Meaning Facets of *Model 1* (How to read the table?)

intentional meaning facets				
ID	**Description**	**Relation**	**Type**	**Subject**
M1	Model 1	`inst_of`	MO	`Model`(SE1, BP0)
SE1	ODE system of M1	`inst_of`	MO	`ODE_System`(equations (1)-(8) of *Model 1*)
BP0	interaction between C2 and Y forming M	`is_a` `is_a`	MO GO	`Biological_Phenomenon` GO:0051726 (regulation of cell cycle)
structural meaning facets				
ID	**Description**	**Relation**	**Type**	**Subject**
C2	cdc2k	`is_a` `is_a`	MO UP	`Substance` UP:P04551 (Cell division control protein 2)
CP	C2-P	`is_a` `has_part`	MO THIS	`Substance` C2, ∼P
Y	cyclin	`is_a` `is_a`	MO IP	`Substance` IPR006670 (Cyclin)
YP	p-Y	`is_a` `has_part`	MO THIS	`Substance` Y, ∼P
M	YP_C2	`is_a` `has_part`	MO THIS	`Substance` C2, YP
pM	YP_CP	`is_a` `has_part`	MO THIS	`Substance` M, ∼P
aa	amino acids	`is_a` `is_a`	MO CH	`Substance` ChEBI:33709 (amino acids)
CT	total cdc2k	`is_a` `has_prop`	MO MO	`Substance` ∀`has_part`.C2
P_i	inorganic phosphate	`is_a` `is_a`	MO CH	`Substance` ChEBI:26082 (phosphorus molecular entities)
∼P	adenosine triphosphate	`is_a` `is_a`	MO CH	`Substance` ChEBI:15422 (ATP)
R1	M dissociation	`inst_of` `is_a`	MO GO	`Reaction`(M → C2 + YP, `MAK`(k_6)) GO:0000079 (regulation of cyclin dependent protein kinase activity)

R2	C2 phosphorylation	`inst_of`
		`is_a`
		
		`is_a`
			MO
			GO
			
			EC
				`Reaction`(C2 + ATP → CP, `MAK`(k_8))
				GO:0006468 (protein amino acid phosphorylation)
				EC 2.7.1.37 (protein kinase, OBSOLETE)

R3	CP dephosphorylation	`inst_of`
		`is_a`
		
		`is_a`
			MO
			GO
			
			EC
				`Reaction`(CP → C2 + P_i, `MAK`(k_9)
				GO:0006470 (protein amino acid dephosphorylation)
				EC 3.1.3.16 (phosphoprotein phosphatase)

R4	Y CP association	`inst_of`	MO	`Reaction`(CP + Y + ∼P → pM, `MAK`(k_3))

R5	deactivation of M	`inst_of`
		`is_a`
		
		`is_a`
		
		`is_a`
			MO
			GO
			
			GO
			
			EC
				`Reaction`(M + ∼P → pM, `MAK`(k_5))
				GO:0045736 (negative regulation of cyclin dependent protein kinase activity)
				GO:0006468 (protein amino acid phosphorylation)
				EC 2.7.1.37 (protein kinase, OBSOLETE)

ID	Description	Relation	Type	Subject
R6	Y biosynthesis	inst_of is_a	MO GO	Reaction(aa → Y, MAK(k_1)) GO:0043037 (translation)
R7	default degradation of Y	inst_of is_a	MO GO	Reaction(Y → aa, MAK(k_2)) GO:0008054 (cyclin catabolism)
R8	M triggered degradation of Y	inst_of is_a	MO GO	Reaction(Y → aa + P_i, MAK(k_7)) GO:0008054 (cyclin catabolism)
R9	activation of M	inst_of is_a	MO GO	Reaction(pM $\xrightarrow{(M)}$ M + P_i, MAK($F([M])$)) GO:0045737 (positive regulation of cyclin dependent protein kinase activity)
$F()$	rate coefficient R9	inst_of	MO	Constraint($F([M]) = k'_4 + k_4([M]/[CT]^2)$)
t	time	represents	MO	Time

behavioural meaning facets

ID	Description	Relation	Type	Subject
B1	steady state with high values of [M]	inst_of has_prop represents	MO MO This	Attractor(Fixed_Point, PS1) Constraint(high([M])) BP1
BP1	metaphase arrest	is_a part_of is_a	MO GO GO	Biological_Phenomenon GO:0051323 (metaphase) GO:0007050 (cell cycle arrest)
B2	spontaneous oscillation	inst_of represents	MO This	Attractor(Limit_Cycle, PS2) BP2
BP2	rapid division cycles in early embryos	is_a is_a	MO GO	Biological_Phenomenon GO:0040016 (embryonic cleavage)
B3	excitable switch	inst_of has_prop represents	MO MO This	Attractor(Fixed_Point, PS3) Constraint(low([M])) BP3
BP3	growth-controlled division cycles in non-embryonic cells	is_a part_of	MO GO	Biological_Phenomenon GO:0051301 (cell division)
PS0	standard parameter setting	inst_of	MO	Constraint($[\sim P] = const.$, $[aa] = const.$, $k_1[aa]/[CT] = 0.015$, $k_2 = 0$, $k_3[CT] = 200$, $10 \leq k_4 \leq 1000$, $k'_4 = 0.018$, $k_5[\sim P] = 0$, $0.1 \leq k_6 \leq 10$, $k_7 = 0.6$, $k_8[\sim P] \gg k_9 \gg k_6$)
PS1	parameter setting for steady state	inst_of	MO	Constraint(PS0, $k_1[aa]/k_6[CT] > \sqrt{k_6/k_4}$)
PS2	parameter setting for spontaneous oscillation	inst_of	MO	Constraint(PS0, $\sqrt{k'_4/k_4} < k_1[aa]/k_6[CT] < \sqrt{k_6/k_4}$)
PS3	parameter setting for excitable switch	inst_of	MO	Constraint(PS0, $k_1[aa]/k_6[CT] < \sqrt{k'_4/k_4}$)

