk

weight, g

time, d

O_2 consumption, ml/h
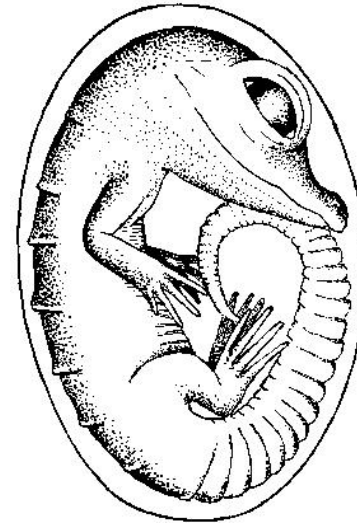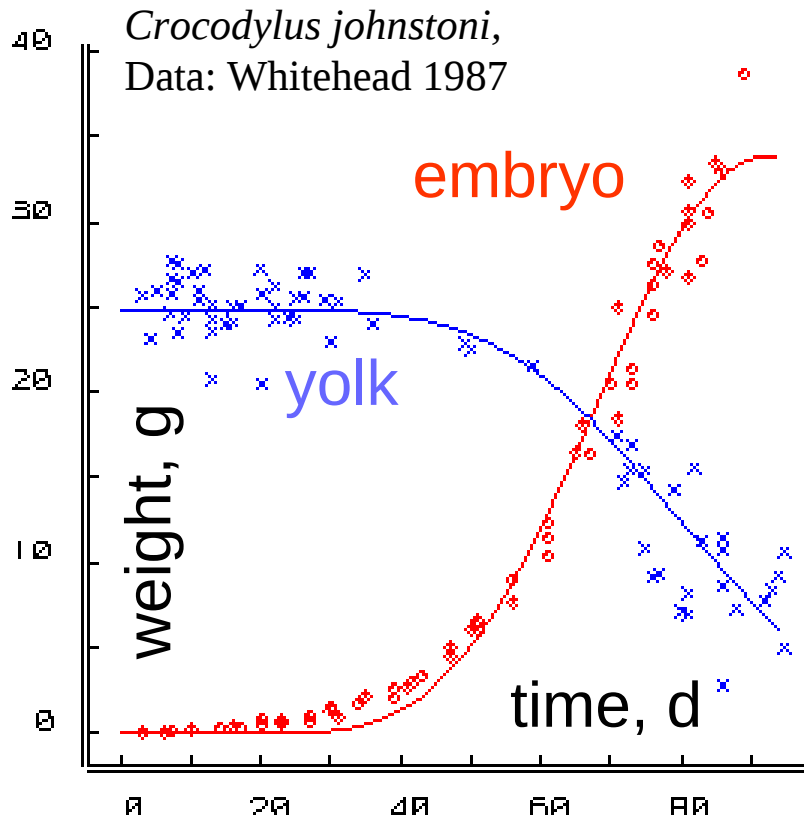
time, d

$$\frac{d}{d\tau}e \;=\; -g\frac{e}{l}; \qquad \frac{d}{d\tau}l = \frac{g}{3}\frac{e-l}{e+g}$$

$$\dot{j}_O \;=\; \dot{j}_{OM}l^3 + \dot{j}_{OG}\frac{d}{d\tau}l^3$$

τ	scaled time
l	scaled length
e	scaled reserve density
g	energy investment ratio

Acceleration of development 7.8.2c

acceleration	no	yes

development

indirect

Pseudophryne bibronii

Crinia georgiana

direct

Geocrinia vitellina

Crinia nimbus
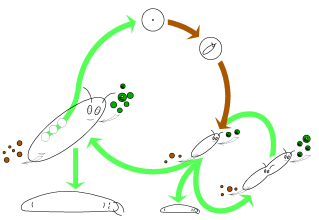
Acceleration of development

