SBML Model Report

Model name: “Westermark2003_Pancreatic-_GlycOsc_extended”

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1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following three authors: Lukas Endler[1], Vijayalakshmi Chelliah[2] and Paal O Westermark[3] at August sixth 2009 at 4:54 p. m. and last time modified at June third 2014 at 2:56 p. m. Table 1 provides an overview of the quantities of all components of this model.

Table 1: Number of components in this model, which are described in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	7
events	0	constraints	0
reactions	4	function definitions	0
global parameters	26	unit definitions	6
rules	8	initial assignments	0

Model Notes

This is the extended model described in eq. 2 of the article:
A model of phosphofructokinase and glycolytic oscillations in the pancreatic beta-cell.

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Westermark PO and Lansner A. Biophys J. 2003 Jul;85(1):126-39. PMID: 12829470, doi:10.1016/S0006-3495(03)74460-9

Abstract:
We have constructed a model of the upper part of the glycolysis in the pancreatic beta-cell. The model comprises the enzymatic reactions from glucokinase to glyceraldehyde-3-phosphate dehydrogenase (GAPD). Our results show, for a substantial part of the parameter space, an oscillatory behavior of the glycolysis for a large range of glucose concentrations. We show how the occurrence of oscillations depends on glucokinase, aldolase and/or GAPD activities, and how the oscillation period depends on the phosphofructokinase activity. We propose that the ratio of glucokinase and aldolase and/or GAPD activities are adequate as characteristics of the glucose responsiveness, rather than only the glucokinase activity. We also propose that the rapid equilibrium between different oligomeric forms of phosphofructokinase may reduce the oscillation period sensitivity to phosphofructokinase activity. Methodologically, we show that a satisfying description of phosphofructokinase kinetics can be achieved using the irreversible Hill equation with allosteric modifiers. We emphasize the use of parameter ranges rather than fixed values, and the use of operationally well-defined parameters in order for this methodology to be feasible. The theoretical results presented in this study apply to the study of insulin secretion mechanisms, since glycolytic oscillations have been proposed as a cause of oscillations in the ATP/ADP ratio which is linked to insulin secretion.

2 Unit Definitions

This is an overview of nine unit definitions of which three are predefined by SBML and not mentioned in the model.

2.1 Unit `substance`

Name mmole

Definition mmol

2.2 Unit `time`

Name seconds

Definition s

2.3 Unit `mM`

Name mM

Definition $\mathrm{mmol} \cdot \mathrm{l}^{-1}$

2.4 Unit `g_per_ml`

Name gramm per ml

Definition $\mathrm{g} \cdot \mathrm{ml}^{-1}$

2.5 Unit `mM_per_s`

Name mM per sec

Definition $\mathrm{mmol} \cdot \mathrm{s}^{-1} \cdot \mathrm{l}^{-1}$

2.6 Unit `mmole_per_min_g`

Name mmole per (min kg)

Definition $\mathrm{mmol} \cdot (60\ \mathrm{s})^{-1} \cdot \mathrm{kg}^{-1}$

2.7 Unit `volume`

Notes Litre is the predefined SBML unit for `volume`.

Definition l

2.8 Unit `area`

Notes Square metre is the predefined SBML unit for `area` since SBML Level 2 Version 1.

Definition m^2

2.9 Unit `length`

Notes Metre is the predefined SBML unit for `length` since SBML Level 2 Version 1.

Definition m

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`cell`	cell	0000290	3	1	litre	☑	

3.1 Compartment `cell`

This is a three dimensional compartment with a constant size of one litre.

