A Petri Net Based Model Validation Technique for the Central Carbon Metabolism of *Solanum Tuberosum* Tubers

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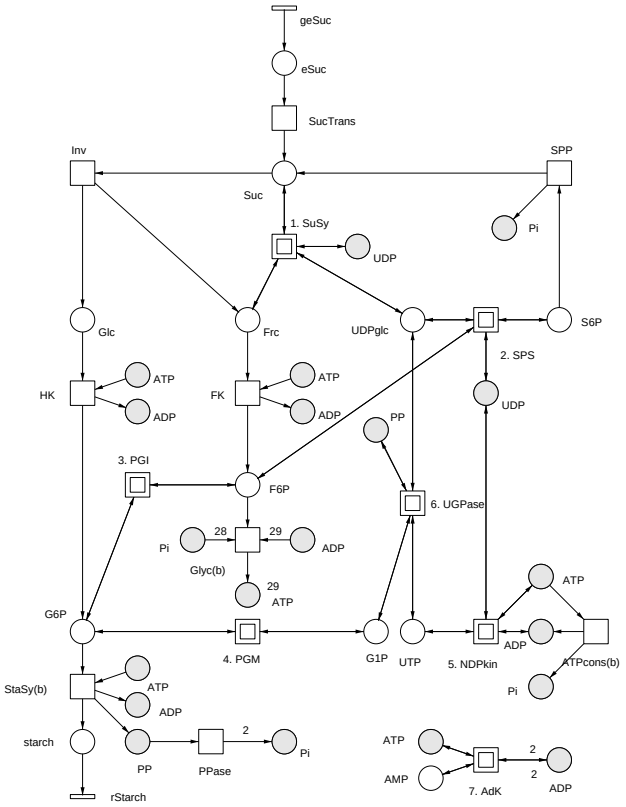
Motivation

Because of the complexity of metabolic pathways and their regulation, formal modelling is a useful method to improve the understanding of these systems. An essential step in pathway modelling is to validate the pathway model before starting a quantitative analysis. Petri net theory provides algorithms and methods, which can be applied directly to metabolic pathway modelling and analysis in order to validate the model [2][3]. The pathway between sucrose and starch in the potato tuber is of great research interest. Even if the pathway is one of the best studied in sink organs, it is not yet fully understood.

The Petri net Model

The modelling was performed according [1] and additional experimental data, using the Petri net editor PED [5]. The metabolism was modelled as place/transition net, where the places represent the metabolites, transitions the enzymes/reactions, and the arc weights the stoichiometric numbers of the underlying chemical reactions.

Top Level



SuSy:	Suc + UDP ↔ UDPglc + Frc	PGM:	G6P ↔ G1P
UGPase:	UDPglc + PP ↔ G1P + UTP	PGI:	G6P ↔ F6P
FK:	Frc + ATP → F6P + ADP	SucTrans:	eSuc → Suc
HK:	Glc + ATP → G6P + ADP	Inv:	Suc → Glc + Frc
SPS:	F6P + UDPglc ↔ S6P + UDP	SPP:	S6P → Suc + Pi
Glyc(b):	F6P + 29 ADP + 28 Pi → 29 ATP	AdK:	ATP + AMP ↔ 2 ADP
NDPkin:	UDP + ATP ↔ UTP + ADP	ATPcons(b):	ATP → ADP + Pi
StaSy(b):	G6P + ATP → starch + ADP + PP	PPase:	PP → 2 Pi

References

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Qualitative Analysis using INA [4]

P-Invariants: The net contains, but is not covered by minimal semi-positive

P-invariants:
(1) UDPglc, UTP, UDP
(2) ATP, AMP, ADP
(3) G6P, F6P, G1P, UTP, ATP(2), ADP, S6P, Pi, PP(2)

T-Invariants: The net is covered by minimal semi-positive T-invariants.

Trivial T-invariants: (1) SPS, SPS_rev; (2) UGPase, UGPase_rev; (3) SuSy, SuSy_rev; (4) PGM, PGM_rev; (5) NDPkin, NDPkin_rev, (6) AdK, AdK_rev; (7) PGI, PGI_rev.

