Sembiotics

Formal Semantics for BioModels

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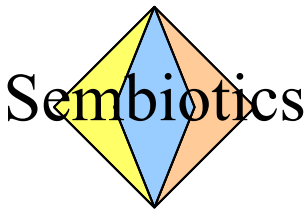
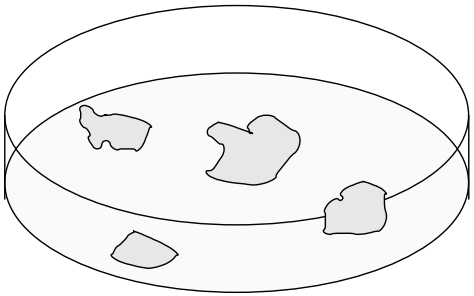
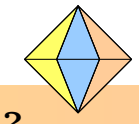


Overview

$$\dot{x} = \ldots$$
$$\dot{y} = \ldots$$

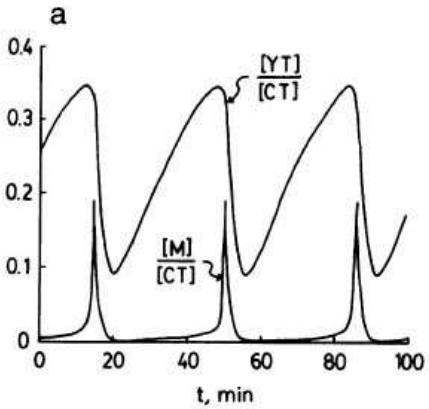




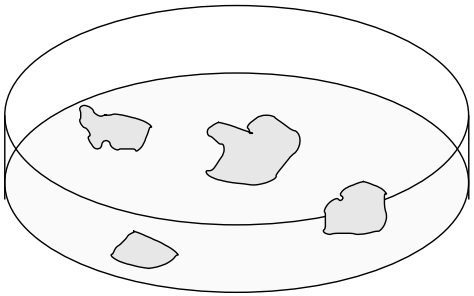
Overview

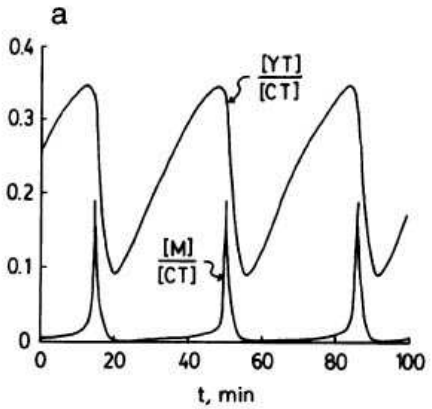
$$\dot{x} = \ldots$$
$$\dot{y} = \ldots$$

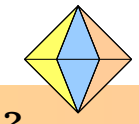
Simulation
Analysis



Observation







Overview

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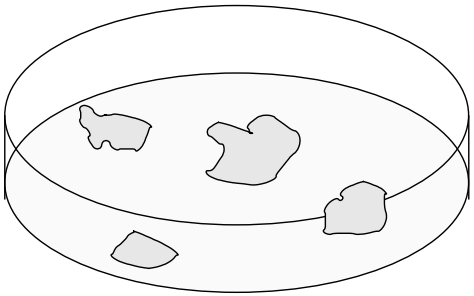
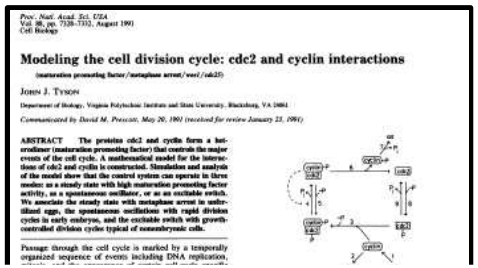
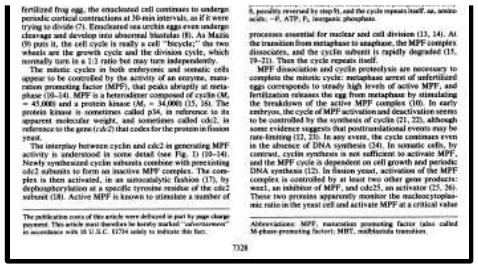
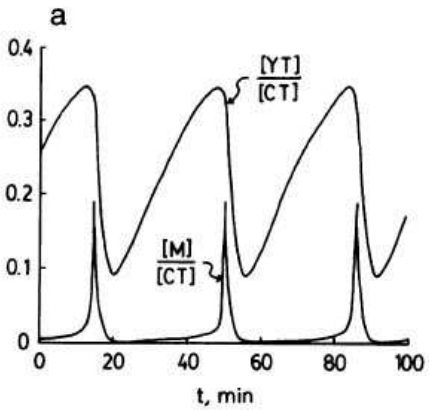
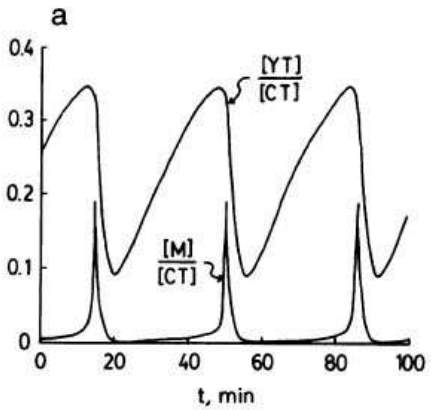