Mueller et al 2012,
Comp. Biochem. Physiol. A
163: 103-110

Crinia georgiana

max dry weight 500 mg
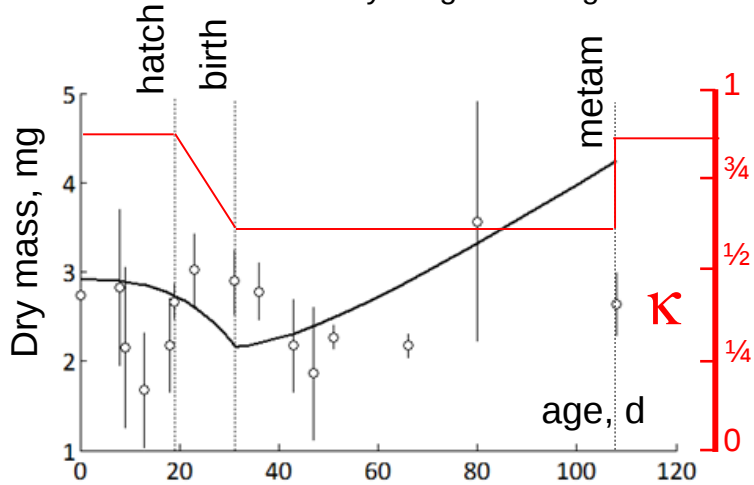
12 °C
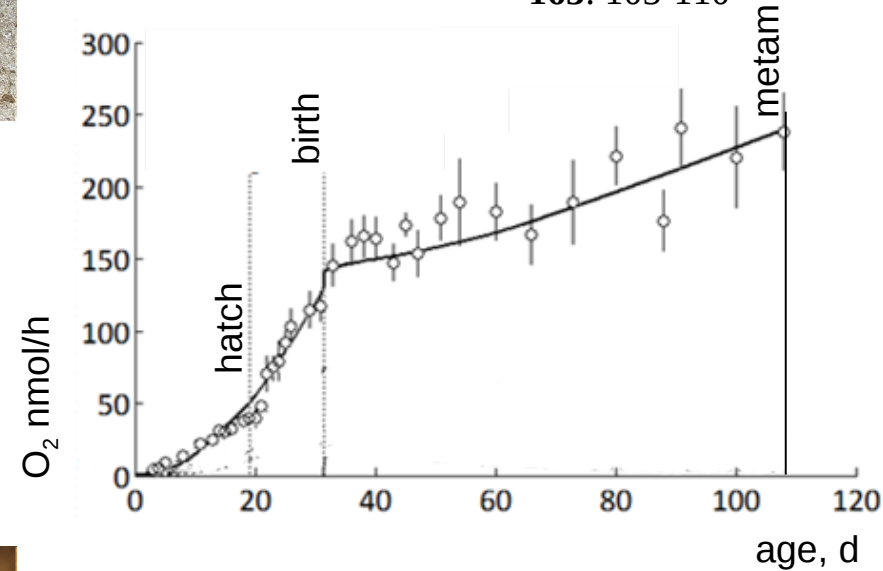
Pseudophryne bibronii