Meaning Facets of *Model 2* (How to read the table?)

intentional meaning facets				
ID	**Description**	**Relation**	**Type**	**Subject**
M2	Model 2	inst_of inst_of	MO MO	Model(SE2, BP0) 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 is_a	MO GO	Biological_Phenomenon GO:0051726 (regulation of cell cycle)
C1		inst_of	MO	Constraint(PS0, $\alpha = k'_4/k_4,\ 0 < \nu < 1$)
structural meaning facets				
ID	**Description**	**Relation**	**Type**	**Subject**
u	relative [M]	is_a	MO	Variable
v	relative sum of [M], [pM], and [Y]	is_a	MO	Variable
α	ratio of rate of R9 without and with M present	is_a	MO	Variable
Y	cyclin	is_a is_a	MO IP	Substance IPR006670 (Cyclin)
M	YP_C2	is_a has_part	MO This	Substance C2, YP
pM	YP_CP	is_a has_part	MO This	Substance M, ∼P
CT	total cdc2k	is_a has_prop	MO MO	Substance ∀has_part.C2
t	time	represents	MO	Time
behavioural meaning facets				
ID	**Description**	**Relation**	**Type**	**Subject**
B1'	steady state with high values of u	inst_of has_prop represents	MO MO M1	Attractor(Fixed_Point, PS1) Constraint(high([u])) B1
B2'	spontaneous oscillation	inst_of represents	MO M1	Attractor(Limit_Cycle, PS2) B2
B3'	excitable switch	inst_of has_prop represents	MO MO M1	Attractor(Fixed_Point, PS3) Constraint(low([M])) B3

Explanation

The first column of the tables contains the identifier (ID) of the model entity described in this row. This ID is used in other entries of the tables to refer to the semantics of this model entity. The IDs are indicated by sans serif font. Entities related to intrinsic meaning facets of the model have red IDs in the first column, extrinsic entities have black IDs. In the second column a description of the regarded model entity is given in "controlled" natural language: This description is tagged with identifiers from other model entities and thereby further constrain it's meaning. The semantics of the regarded model entity is covered by typed (column 4) binary relations (column 3). These binary relations can refer to other entities of the same model (THIS), to concepts of our preliminary Model Ontology (MO), or to external references (hyperlinks) specified in the last column of the tables. The used concepts from the proposed Model Ontology are described in the text. The following table summarises the used relations and types:

Relation	**Intended Meaning**
`has_prop`	defining property of a concept
`inst_of`	instance of a concept
`is_a`	subclass of a concept
`part_of`	part-whole relation
`has_part`	inverse of `part_of`
`represents`	model entity standing for some extrinsic entity
Type	**Intended Meaning**
MO	proposed Model Ontology
THIS	refers to another identifier from the semantics of this model
CH	Chemical Compounds of Biological Interest (ChEBI)
EC	Enzyme Nomenclature – online version INTENZ
GO	Gene Ontology – browser QUICKGO
IP	InterPro – integrated protein database
UP	Universal Protein Resource (UniProt)

We derived those tables by starting from the corresponding entry (BIOMD0000000005) of the *BioModels* database. The resulting formalisation of the semantics of *Model 1* goes beyond the annotation of the *BioModels* entry especially with respect to the behavioural level and the meaning of mathematical expressions in the model. Strong effort has been devoted to give the model a computer-understandable meaning. We use `is_a` instead of the relation "`is_version_of`" in *BioModels* which has no precise meaning. The subject of `is_a` has to be a super-concept of the regarded model entity. In order to ensure this formal reading of `is_a` the relevant parts of the external source must be imported in a suitable way.

The *BioModels*[1] references to *Reactome* for *Model 1* seem to be obsolete. Also the *BioModels* reference to the Enzyme Nomenclature EC 2.7.1.37 is out of date: in 2005 this entry was split up into different new entries and marked as "inactive entry" (we indicate this also in the table). This shows a major semantical problem of cross-linking: How can the validity of this cross-linking and of the semantics based on it be maintained in an ever changing world? The problem of sound revision of hybrid knowledge of this kind will certainly become a challenge in the "post-ontology" era.

[1]This refers to the forth release of the *BioModels* Database. In the current release from June 2006 the entry was corrected. But the general problem of revision in hybrid systems remains.