

British outstation of the European Molecular Biology Laboratory

■ Databases

- Sequences, structures
- Transcriptomics, Proteomics pathways, models
- Controlled vocabularies and dictionaries

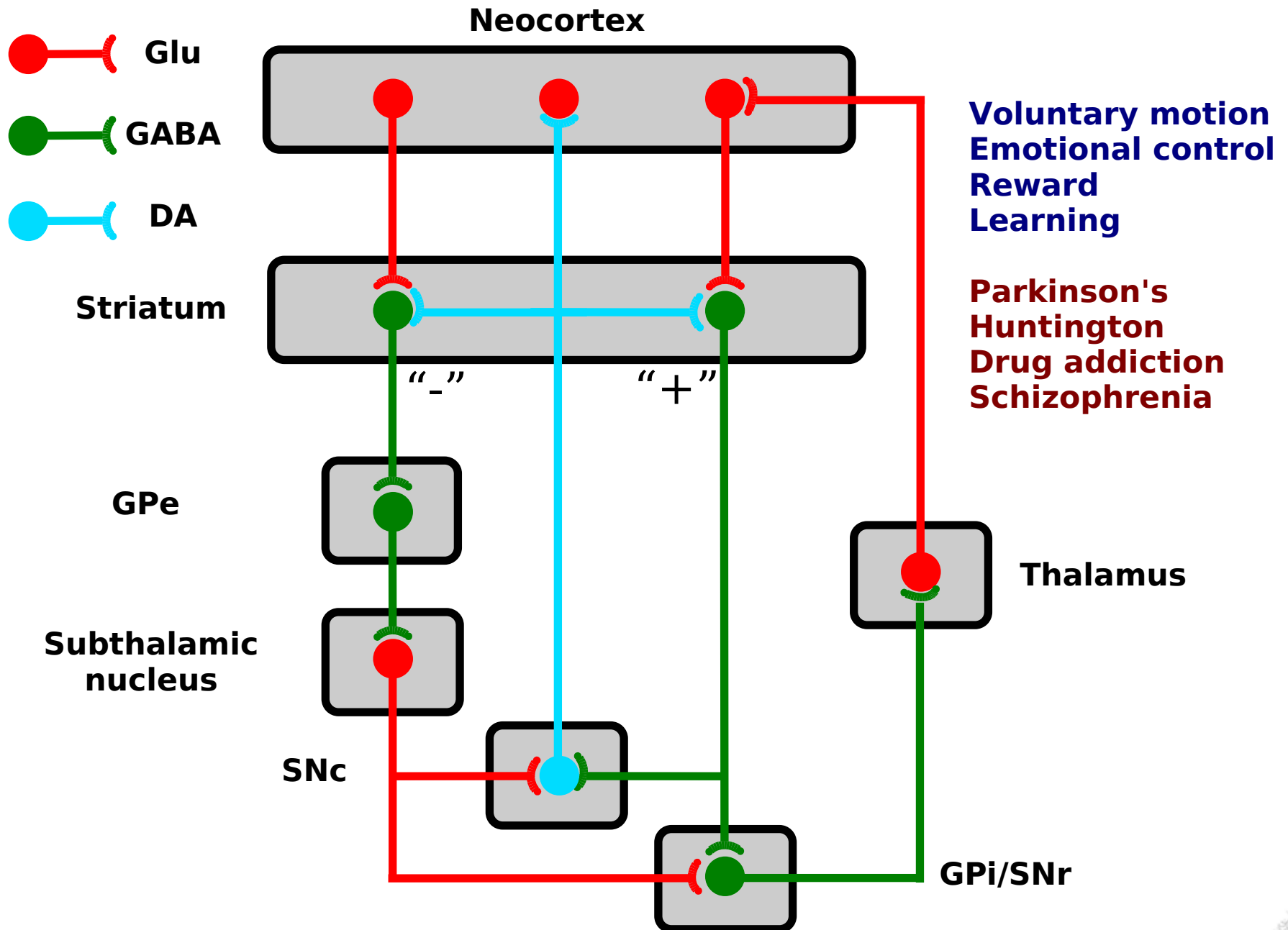


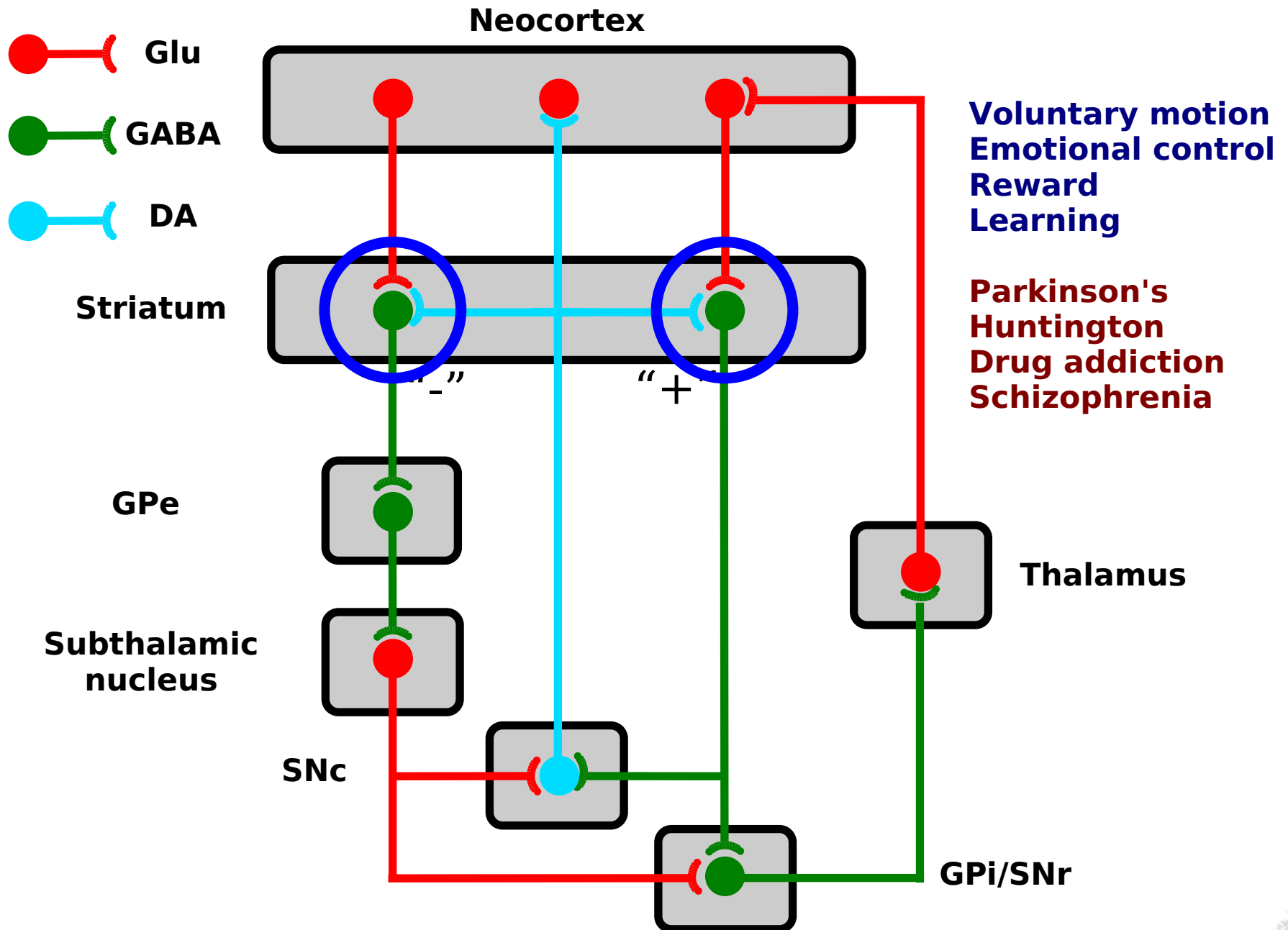
■ Research groups

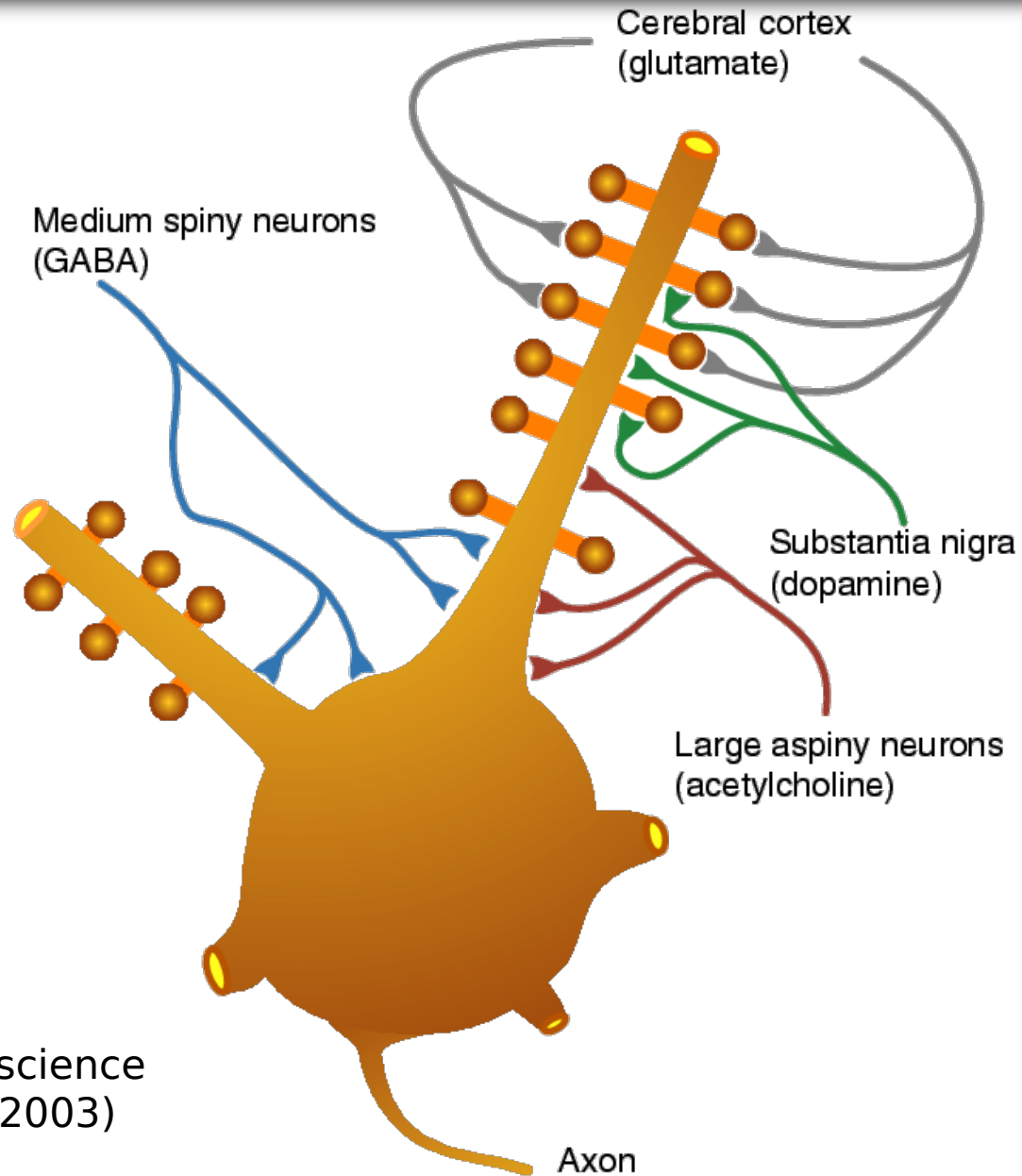
- Structural Genomics (Thornton)
- Molecular Evolution (Goldman)
- Text-Mining (Rebholz-Schumman)
- Computational Systems Biology (Le Novère)
- Statistical array analysis (Huber)
- Genomic analysis of regulatory systems (Luscombe)
- Systems Biology of ES cells (Bertone)