max dry weight 200 mg
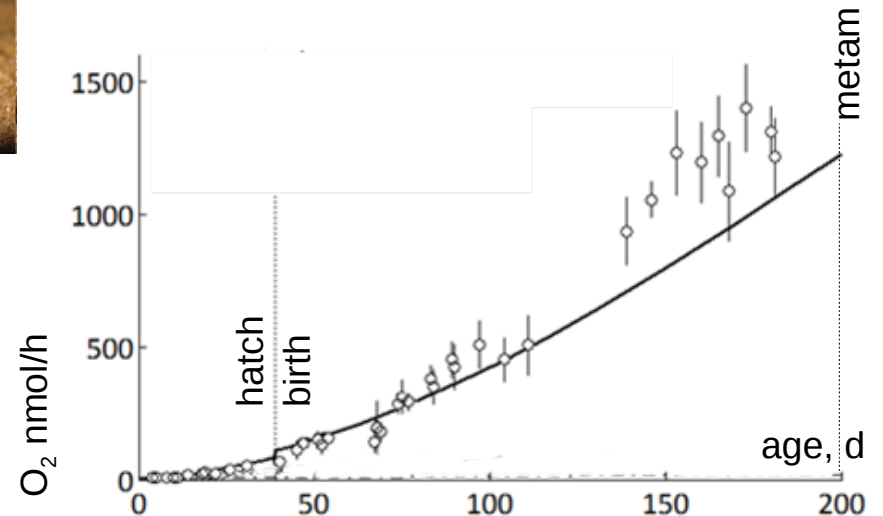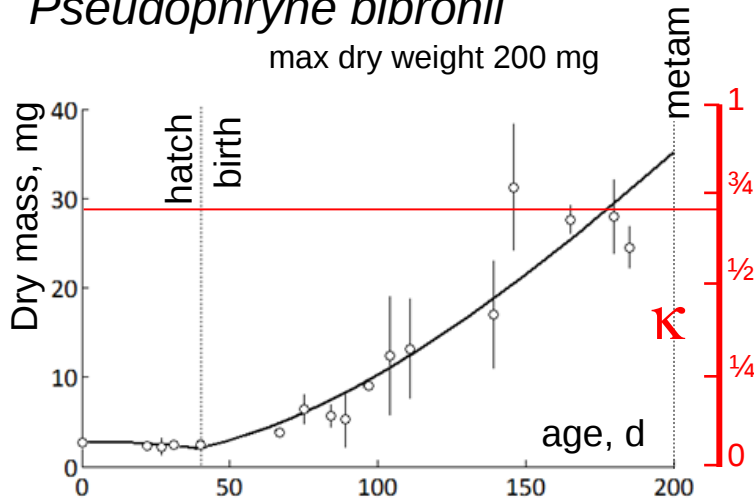
Acceleration of metabolism
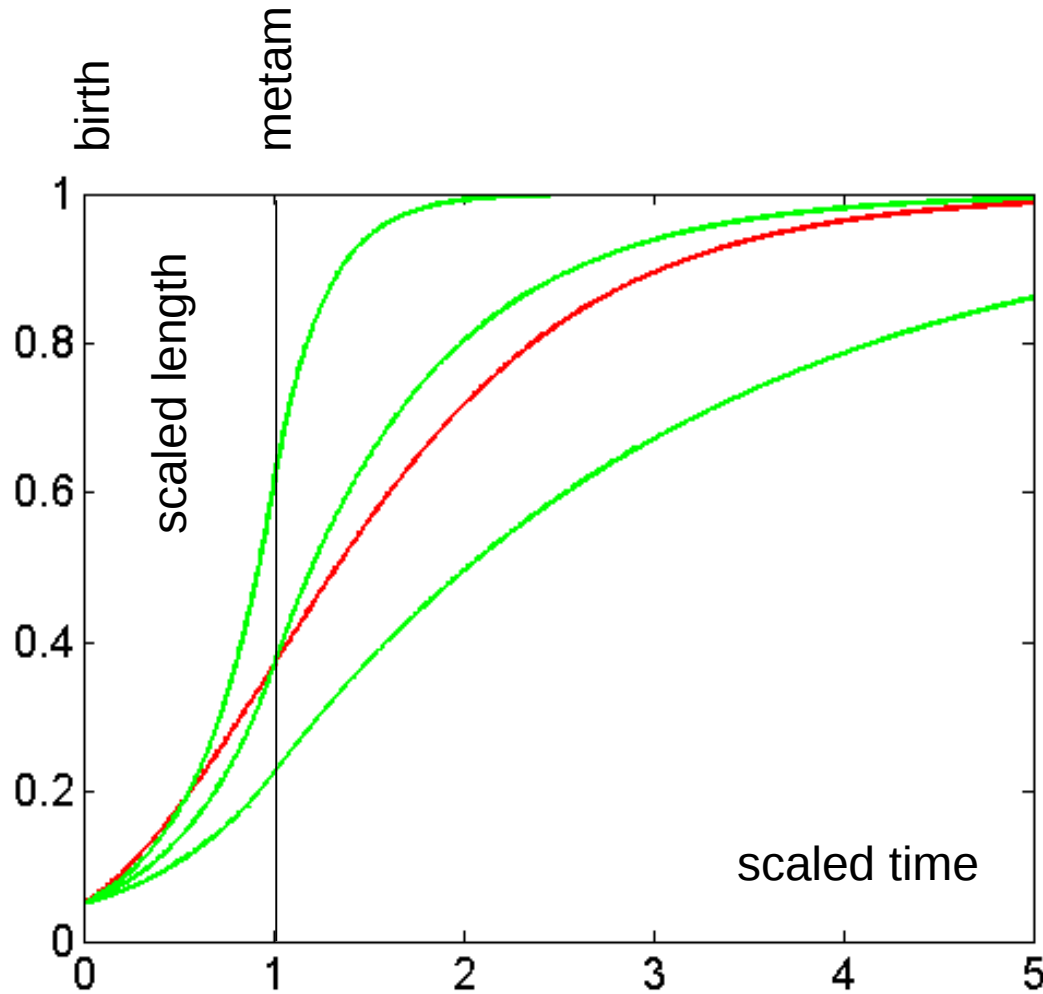
Morph: $V\frac{2}{3}$ | $V1$ | $V\frac{2}{3}$