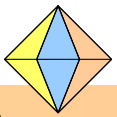


Scientific Paper









Overview

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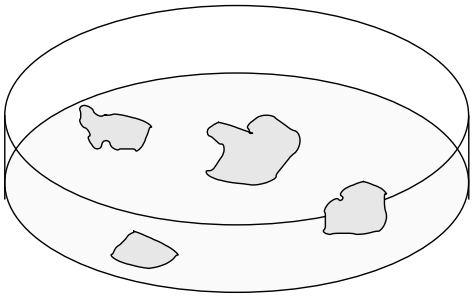
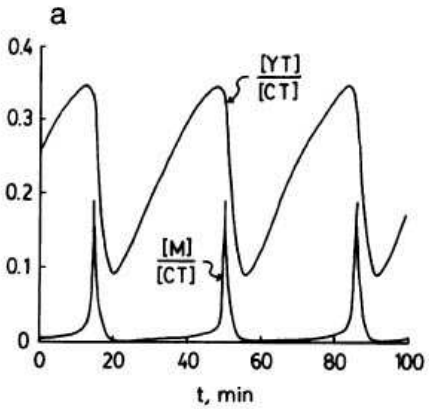
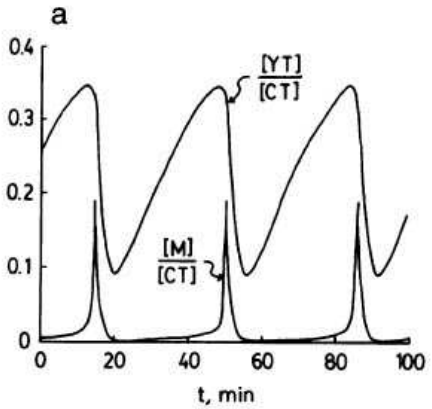
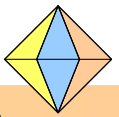
BioModels Database



SBML







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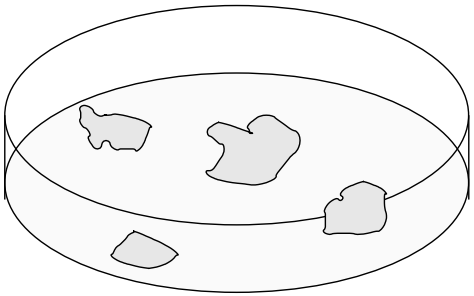

SBML

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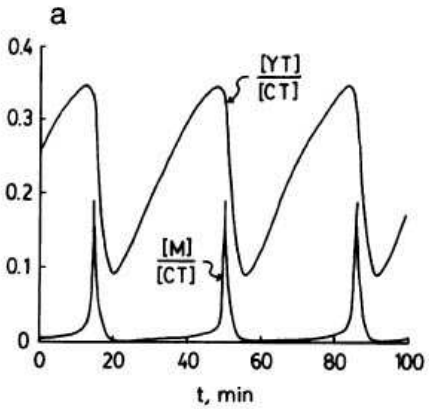
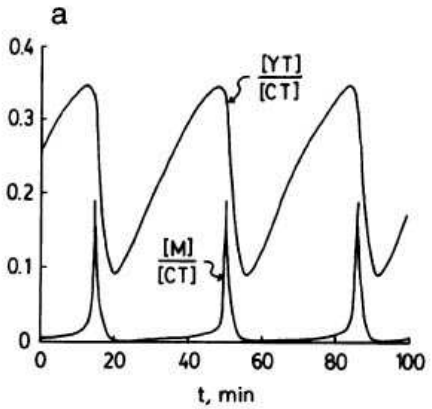
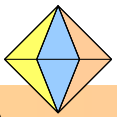


Sembiotics

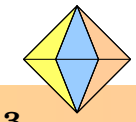




Computer-Aided Modelling

- development
- curation
- retrieval
- composition
- integration
- usage
- modification

of bio-models

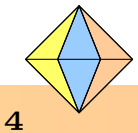


What do we Need?