Name cell

SBO:0000290 physical compartment

4 Species

This model contains seven species. The boundary condition of four of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 8 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
`GLC`	intracellular glucose	`cell`	$\text{mmol} \cdot \text{l}^{-1}$	☑	☑
`G6P_F6P`	G6P_F6P	`cell`	$\text{mmol} \cdot \text{l}^{-1}$	⊟	⊟
`F6P`	fructose-6-phosphate	`cell`	$\text{mmol} \cdot \text{l}^{-1}$	⊟	☑
`FBP`	fructose-1,6-biphosphate	`cell`	$\text{mmol} \cdot \text{l}^{-1}$	⊟	⊟
`G3P`	glyceraldehyde–phosphate	`cell`	$\text{mmol} \cdot \text{l}^{-1}$	⊟	☑
`DHAP`	dihydroxyacetone-phosphate	`cell`	$\text{mmol} \cdot \text{l}^{-1}$	⊟	☑
`DHAP_G3P`	DHAP-G3P pool	`cell`	$\text{mmol} \cdot \text{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 26 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Vgk	Vgk		0.000	$\mathrm{mmol} \cdot \mathrm{s}^{-1} \cdot \mathrm{l}^{-1}$	☐
hGK	hGK		1.700	dimensionless	☑
KeqGPI	KeqGPI		0.300	dimensionless	☑
KeqTPI	KeqTPI		0.045	dimensionless	☑
Vpfk	Vpfk		0.000	$\mathrm{mmol} \cdot \mathrm{s}^{-1} \cdot \mathrm{l}^{-1}$	☐
Vfba	Vfba		0.000	$\mathrm{mmol} \cdot \mathrm{s}^{-1} \cdot \mathrm{l}^{-1}$	☐
Vgapdh	Vgapdh		0.000	$\mathrm{mmol} \cdot \mathrm{s}^{-1} \cdot \mathrm{l}^{-1}$	☐
Sgk	Sgk		8.000	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
Spfk	Spfk		4.000	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
Sfba	Sfba		0.005	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
Sgapdh	Sgapdh		0.005	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
Xpfk	Xpfk		0.010	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
alpha	alpha		5.000	dimensionless	☑
hx	hx		2.500	dimensionless	☑
hpfk	hpfk		2.500	dimensionless	☑
hact	hact		1.000	dimensionless	☑
dw_per_ml	dw_per_ml		0.333	$\mathrm{g} \cdot \mathrm{ml}^{-1}$	☑
min_to_sec	min_to_sec		60.000	dimensionless	☑
Vgk_min	Vgk_min		10.000	$\mathrm{mmol} \cdot (60\,\mathrm{s})^{-1} \cdot \mathrm{kg}^{-1}$	☑
Vpfk_min	Vpfk_min		100.000	$\mathrm{mmol} \cdot (60\,\mathrm{s})^{-1} \cdot \mathrm{kg}^{-1}$	☑
Vfba_min	Vfba_min		25.000	$\mathrm{mmol} \cdot (60\,\mathrm{s})^{-1} \cdot \mathrm{kg}^{-1}$	☑
Vgapdh_min	Vgapdh_min		250.000	$\mathrm{mmol} \cdot (60\,\mathrm{s})^{-1} \cdot \mathrm{kg}^{-1}$	☑
Pfba	Pfba		0.500	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
Qfba	Qfba		0.275	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
KeqFBA	KeqFBA		0.100	$\mathrm{mmol} \cdot \mathrm{l}^{-1}$	☑
sigma	sigma		0.000		☐

6 Rules

This is an overview of eight rules.

6.1 Rule sigma

Rule `sigma` is an assignment rule for parameter `sigma`:

$$\text{sigma} = \frac{[\text{F6P}]}{\text{Spfk}} \tag{1}$$

Derived unit dimensionless

6.2 Rule Vgk

Rule `Vgk` is an assignment rule for parameter `Vgk`:

$$\text{Vgk} = \frac{\text{Vgk\_min} \cdot \text{dw\_per\_ml}}{\text{min\_to\_sec}} \tag{2}$$

Derived unit $\text{mmol} \cdot (60\ \text{s})^{-1} \cdot \text{ml}^{-1}$

6.3 Rule Vpfk

Rule `Vpfk` is an assignment rule for parameter `Vpfk`:

$$\text{Vpfk} = \frac{\text{Vpfk\_min} \cdot \text{dw\_per\_ml}}{\text{min\_to\_sec}} \tag{3}$$

Derived unit $\text{mmol} \cdot (60\ \text{s})^{-1} \cdot \text{ml}^{-1}$

6.4 Rule Vfba

Rule `Vfba` is an assignment rule for parameter `Vfba`:

$$\text{Vfba} = \frac{\text{Vfba\_min} \cdot \text{dw\_per\_ml}}{\text{min\_to\_sec}} \tag{4}$$

Derived unit $\text{mmol} \cdot (60\ \text{s})^{-1} \cdot \text{ml}^{-1}$

6.5 Rule Vgapdh

Rule `Vgapdh` is an assignment rule for parameter `Vgapdh`:

$$\text{Vgapdh} = \frac{\text{Vgapdh\_min} \cdot \text{dw\_per\_ml}}{\text{min\_to\_sec}} \tag{5}$$

Derived unit $\text{mmol} \cdot (60\ \text{s})^{-1} \cdot \text{ml}^{-1}$

6.6 Rule F6P

Rule `F6P` is an assignment rule for species `F6P`:

$$\text{F6P} = \frac{[\text{G6P\_F6P}] \cdot \text{KeqGPI}}{1 + \text{KeqGPI}} \tag{6}$$