**Modeling the intracellular dopamine
signaling network :
DARPP32 – a robust signal integrator**





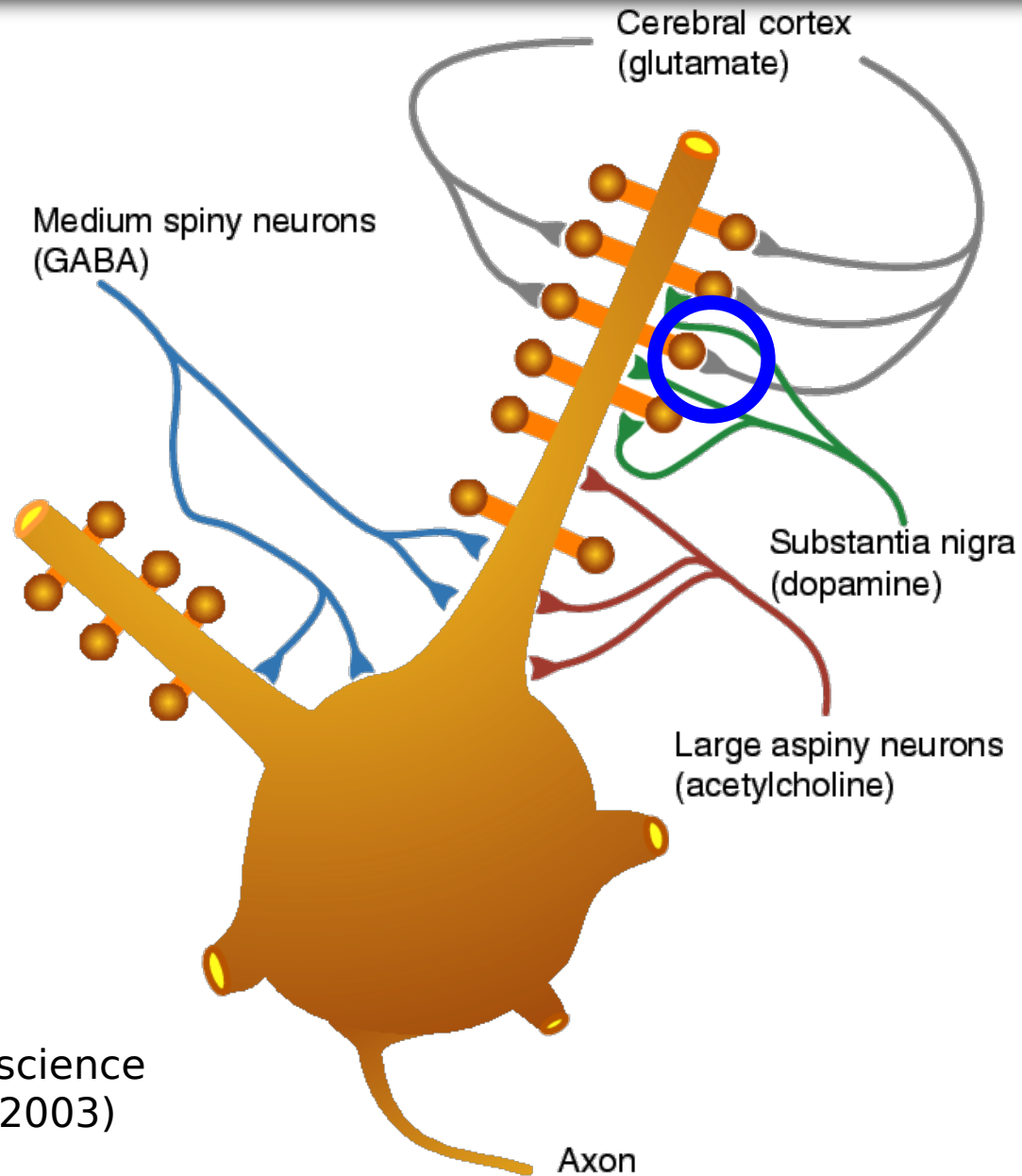




Fundamental Neuroscience
Squire et al. 2nd ed(2003)

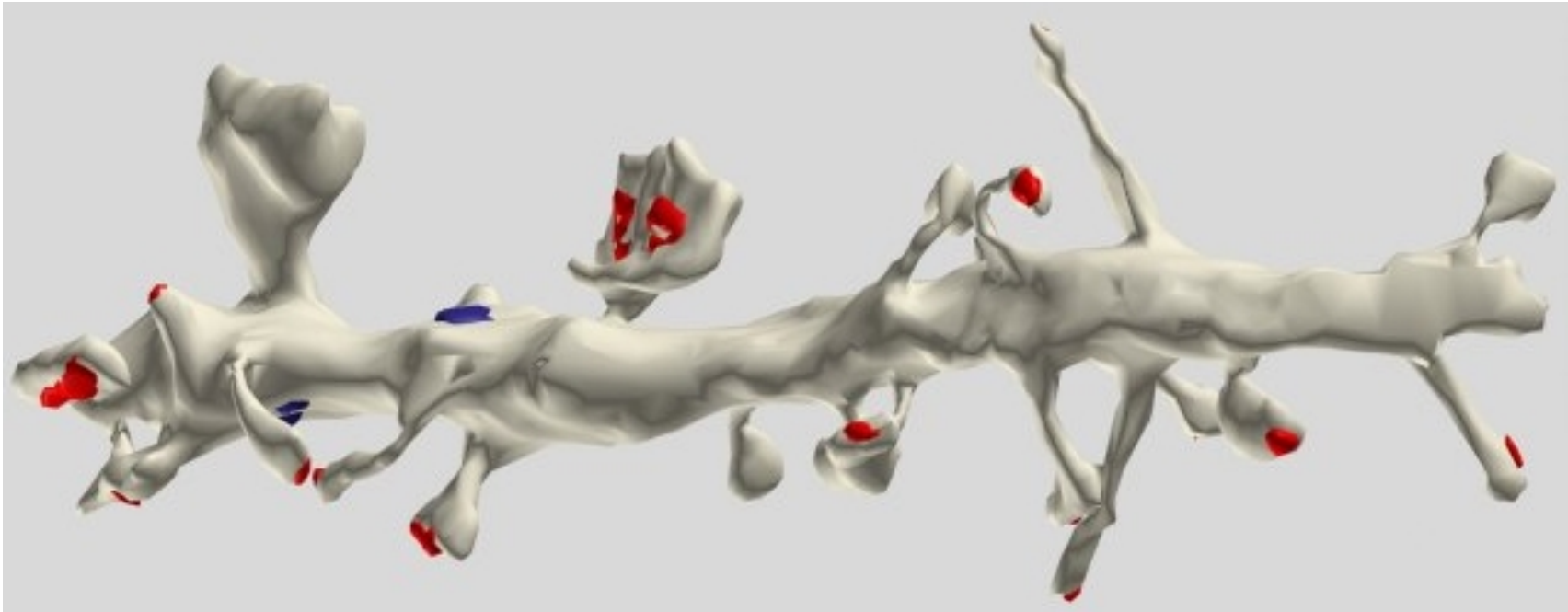
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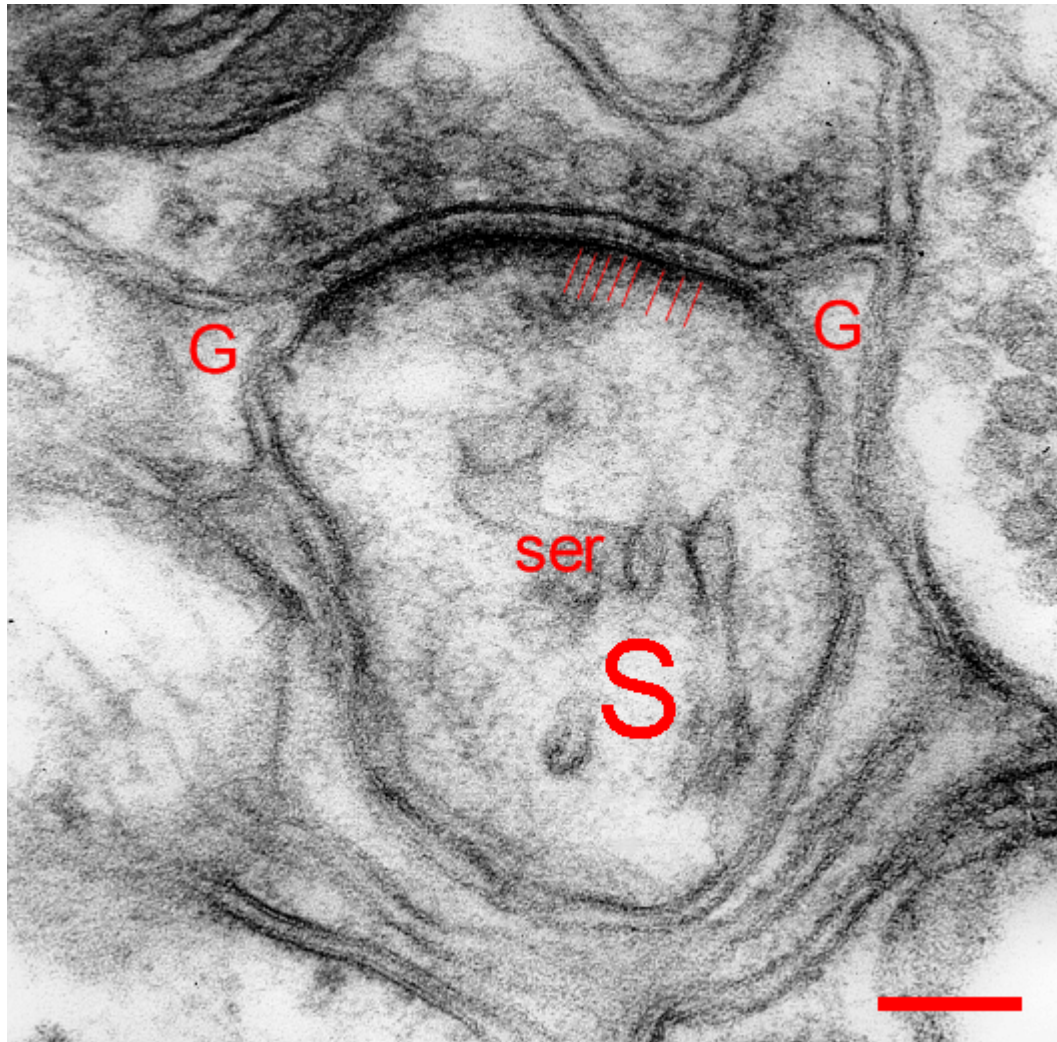