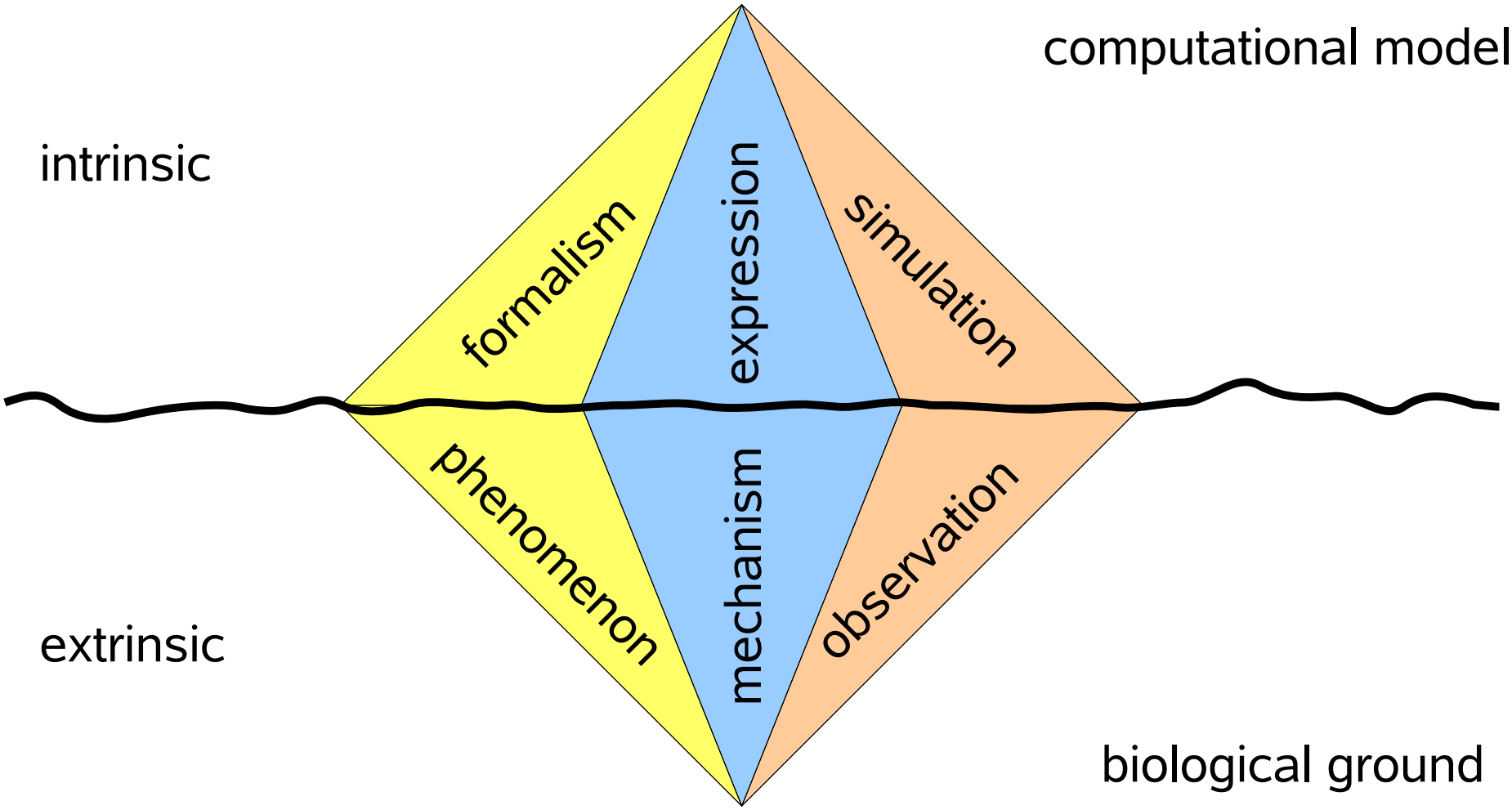
- computer-understanding
- reasoning

Formal Semantics