Gompertz
expo-von Bertalanffy

Acceleration of metabolism

scaled functional response f
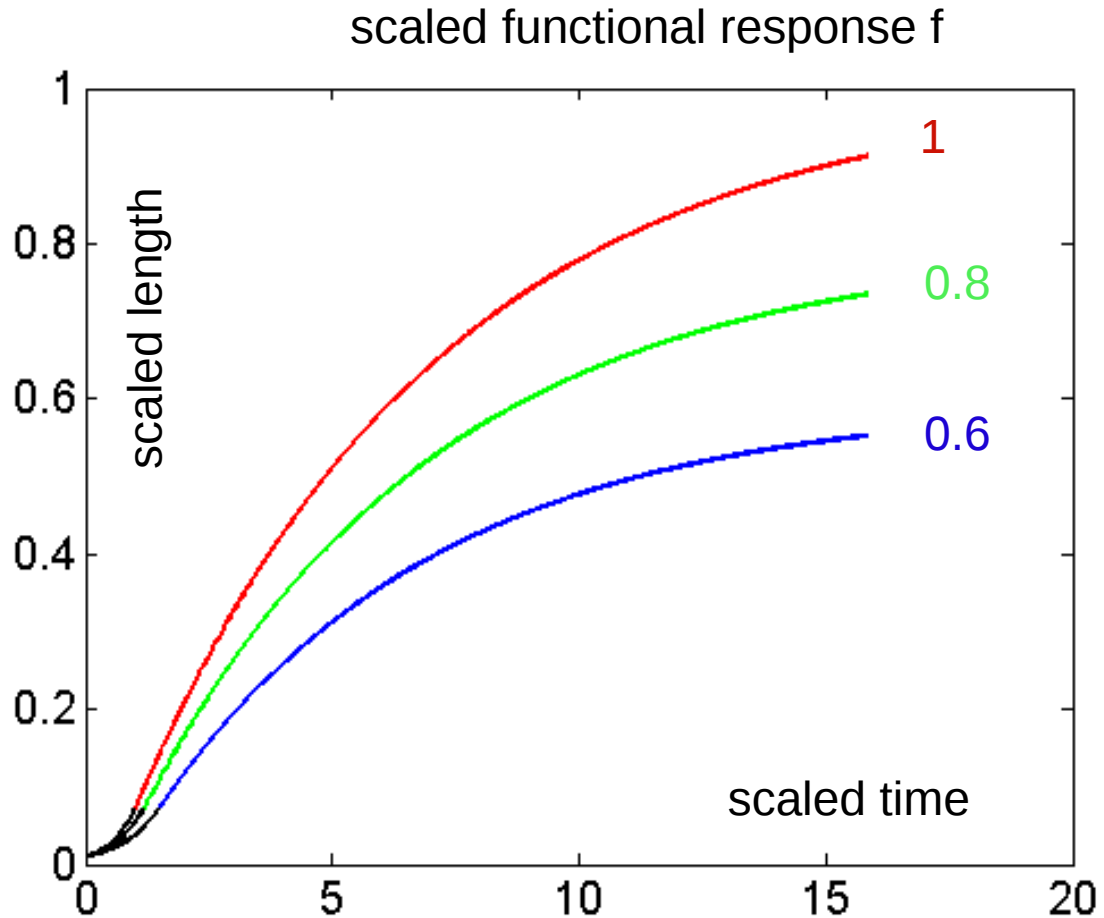
Stage transitions at maturity thresholds