Invariants with sucrose cleavage by sucrose synthase

(8) geSuc, SucTrans, SuSy(29), UGPase, PGM_rev, FK(29), Glyc(b), StaSy(b), rStarch, SPS(28), SPP(28), NDPkin_rev.
(9 geSuc, SucTrans, SuSy, UGPase, PGM_rev, FK, Glyc(b), StaSy(b), rStarch, ATPcons(b)(28), NDPkin_rev.
(10) geSuc(15), SucTrans(15), SuSy(15), PGI_rev(14), UGPase(15), PGM_rev(15), FK(15), Glyc(b), StaSy(b)(29), rStarch(29), NDPkin_rev(15), PPase(14).

Invariants with sucrose cleavage by invertase

(11) geSuc, SucTrans, Inv(14), UGPase_rev(13), PGM(13), HK(14), FK, Glyc(b), StaSy(b), rStarch, SuSy_rev(13), NDPkin(13), PPase(14).
(12) geSuc(3), SucTrans(3), Inv(29), UGPase_rev(26), PGM(26), HK(29), FK(29), Glyc(b)(3), StaSy(b)(3), rStarch(3), SPS(26), SPP(26), NDPkin(26), PPase(29).
(13) geSuc, SucTrans, Inv, HK, FK(27), Glyc(b), StaSy(b), rStarch, SuSy(26), SPS(26), SPP(26), PPase.
(14) geSuc, SucTrans, Inv, HK, FK, Glyc(b), StaSy(b), rStarch, ATPcons(b)(26), PPase.
(15) geSuc(15), SucTrans(15), Inv(15), HK(15), FK(15), PGI_rev(13), Glyc(b)(2), StaSy(b)(28), rStarch(28), PPase(28).
(16) geSuc, SucTrans, Inv(29), HK(29), FK, PGI, UGPase_rev(28), PGM(28), Glyc(b)(2), SuSy_rev(28), NDPkin(28), PPase(28).
(17) geSuc(3), SucTrans(3), Inv(59), HK(59), FK(59), UGPase_rev(56), PGM(56), PGI(3), Glyc(b)(6), SPS(56), SPP(56), NDPkin(56), PPase(56).
(18) geSuc, SucTrans, Inv, HK, FK(57), PGI, Glyc(b)(2), SuSy_rev(56), SPS(56), SPP(56).
(19) geSuc, SucTrans, Inv, HK, FK, PGI, Glyc(b)(2), ATPkons(b)(56).

Distribution of the 12 non-trivial T-invariants

invariant no.	Suc cleavage Susy	Suc cleavage Inv	hexoses go into Glyc	hexoses go into StaSy	ATP used for cycling ATP cons	ATP used for cycling Inv Susy_rev	ATP used for cycling Inv SPS, SPP	ATP used for cycling SuSy SPS, SPP
8	x		x	x				x
9	x		x	x	x			
10	x		x	x				
11		x	x	x		x		
12		x	x	x			x	
13		x	x	x				x
14		x	x	x	x			
15		x	x	x				
16		x	x			x		
17		x	x				x	
18		x	x					x
19		x	x		x			

Other net properties: The net is unbounded, not ordinary, not homogenous, not conservative; pure, not static conflict free, connected, but not strongly connected.

Conclusions

- Petri nets provide methods for qualitative analysis, which can be used for model validation before starting quantitative analyses and simulation experiments.
- P-invariants reflect substance preservations.
- T-invariants reflect the main processes (pathways) taking place in reality.
- The model is covered by T-invariants, which all enjoy biological meaning.
- The occurring T-invariants explain the net behaviour as possible combinations of sub-processes, which mirrors correctly experimentally known results.

Outlook

- Extension of the validated model by other central metabolic processes (e.g. glycolysis, respiration, amino acid metabolism).
- Exploration of Petri net methods for larger and more complex networks.

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