6.7 Rule G3P

Rule G3P is an assignment rule for species G3P:

$$\mathrm{G3P} = \frac{[\mathrm{DHAP\_G3P}] \cdot \mathrm{KeqTPI}}{1 + \mathrm{KeqTPI}} \tag{7}$$

6.8 Rule DHAP

Rule DHAP is an assignment rule for species DHAP:

$$\mathrm{DHAP} = [\mathrm{DHAP\_G3P}] - [\mathrm{G3P}] \tag{8}$$

Derived unit $\mathrm{mmol} \cdot \mathrm{l}^{-1}$

7 Reactions

This model contains four reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	`vgk`	vgk	$\mathrm{GLC} \rightleftharpoons \mathrm{G6P\_F6P}$	0000167
2	`vpfk`	vpfk	$\mathrm{G6P\_F6P} \xrightleftharpoons{\mathrm{F6P}} \mathrm{FBP}$	0000216
3	`vfba`	vfba	$\mathrm{FBP} \xrightleftharpoons{\mathrm{G3P,\ DHAP}} 2\,\mathrm{DHAP\_G3P}$	0000178
4	`vgapdh`	vgapdh	$\mathrm{DHAP\_G3P} \xrightarrow{\mathrm{G3P}} \emptyset$	0000201

7.1 Reaction vgk

This is a reversible reaction of one reactant forming one product.

Name vgk

SBO:0000167 biochemical or transport reaction

Reaction equation

$$\mathrm{GLC} \rightleftharpoons \mathrm{G6P\_F6P} \tag{9}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
GLC	intracellular glucose	

Product

Table 7: Properties of each product.

Id	Name	SBO
G6P_F6P	G6P_F6P	

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{\mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{Vgk} \cdot \left(\frac{[\mathrm{GLC}]}{\mathrm{Sgk}}\right)^{\mathrm{hGK}}}{1 + \left(\frac{[\mathrm{GLC}]}{\mathrm{Sgk}}\right)^{\mathrm{hGK}}} \tag{10}$$

7.2 Reaction vpfk

This is a reversible reaction of one reactant forming one product influenced by one modifier.

Name vpfk

SBO:0000216 phosphorylation

Reaction equation

$$\mathrm{G6P\_F6P} \xrightleftharpoons{\mathrm{F6P}} \mathrm{FBP} \tag{11}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
G6P_F6P	G6P_F6P	

Modifier

Table 9: Properties of each modifier.

Id	Name	SBO
F6P	fructose-6-phosphate	

Product

Table 10: Properties of each product.

Id	Name	SBO
FBP	fructose-1,6-biphosphate	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \frac{\mathrm{vol}\left(\mathrm{cell}\right) \cdot \mathrm{Vpfk} \cdot \left(\frac{[\mathrm{F6P}]}{\mathrm{Spfk}}\right)^{\mathrm{hpfk}-(\mathrm{hpfk}-\mathrm{hact}) \cdot \frac{\frac{[\mathrm{FBP}]}{\mathrm{Sfba}}}{1+\frac{[\mathrm{FBP}]}{\mathrm{Sfba}}}}}{\left(\frac{[\mathrm{F6P}]}{\mathrm{Spfk}}\right)^{\mathrm{hpfk}-(\mathrm{hpfk}-\mathrm{hact}) \cdot \frac{\frac{[\mathrm{FBP}]}{\mathrm{Sfba}}}{1+\frac{[\mathrm{FBP}]}{\mathrm{Sfba}}}} + \frac{1+\left(\frac{[\mathrm{FBP}]}{\mathrm{Xpfk}}\right)^{\mathrm{hx}}}{1+\mathrm{alpha}^{\mathrm{hpfk}-(\mathrm{hpfk}-\mathrm{hact}) \cdot \frac{\frac{[\mathrm{FBP}]}{\mathrm{Sfba}}}{1+\frac{[\mathrm{FBP}]}{\mathrm{Sfba}}}} \cdot \left(\frac{[\mathrm{FBP}]}{\mathrm{Xpfk}}\right)^{\mathrm{hx}}}} \tag{12}$$

7.3 Reaction `vfba`

This is a reversible reaction of one reactant forming one product influenced by two modifiers.

Name vfba

SBO:0000178 cleavage

Reaction equation

$$\mathrm{FBP} \xrightleftharpoons{\mathrm{G3P},\ \mathrm{DHAP}} 2\,\mathrm{DHAP\_G3P} \tag{13}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
FBP	fructose-1,6-biphosphate	

Modifiers

Table 12: Properties of each modifier.