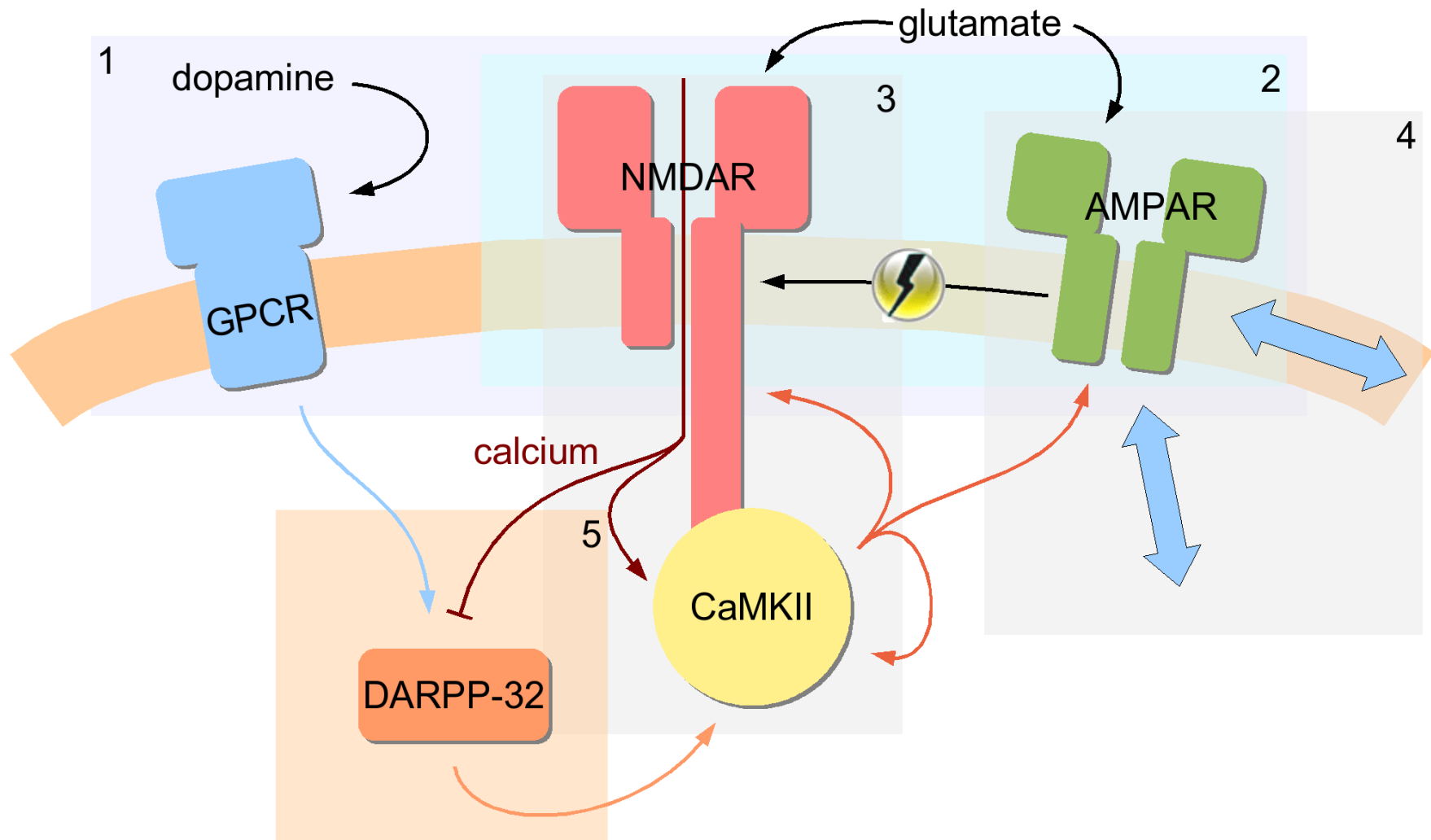


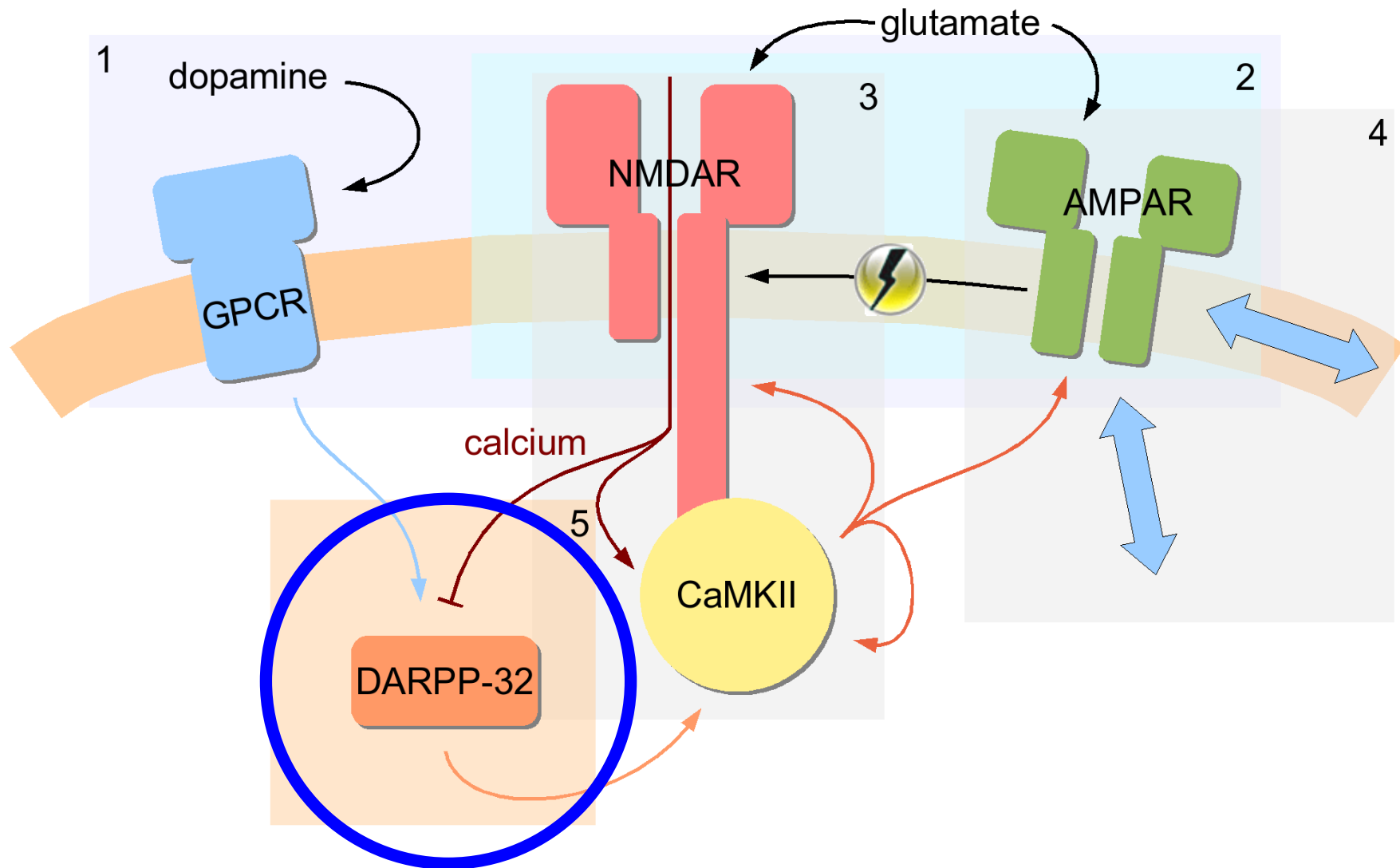
Fundamental Neuroscience
Squire et al. 2nd ed(2003)