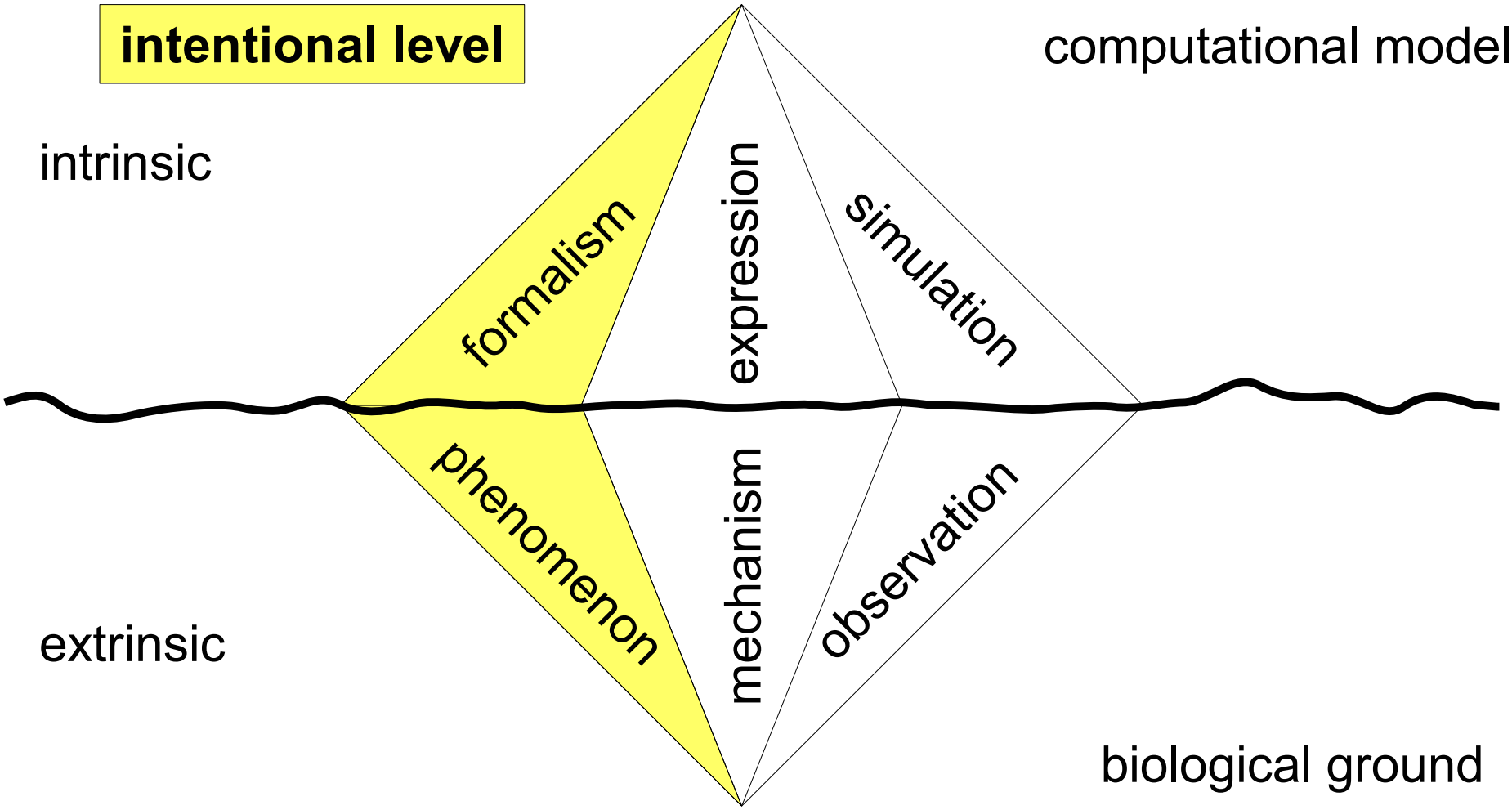
- all relevant aspects of the meaning
- relations between them
- rich model ontology