Id	Name	SBO
G3P	glyceraldehyde–phosphate	
DHAP	dihydroxyacetone-phosphate	

Product

Table 13: Properties of each product.

Id	Name	SBO
DHAP_G3P	DHAP-G3P pool	

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \frac{\mathrm{vol}\left(\mathrm{cell}\right) \cdot \mathrm{Vfba} \cdot \left(\frac{[\mathrm{FBP}]}{\mathrm{Sfba}} - \frac{[\mathrm{G3P}] \cdot [\mathrm{DHAP}]}{\mathrm{Pfba} \cdot \mathrm{Qfba} \cdot \mathrm{KeqFBA}}\right)}{1 + \frac{[\mathrm{FBP}]}{\mathrm{Sfba}} + \frac{[\mathrm{DHAP}]}{\mathrm{Qfba}} + \frac{[\mathrm{G3P}] \cdot [\mathrm{DHAP}]}{\mathrm{Pfba} \cdot \mathrm{Qfba}}} \tag{14}$$

7.4 Reaction vgapdh

This is an irreversible reaction of one reactant forming no product influenced by one modifier.

Name vgapdh

SBO:0000201 oxidation

Reaction equation

$$\mathrm{DHAP\_G3P} \xrightarrow{\mathrm{G3P}} \emptyset \tag{15}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
DHAP_G3P	DHAP-G3P pool	

Modifier

Table 15: Properties of each modifier.

Id	Name	SBO
G3P	glyceraldehyde–phosphate	

Kinetic Law

Derived unit $0.0010 \text{ mol} \cdot \text{s}^{-1}$

$$v_4 = \frac{\text{vol}(\text{cell}) \cdot \text{Vgapdh} \cdot [\text{G3P}]}{\text{Sgapdh} + [\text{G3P}]} \tag{16}$$

8 Derived Rate Equations

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rates of change of each species.

8.1 Species GLC

Name intracellular glucose

SBO:0000247 simple chemical

Initial concentration $10 \text{ mmol} \cdot \text{l}^{-1}$

This species takes part in one reaction (as a reactant in vgk), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\text{d}}{\text{d}t}\text{GLC} = 0 \tag{17}$$

8.2 Species G6P_F6P

Name G6P_F6P

SBO:0000247 simple chemical

Initial concentration $3.71728 \text{ mmol} \cdot \text{l}^{-1}$

This species takes part in two reactions (as a reactant in vpfk and as a product in vgk).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{G6P\_F6P} = v_1 - v_2 \tag{18}$$

8.3 Species F6P

Name fructose-6-phosphate

SBO:0000247 simple chemical

Involved in rule F6P

This species takes part in one reaction (as a modifier in vpfk). Not this but one rule determines the species' quantity because this species is on the boundary of the reaction system.

8.4 Species FBP

Name fructose-1,6-biphosphate

SBO:0000247 simple chemical

Initial concentration $6.3612 \cdot 10^{-4}$ mmol $\cdot$ l^{-1}

This species takes part in two reactions (as a reactant in vfba and as a product in vpfk).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{FBP} = v_2 - v_3 \tag{19}$$

8.5 Species G3P

Name glyceraldehyde–phosphate

SBO:0000247 simple chemical

Involved in rule G3P

This species takes part in two reactions (as a modifier in vfba, vgapdh). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

8.6 Species DHAP

Name dihydroxyacetone-phosphate

SBO:0000247 simple chemical

Involved in rule DHAP

This species takes part in one reaction (as a modifier in vfba). Not this but one rule determines the species' quantity because this species is on the boundary of the reaction system.

8.7 Species DHAP_G3P

Name DHAP-G3P pool

SBO:0000247 simple chemical

Initial concentration $0.00262966 \text{ mmol} \cdot \text{l}^{-1}$

This species takes part in two reactions (as a reactant in vgapdh and as a product in vfba).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{DHAP\_G3P} = 2v_3 - v_4 \quad (20)$$

A Glossary of Systems Biology Ontology Terms

SBO:0000167 **biochemical or transport reaction:** An event involving one or more physical entities that modifies the structure, location or free energy of at least one of the participants

SBO:0000178 **cleavage:** Rupture of a covalent bond resulting in the conversion of one physical entity into several physical entities

SBO:0000201 **oxidation:** Chemical process during which a molecular entity loses electrons

SBO:0000216 **phosphorylation:** Addition of a phosphate group (-H2PO4) to a chemical entity

SBO:0000247 **simple chemical:** Simple, non-repetitive chemical entity

SBO:0000290 **physical compartment:** Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions

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