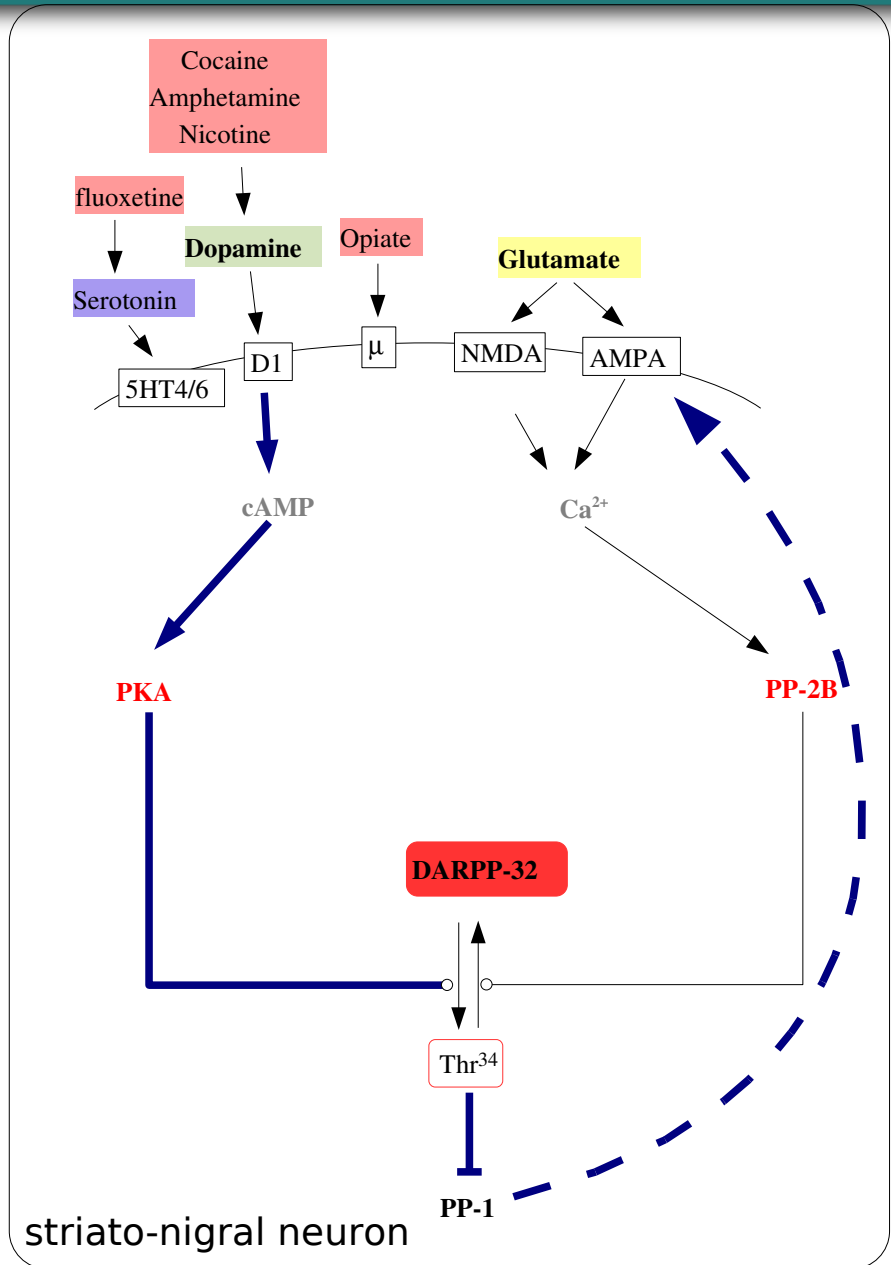
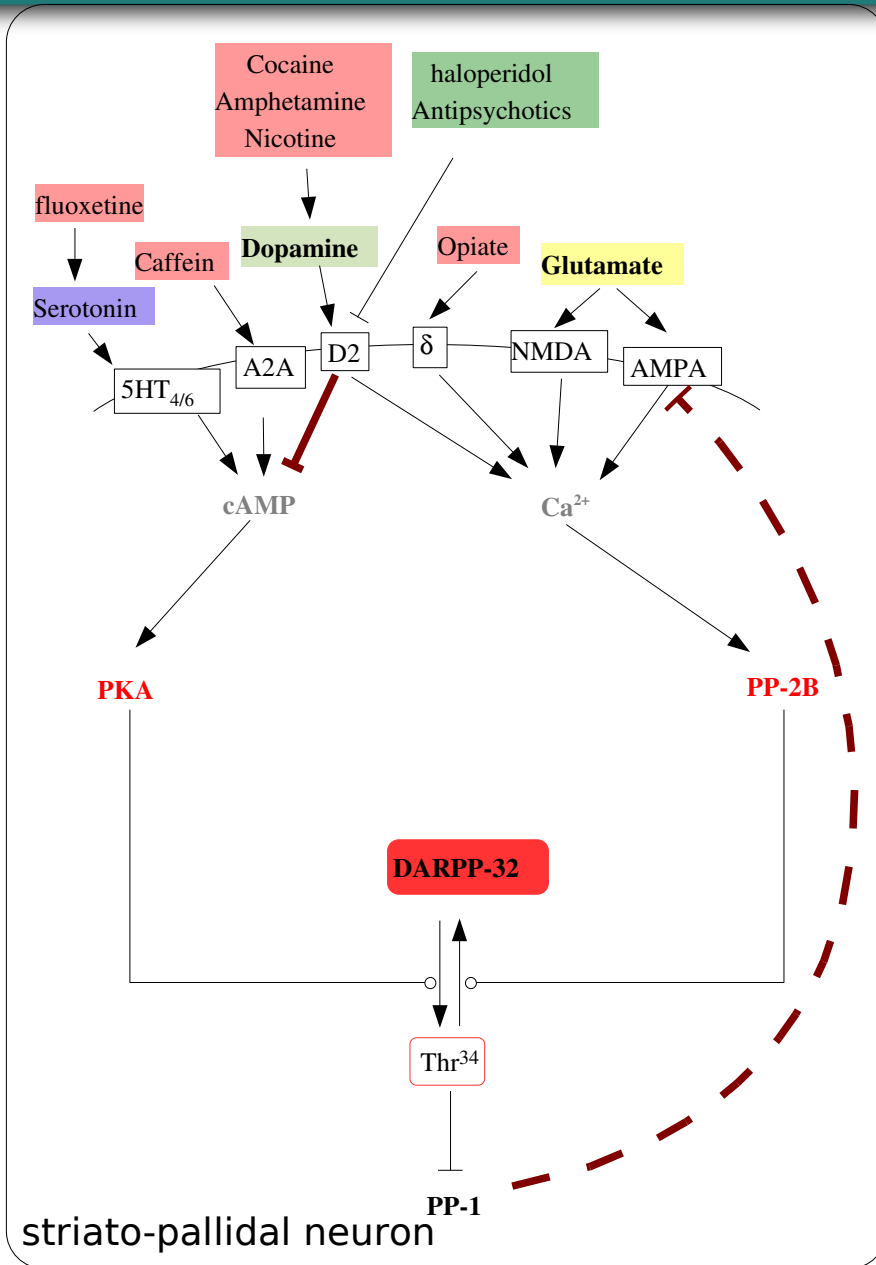


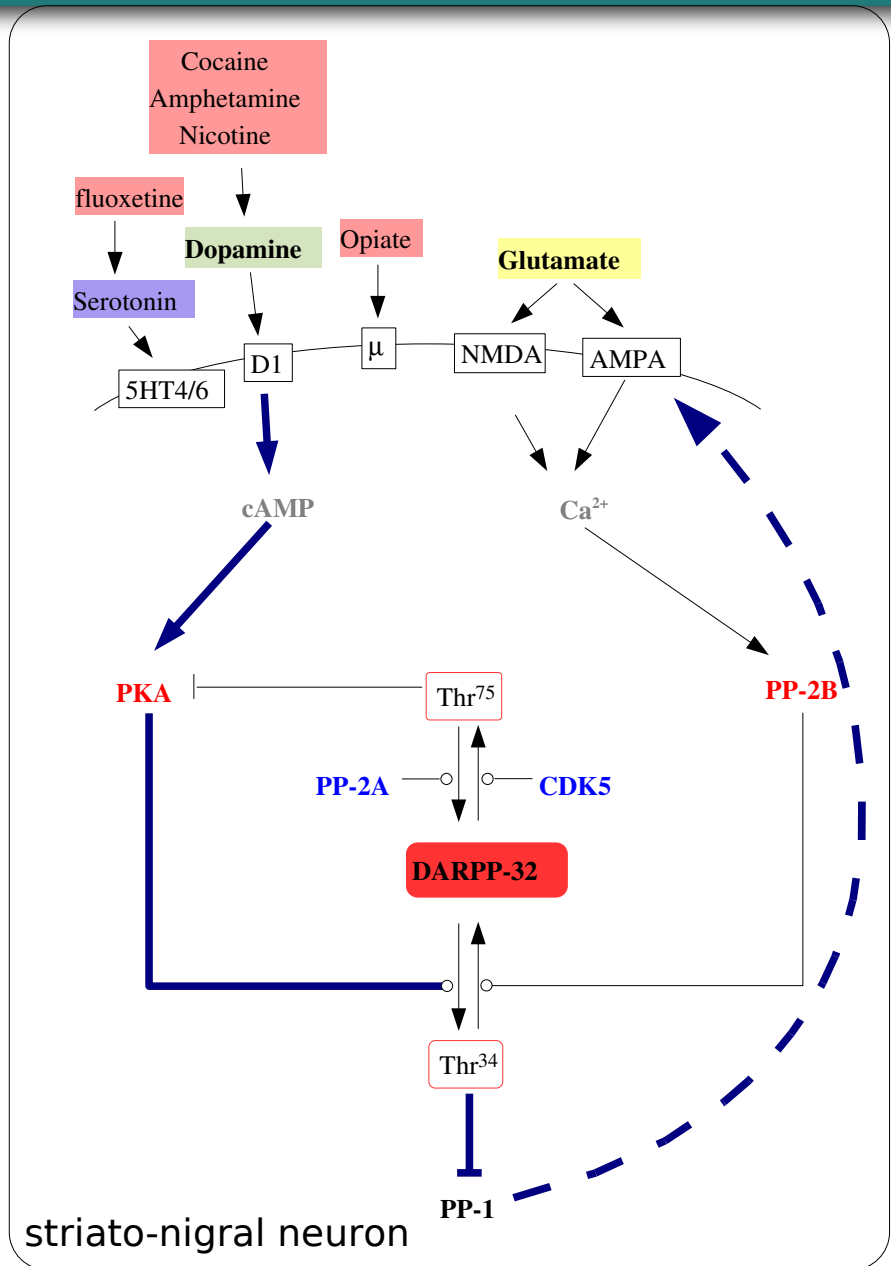
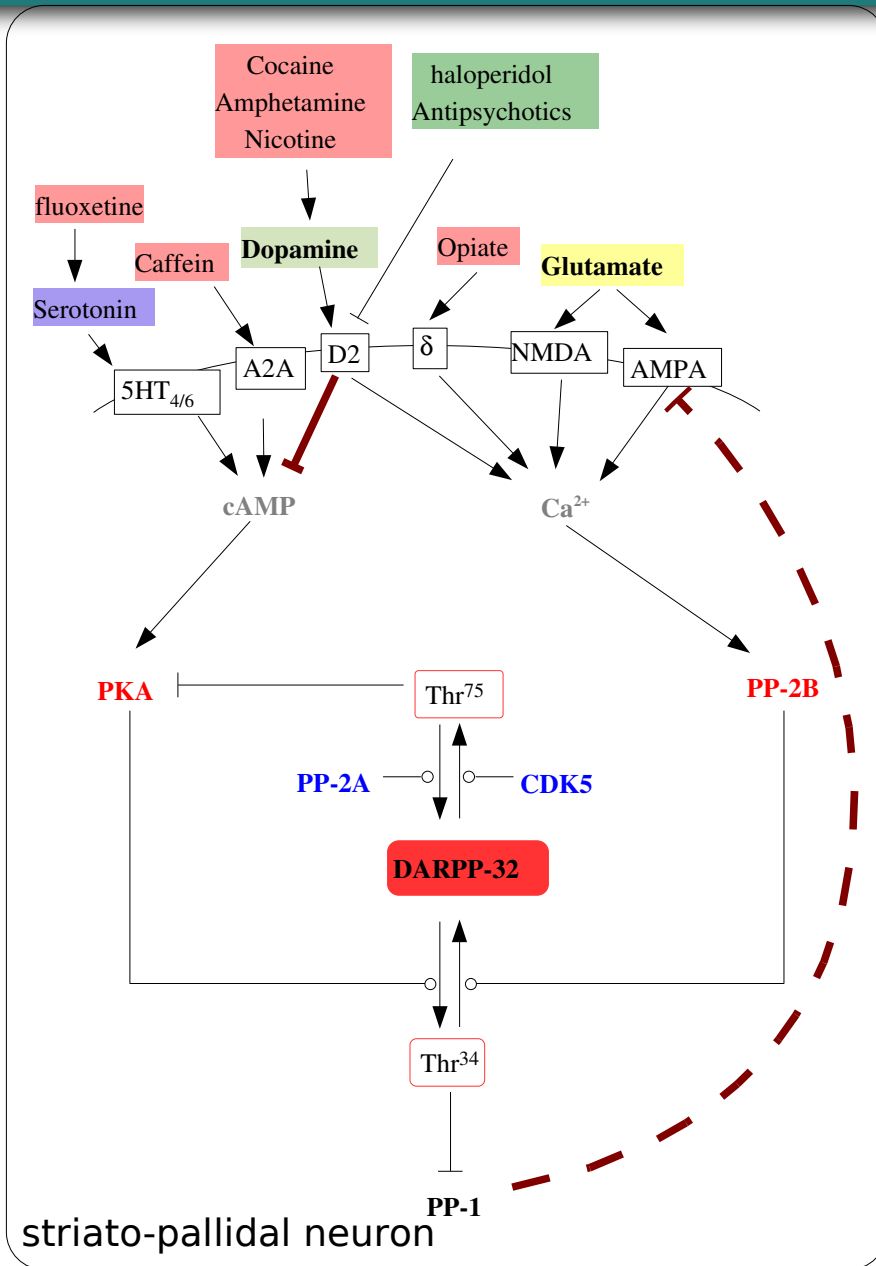