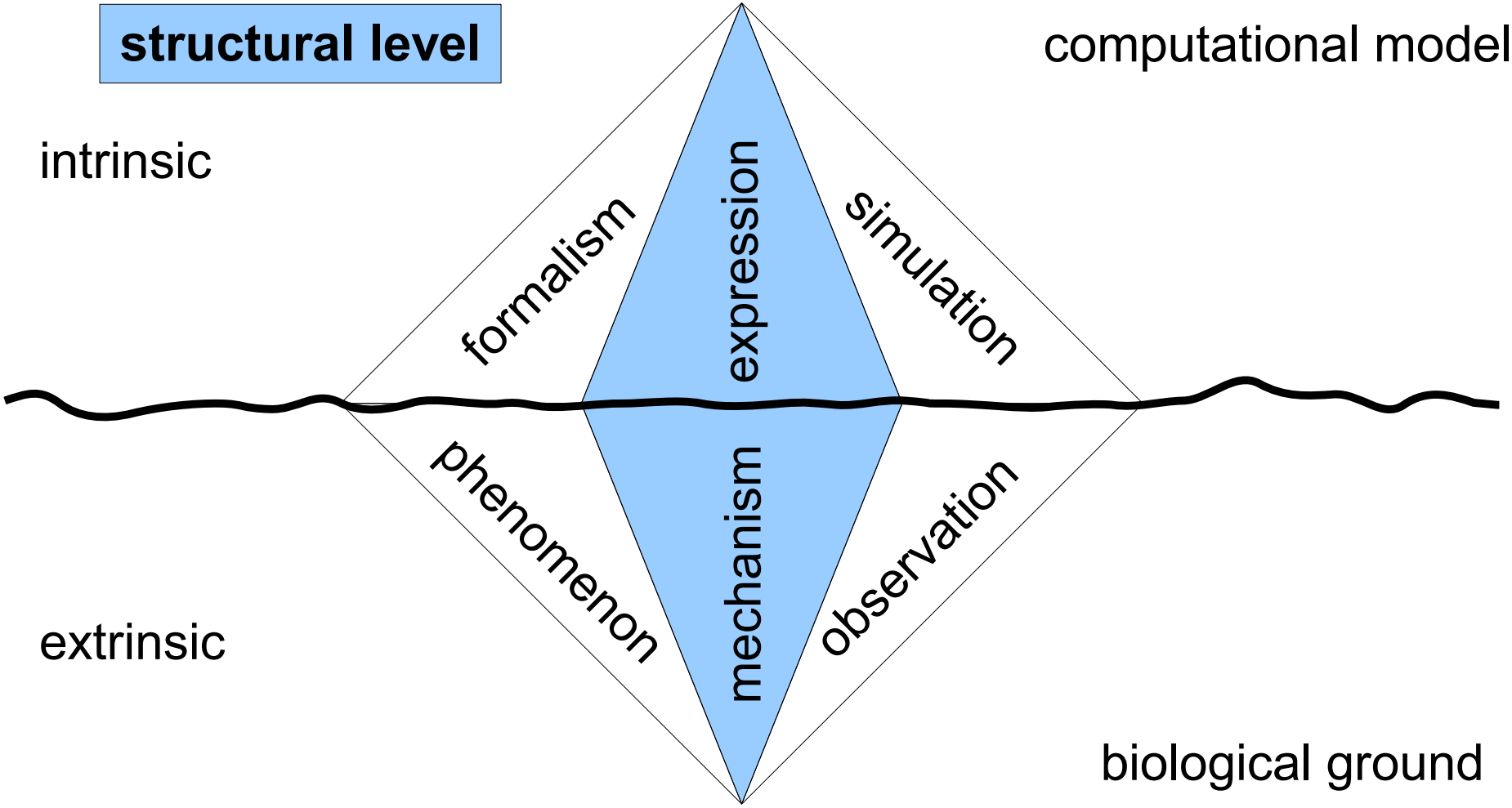
Meaning Facets



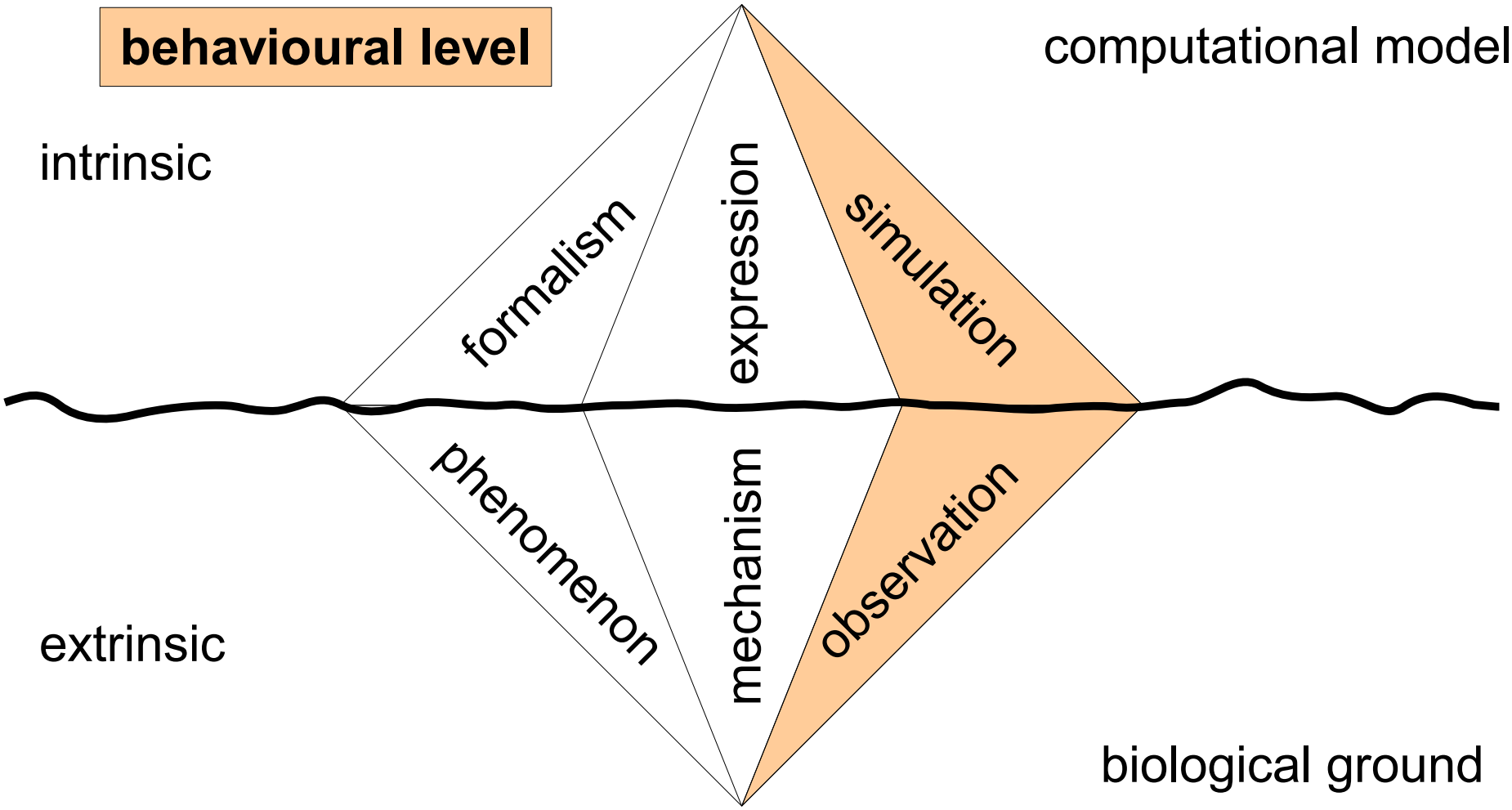
Meaning Facets



Meaning Facets

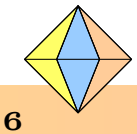


Meaning Facets



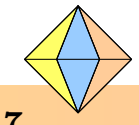
Sembiotics Framework

- formal specification of the meaning of bio-models
- commitment to meaning facets
- formal model ontology
- automated reasoning services



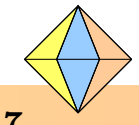
Sembiotics

Bio-models as computational codes of biological systems



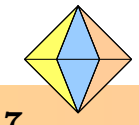
Sembiotics

Bio-models as computational codes of biological systems



Sembiotics

Bio-models as computational codes of biological systems