7.8.2a

Danio rerio
28.5°C

	Stage	Age hpf	E_H mJ
	2-cell	0.75	0.01
	4-cell	1	0.02
	8-cell	1.25	0.02
	16-cell	1.5	0.02
	32-cell	1.75	0.02
	64-cell	2	0.03
	128-cell	2.25	0.03
	256-cell	2.5	0.04
	512-cell	2.75	0.05
	1k-cell	3	0.07
	High	3.33	0.088
	Oblong	3.66	0.11
	Sphere	4	0.14
	Dome	4.33	0.171
	30%-epiboly	4.66	0.20
	50%-epiboly	5.25	0.27
	Germ-ring	5.66	0.33

	Stage	Age hpf	E_H mJ
	Shield	6	0.38
	75%-epiboly	8	0.71
	90%-epiboly	9	0.96
	Bud	10	1.3
	3-somite	11	1.7
	6-somite	12	2.1
	14-somite	16	4.6
	21-somite	19.5	8.0
	26-somite	22	11.2
	Prim-6	25	16.0
	Prim-16	31	29.5
	Prim-22	35	41.4
	High-pec	42	68.9
	Long-pec	48	99.6
	Pec-fin	60	180
	Protruding-mouth	72	280

Stage transitions at maturity thresholds

< birth : isomorph
birth-metamorphosis: V1-morph
> metamorphosis : isomorph

7.8.2b

Danio rerio
28.5°C

Stage	age dpf	SL cm	age dpf	SL cm	E_H J
		$f=0.63$		$f=1$	
pSB+ swim bladder inflation	4.5	3.8	4.0	3.7	**0.5**
Fle early flexion	7.2	4.5	6.3	4.6	**1.1**
CR caudal fin ray	8.9	4.9	7.4	5.1	**1.6**
AC anal fin condensation	10.5	5.4	8.5	5.9	**2.3**
DC dorsal fin condensation	12.3	5.7	9.6	5.8	**3.3**
MMA metamorphic melanophore app.	12.9	5.9	10.0	6.0	**3.8**
AR anal fin ray appearance	14.2	6.2	10.9	6.3	**5**
DR dorsal fin ray appearance	15.0	6.4	11.4	6.5	**5.9**
PB+ following pelvic fin bud app.	18.7	7.6	13.8	7.7	**12.7**
PR pelvic fin ray appearance	21.3	8.5	15.5	8.5	**21.9**
PR+ following pelvic fin ray app.	22.5	9.2	16.3	9.3	**27.9**
SP onset of posterior squamation	23.8	9.8	17.2	9.8	**34.9**
SA onset of anterior squamation	25.0	10.4	17.9	10.5	**42.3**
J juvenile	26.2	11.0	18.7	11.0	**50.9**
J+ following juvenile	30.8	13.0	21.6	13.2	**91.7**
J++ following juvenile	40.7	16.0	27.5	16.4	**221.6**
A adults	218	26.0	59.9	30.6	**2061**
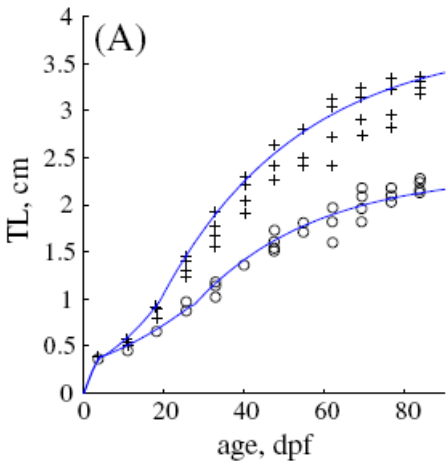
Data:
Lauwrence et al 2008