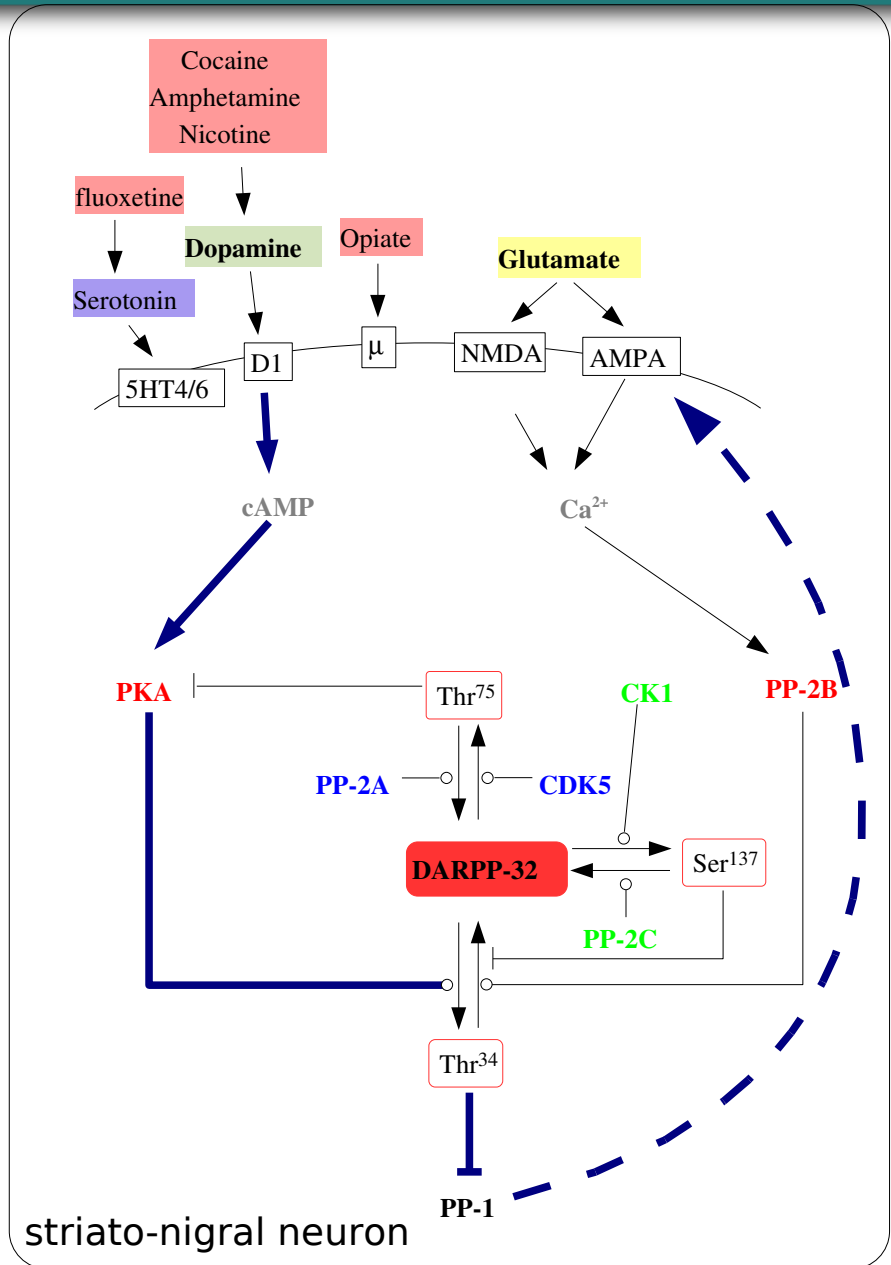
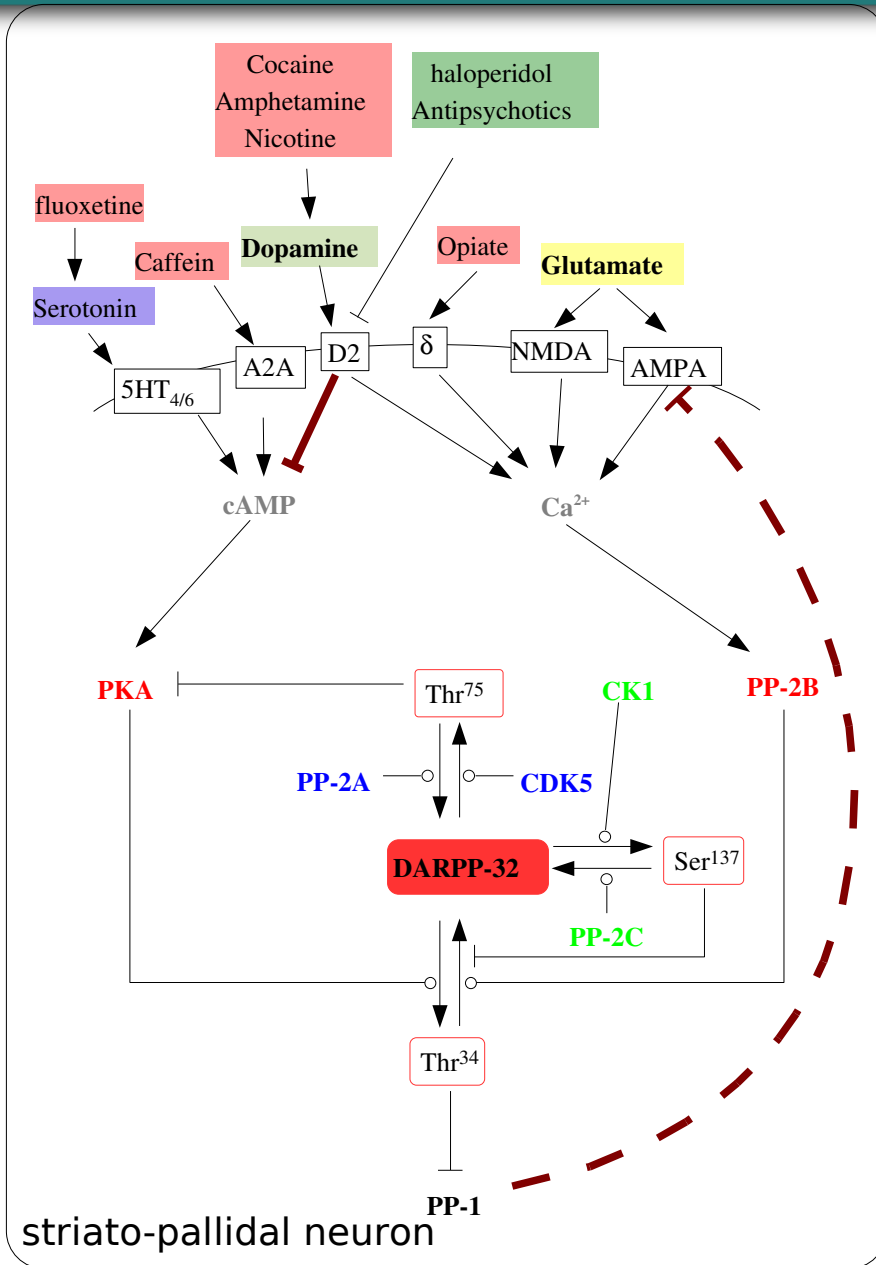