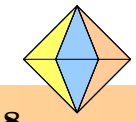


Common Goals

Improve

- access
- usage
- reuse
- exchange
- integration

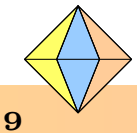
of bio-models



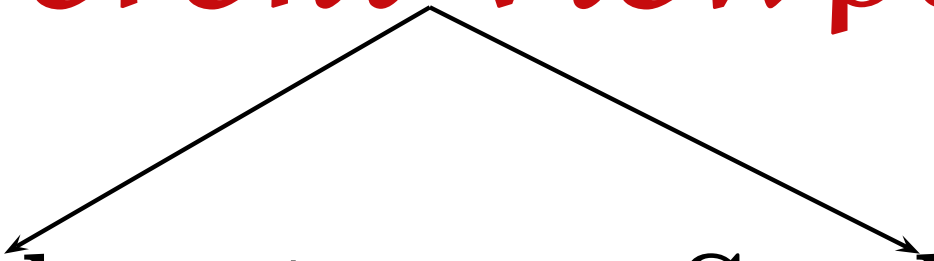
Common Means

- precise
- explicit
- structured
- standardised
- concise

description of computational bio-models



Different Viewpoints



BioModels.net

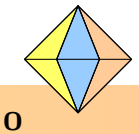
biologist viewpoint

model database for modellers

Sembiotics

KR viewpoint

methodology for formal model descriptions



Case Study: Model 1

$$\mathrm{d}[\mathsf{C2}]/dt = k_6[\mathsf{M}] - k_8[\sim\mathsf{P}][\mathsf{C2}] + k_9[\mathsf{CP}] \quad (1)$$