caloric restriction
Data: Augustine
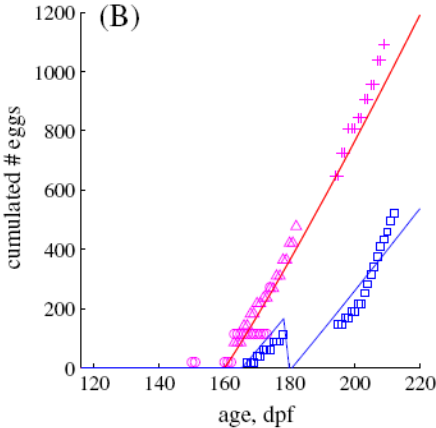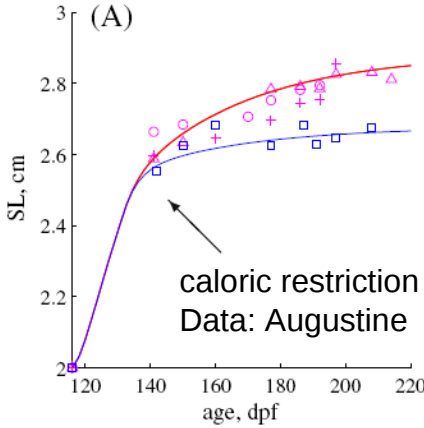
*Augustine et al 2011
Comp. Biochem. Physiol. A
159 :275–283*