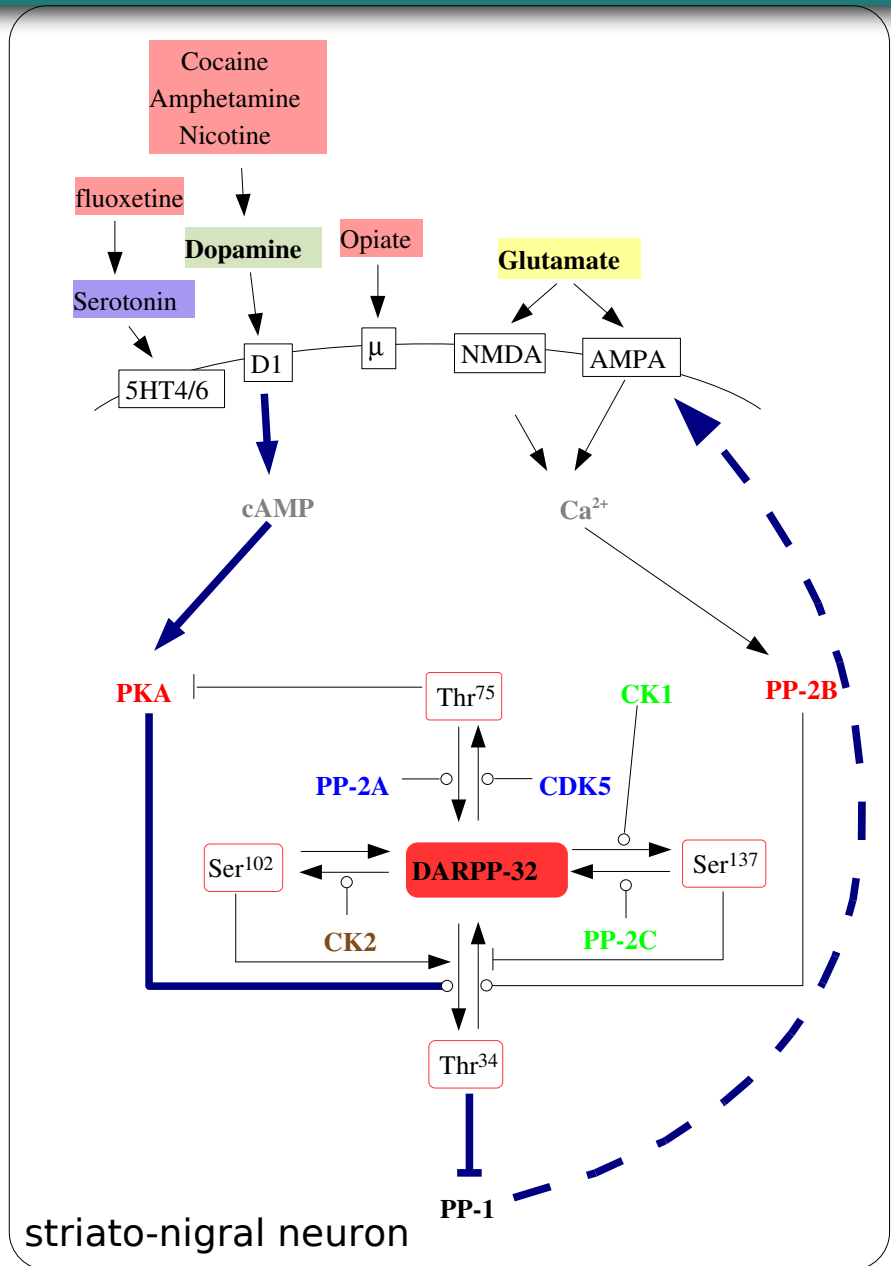
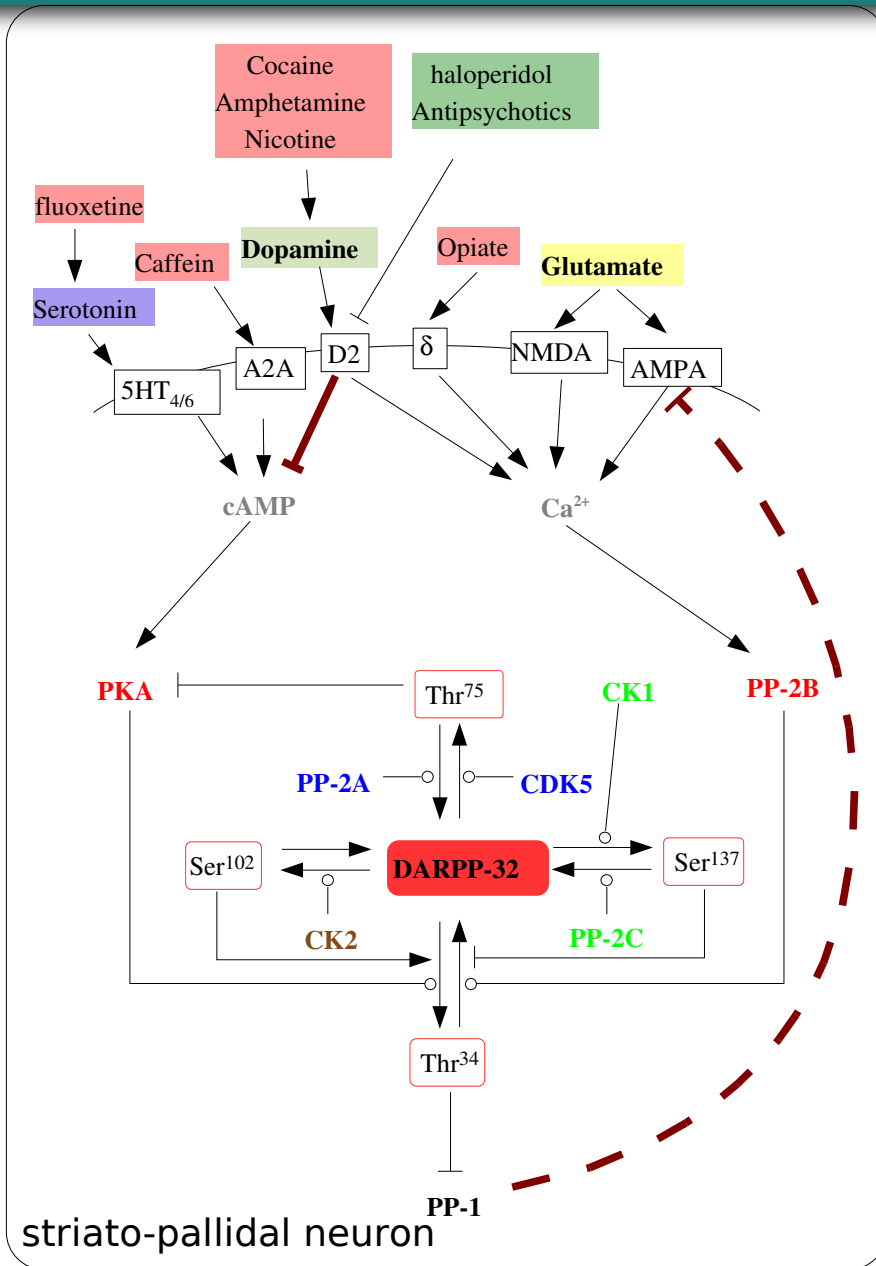
Fernandez E, Schiappa R, Girault JA, Le Novère N (2006)
DARPP-32 is a robust integrator of dopamine and glutamate signals.
PLoS Computational Biology, 2(12): e176.

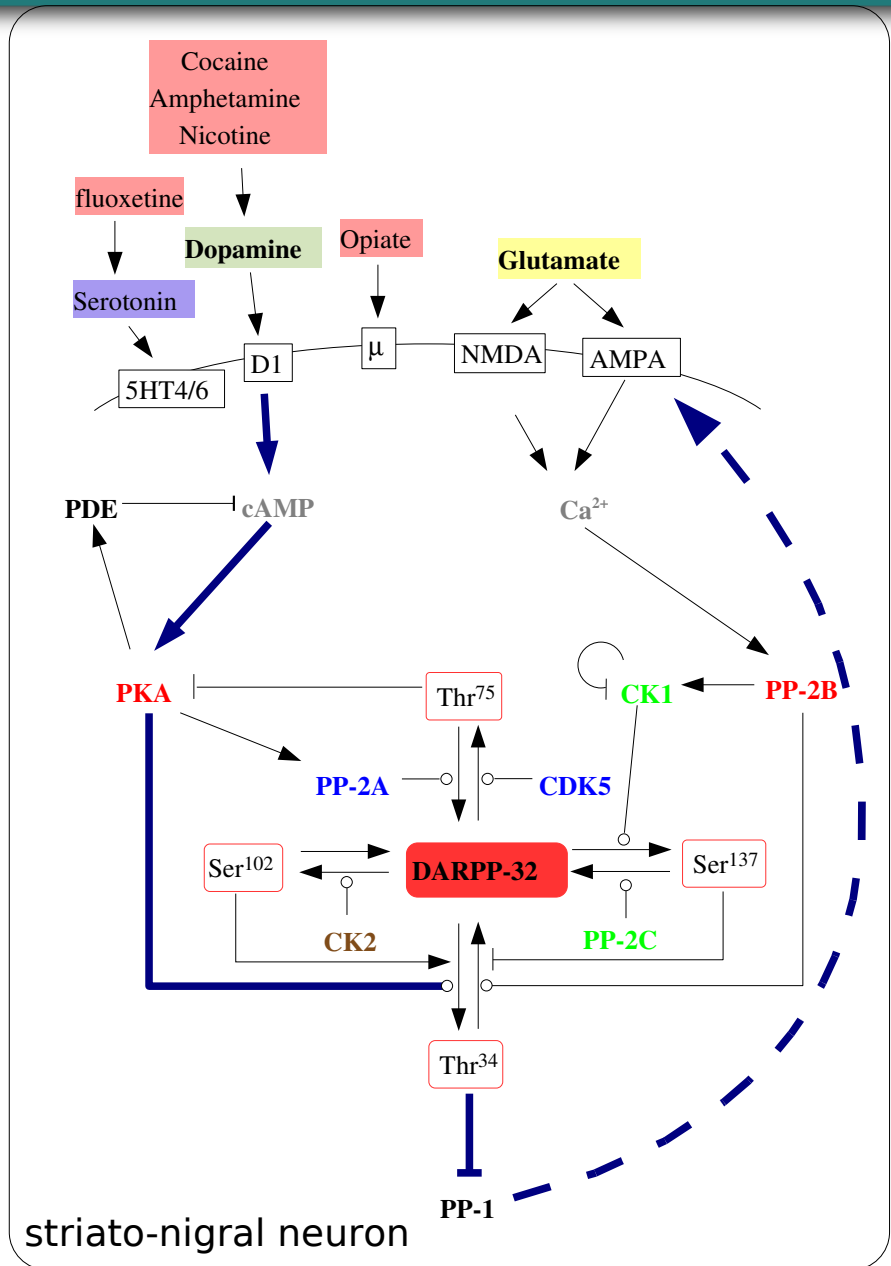
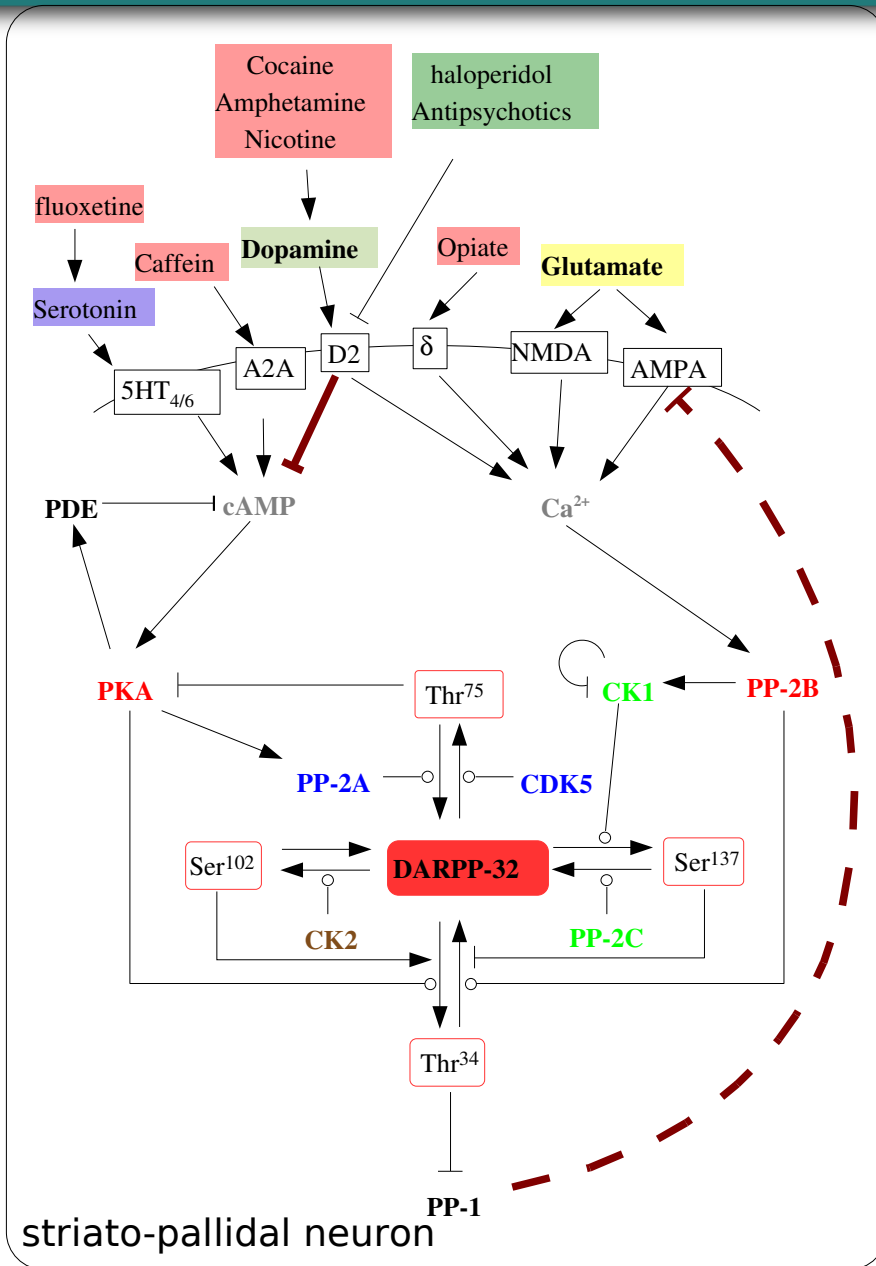