$$\mathrm{d}[\mathsf{CP}]/dt = -k_3[\mathsf{CP}][\mathsf{Y}] + k_8[\sim\mathsf{P}][\mathsf{C2}] - k_9[\mathsf{CP}] \quad (2)$$

$$\mathrm{d}[\mathsf{pM}]/dt = k_3[\mathsf{CP}][\mathsf{Y}] - [\mathsf{pM}]F([\mathsf{M}]) + k_5[\sim\mathsf{P}][\mathsf{M}] \quad (3)$$

$$\mathrm{d}[\mathsf{M}]/dt = [\mathsf{pM}]F([\mathsf{M}]) - k_5[\sim\mathsf{P}][\mathsf{M}] - k_6[\mathsf{M}] \quad (4)$$

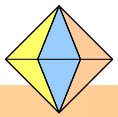
$$\mathrm{d}[\mathsf{Y}]/dt = k_1[\mathsf{aa}] - k_2[\mathsf{Y}] - k_3[\mathsf{CP}][\mathsf{Y}] \quad (5)$$

$$\mathrm{d}[\mathsf{YP}]/dt = k_6[\mathsf{M}] - k_7[\mathsf{YP}] \quad (6)$$

$$F([\mathsf{M}]) = k'_4 + k_4([\mathsf{M}]/[\mathsf{CT}])^2 \quad (7)$$

$$[\mathsf{CT}] = [\mathsf{C2}] + [\mathsf{CP}] + [\mathsf{pM}] + [\mathsf{M}] \quad (8)$$

Tyson1991_CellCycle_6var (BIOMD0000000005)



Case Study: Model 2

$$\mathrm{du}/d\mathrm{t} = k_4(\nu - u)(\alpha + u^2) - k_6 u \quad (9)$$

$$\mathrm{d}\nu/d\mathrm{t} = (k_1[\mathsf{aa}]/[\mathsf{CT}]) - k_6 u \quad (10)$$

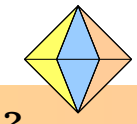
$$u = [\mathsf{M}]/[\mathsf{CT}] \quad (11)$$

$$\nu = ([\mathsf{Y}] + [\mathsf{pM}] + [\mathsf{M}])/[\mathsf{CT}] \quad (12)$$

$$[\mathsf{CT}] = [\mathsf{C2}] + [\mathsf{CP}] + [\mathsf{pM}] + [\mathsf{M}] \quad (13)$$

$$\alpha = k_4'/k_4 \quad (14)$$

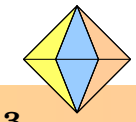
Tyson1991_CellCycle_2var (BIOMD0000000006)



Mathematical Structure

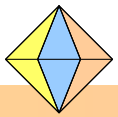
$$\begin{aligned} \mathrm{du}/d\mathsf{t} &= k_4(\nu - u)(\alpha + u^2) - k_6 u \\ u &= [\mathsf{M}]/[\mathsf{CT}] \end{aligned}$$

ID	Description	Relation	Type	Subject
u	relative [M]	is_a	MO	Variable
M	YP_C2	is_a	MO	Substance
		has_part	THIS	C2, YP
CT	total cdc2k	is_a	MO	Substance
		has_prop	MO	∀has_part.C2



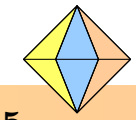
Behavioural Modes

behavioural meaning facets of *Model 1*				
ID	**Description**	**Relation**	**Type**	**Subject**
B1	steady state with high values of [M]	`inst_of`	MO	`Attractor(Fixed_Point, PS1)`
		`has_prop`	MO	`Constraint(high([M]))`
		`represents`	THIS	BP1
BP1	metaphase arrest	`is_a`	MO	`Biological_Phenomenon`
		`part_of`	GO	GO:0051323 (metaphase)
		`is_a`	GO	GO:0007050 (cell cycle arrest)
B2	spontaneous oscillation	`inst_of`	MO	`Attractor(Limit_Cycle, PS2)`
		`represents`	THIS	BP2
BP2	rapid division cycles in early embryos	`is_a`	MO	`Biological_Phenomenon`
		`is_a`	GO	GO:0040016 (embryonic cleavage)