Crustacea

Arachnida

Nematoda

Platyhelminthes

Anthocephala

Gastrotricha

Ecdysozoa

Enthognatha

Tardigrada

Rotifera

Platyzoa

Insecta

Bryozoa

Lophotrochozoa

Annelida

Chaetognatha

Mollusca

Echinodermata

Ctenophora

Tunicata

Mammali

Deuterostomia

Mixini

Amphibia

Cnidaria

Leptocardii

Sarcopterygii

Radiata

Aves

Cephalaspidorphi

Reptilia

Chondrichthyes

Actinopterygii

1	2	5	10

Twinning: separation of cells 2.6.4
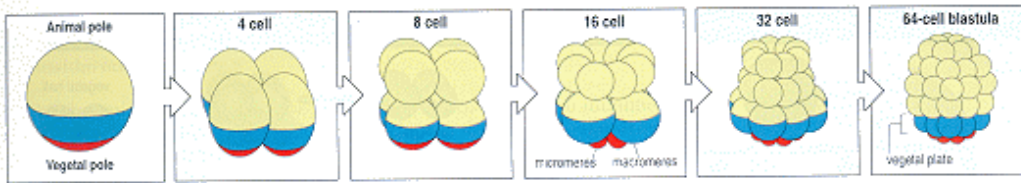
Kooijman 2009
J. Math. Biol.
58: 377--394
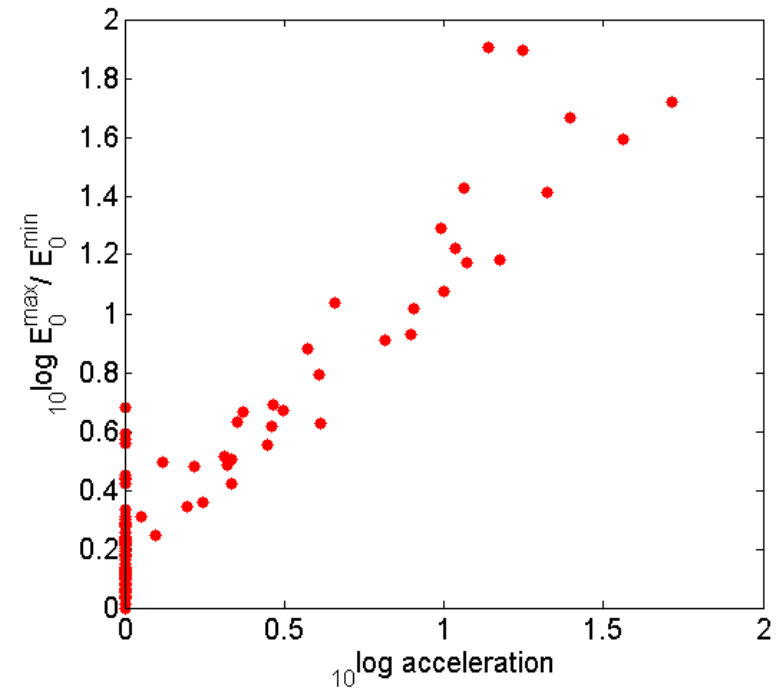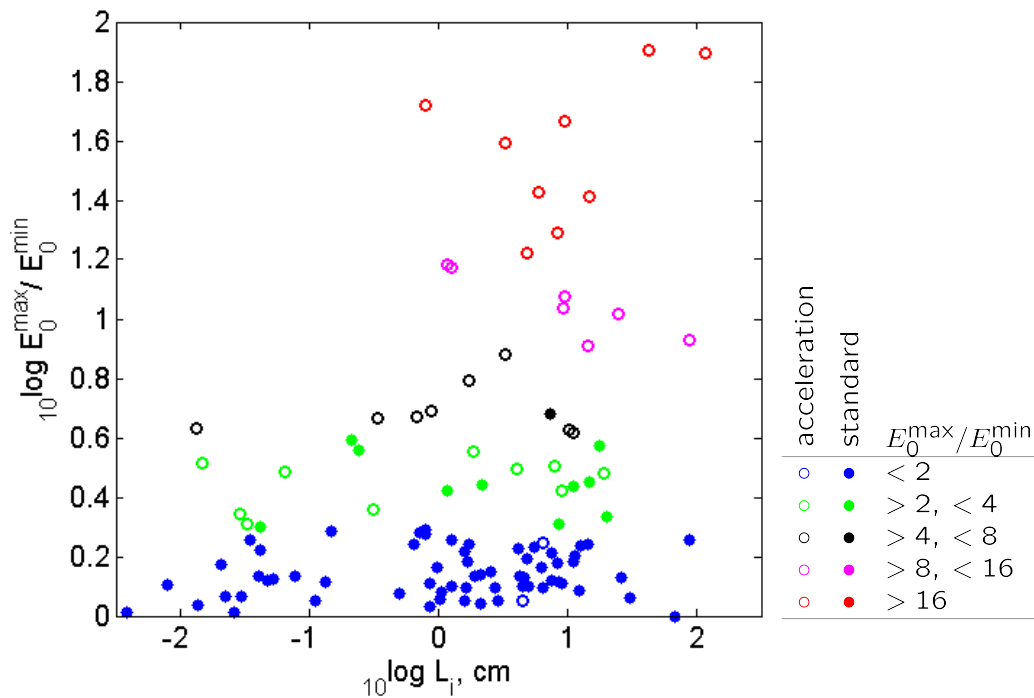
E_0^{max} initial reserve at max nutrition
E_0^{min} initial reserve at min nutrition
L_i max structural length of species

Maternal effect:
reserve density at birth =
    reserve density of mother

Parameter estimates from
add_my_pet 2012/06/17,
egg development only

Evolution of DEB systems 10.3

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

Symbol	Meaning
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 → embryo + adult

animals

strong homeostasis for reserve

plants

specialization of structure

Evolution of DEB systems 10.3a

- Start: variable biomass composition, passive uptake
- Strong homeostasis $\rightarrow$ stoichiometric constraints
- Reserves: delay of use of internalised substrates $\rightarrow$ storage, weak homeostasis
- Maintenance requirements: turnover (e.g. active uptake by carriers), regulation
- Maintenance from reserve instead of substrate; increase reserve capacity
- Control of morphology via maturation; κ-rule $\leftrightarrow$ cell cycle
- Diversification of assimilation (litho- $\rightarrow$ photo- $\rightarrow$ heterotrophy)

Eukaryotisation: heterotrophic start; unique event?
- Syntrophy & compartmentalisation: mitochondria, genome reorganisation
- Phagocytosis, plastids (acquisition of phototrophy)

Animal trajectory: biotrophy
- Reduction of number of reserves
- Emergence of life stages
- Further increase of maintenance costs
- Further increase of reserve capacity
- Socialisation
- Supply $\rightarrow$ demand systems

Plant trajectory: site fixation
- Differentiation of root and shoot
- Emergence of life stages
- Increase of metabolic flexibility (draught)
- Nutrient acquisition via transpiration
- Symbioses with animals, fungi, bacteria
  (e.g. re-mineralisation leaf litter, pollination)