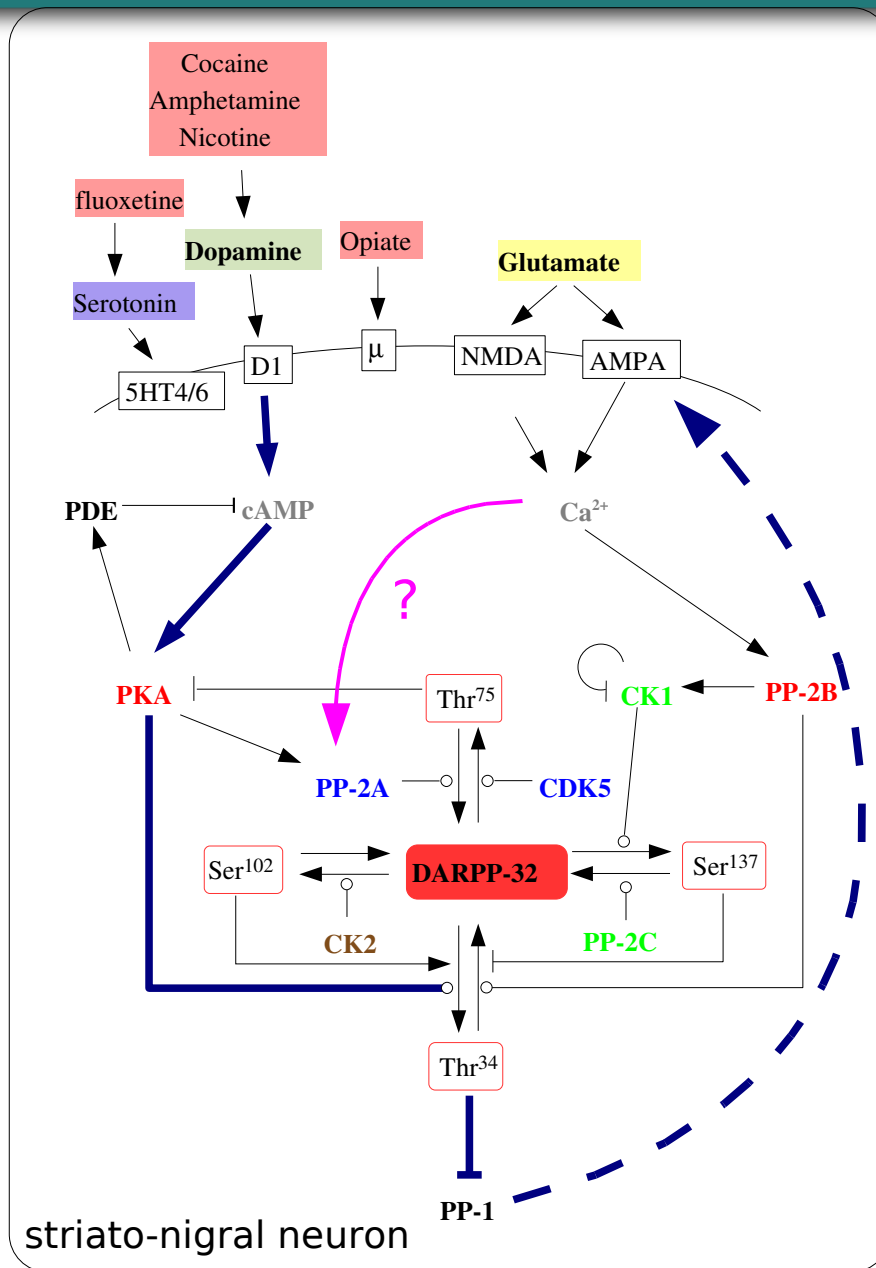
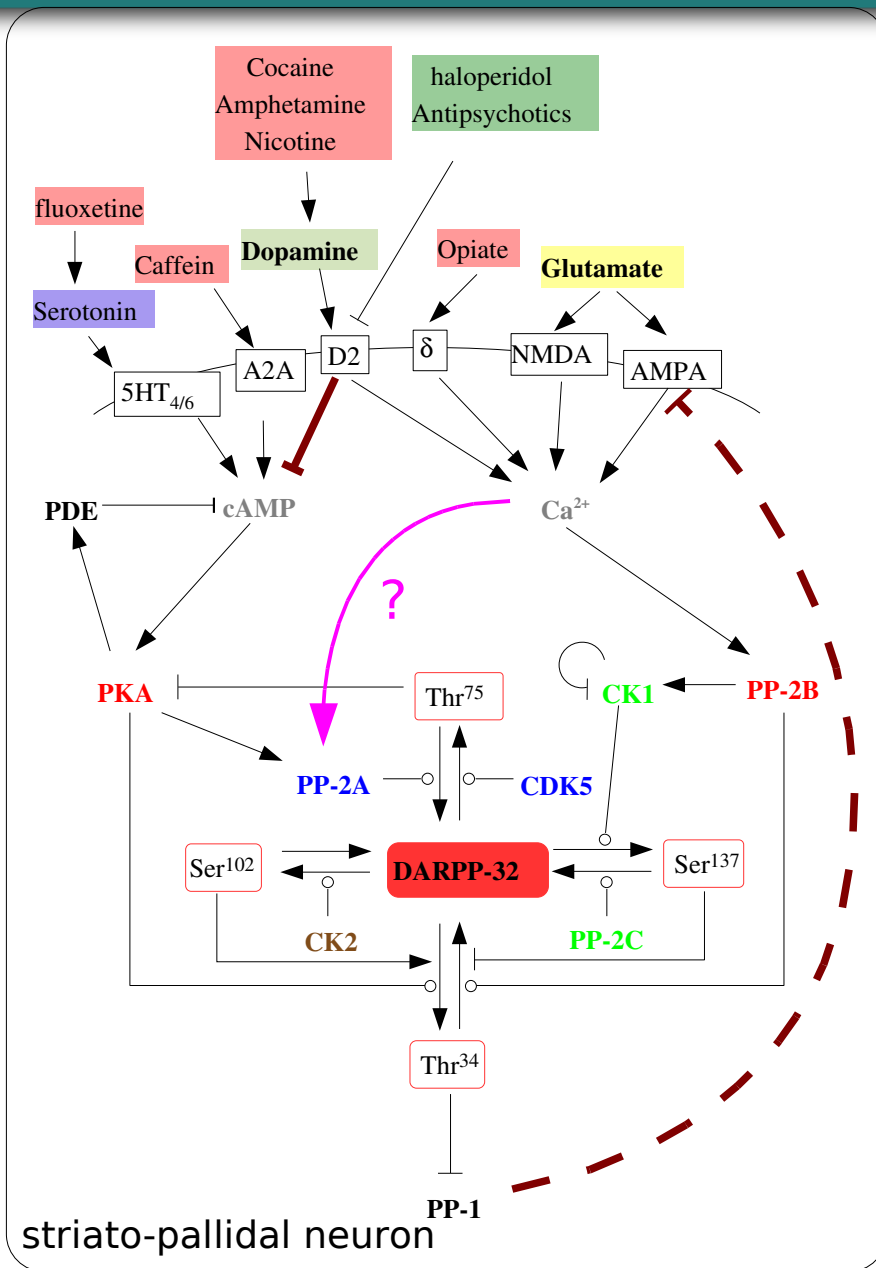