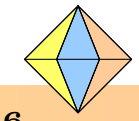
Parameter Settings

ID	Description	Relation	Type	Subject
PS0	standard parameter setting	`inst_of`	MO	`Constraint`$\big($ $[\sim\mathsf{P}] = const.$, $[\mathsf{aa}] = const.$, $k_1[\mathsf{aa}]/[\mathsf{CT}] = 0.015$, $k_2 = 0$, $k_3[\mathsf{CT}] = 200$, $10 \leq k_4 \leq 1000$, $k'_4 = 0.018$, $k_5[\sim\mathsf{P}] = 0$, $0.1 \leq k_6 \leq 10$, $k_7 = 0.6$, $k_8[\sim\mathsf{P}] \gg k_9 \gg k_6$ $\big)$
PS1	parameter setting for steady state	`inst_of`	MO	`Constraint`$\big($PS0, $k_1[\mathsf{aa}]/k_6[\mathsf{CT}] > \sqrt{k_6/k_4}$ $\big)$
PS2	parameter setting for spontaneous oscillation	`inst_of`	MO	`Constraint`$\big($PS0, $\sqrt{k'_4/k_4} < k_1[\mathsf{aa}]/k_6[\mathsf{CT}] < \sqrt{k_6/k_4}$ $\big)$
PS3	parameter setting for excitable switch	`inst_of`	MO	`Constraint`$\big($PS0, $k_1[\mathsf{aa}]/k_6[\mathsf{CT}] < \sqrt{k'_4/k_4}$ $\big)$



Relations between Models

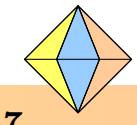
intentional meaning facets of *Model 2*				
ID	**Description**	**Relation**	**Type**	**Subject**
M2	Model 2	`inst_of`	MO	`Model`(SE2, BP0)
		`inst_of`	MO	`Projection`(`Specialisation`(M1,C1),$\{u, v\}$)
SE2	ODE system of M2	`inst_of`	MO	`ODE_System`(equations (9)-(14) of *Model 2*)
BP0	interaction between C2 and Y forming M	`is_a`	MO	`Biological_Phenomenon`
		`is_a`	GO	GO:0051726 (regulation of cell cycle)
C1		`inst_of`	MO	`Constraint`(PS0, $\alpha = k'_4/k_4,\ 0 < \nu < 1$)



Direct Benefits

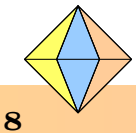
Extensions of the BioModels Database:

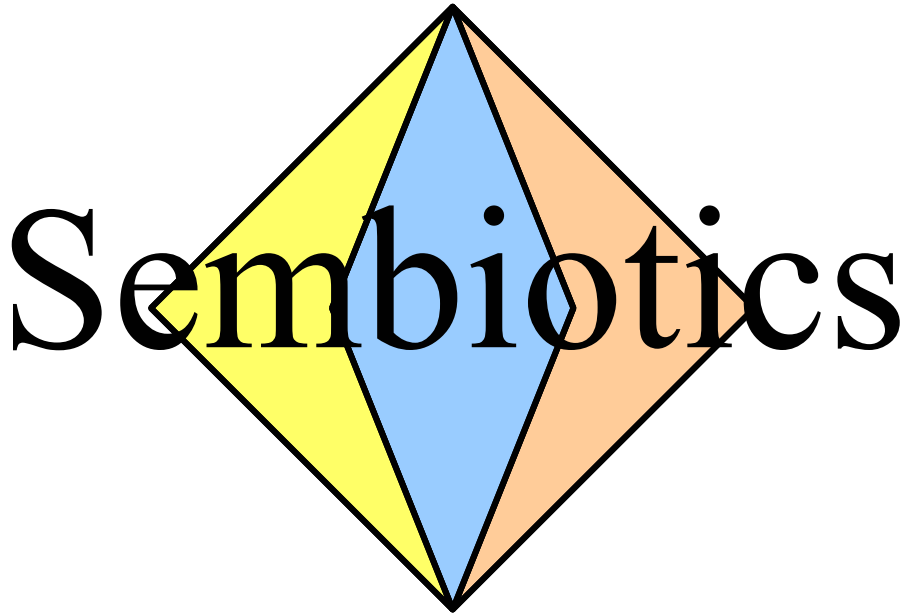
- behavioural level
- mathematical structure
- assumptions, parameter settings
- relations between models



Conclusion/Outlook

- BioModels.net and Sembiotics are complementary.
- They can benefit form each other.
- Computer-aided modelling needs formal semantics of bio-models.
- Sembiotics will provide the conceptual and methodological framework.





http://www.informatik.uni-jena.de/csb/prj/sembiotics/