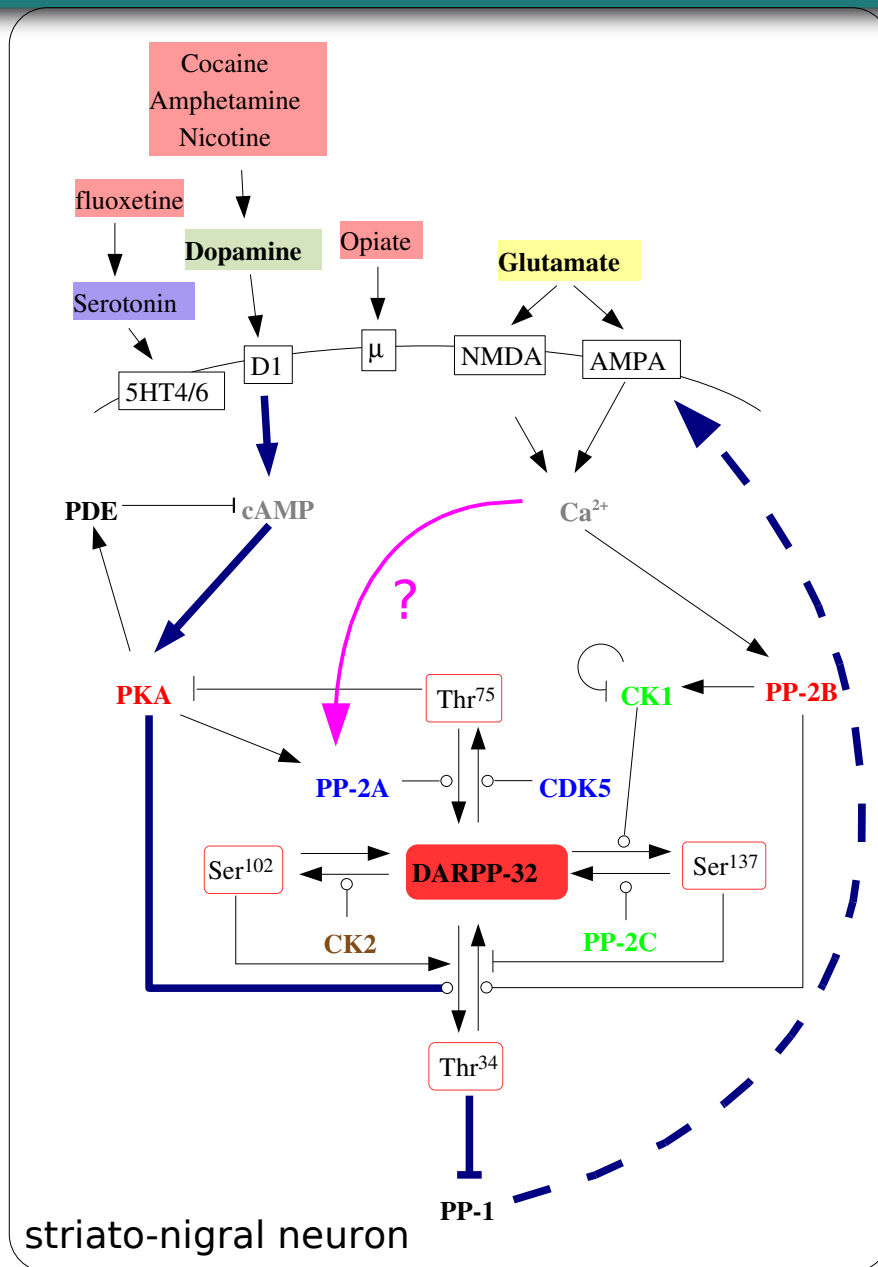
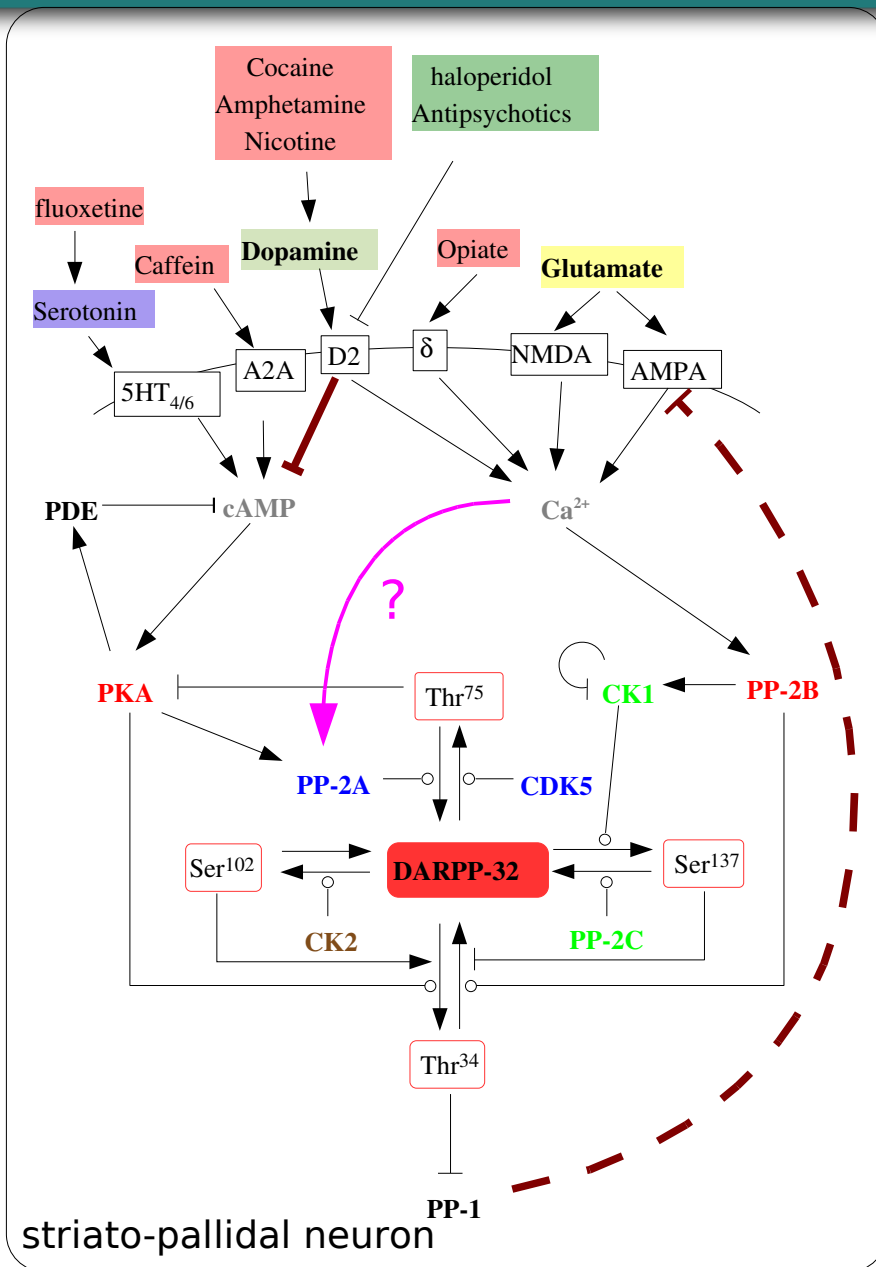






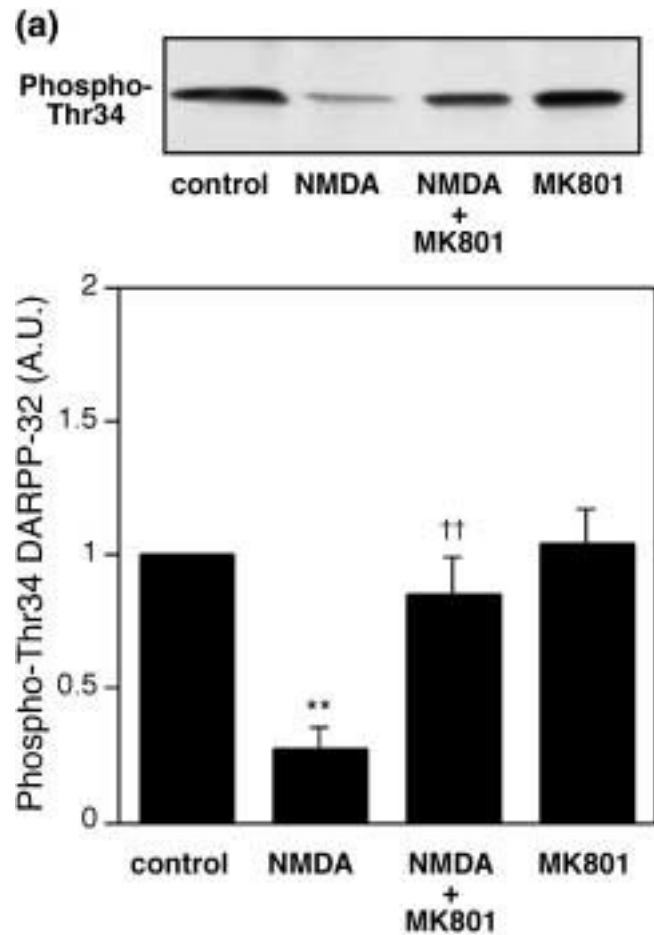






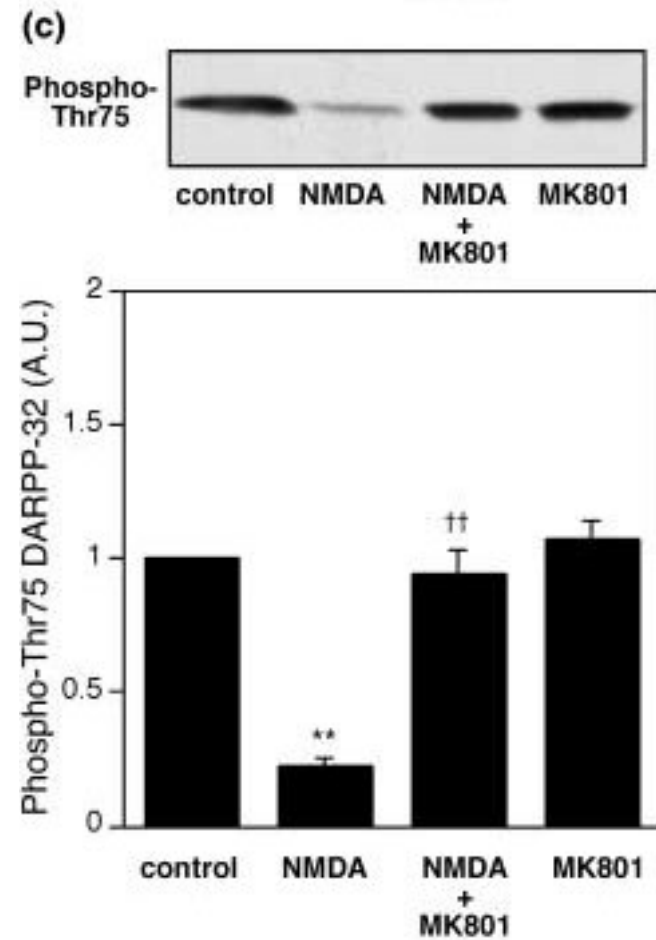
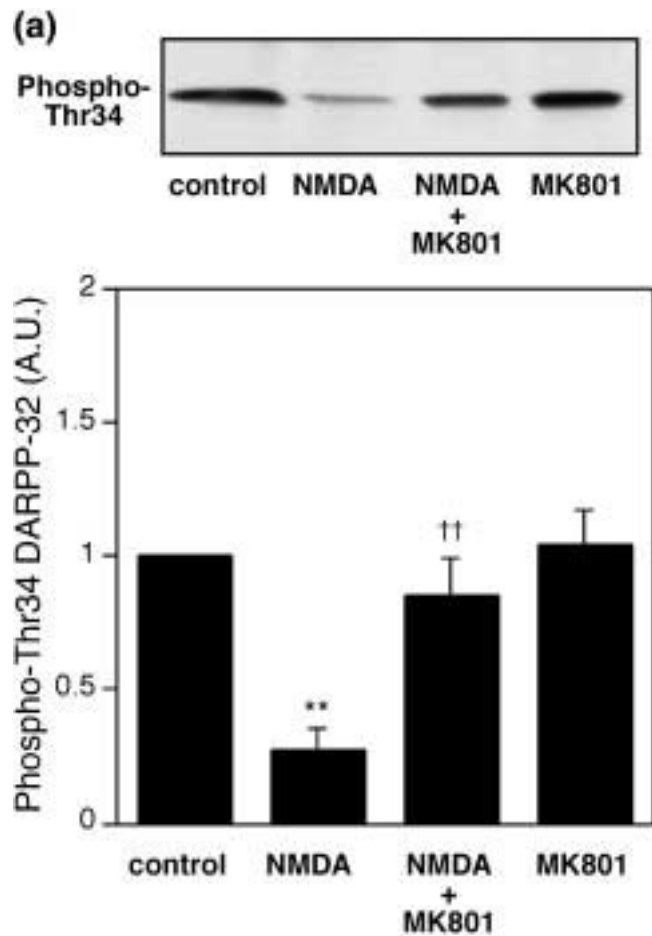
DARPP-32 is a “hub” for phosphatases and kinase in the post-synaptic compartment





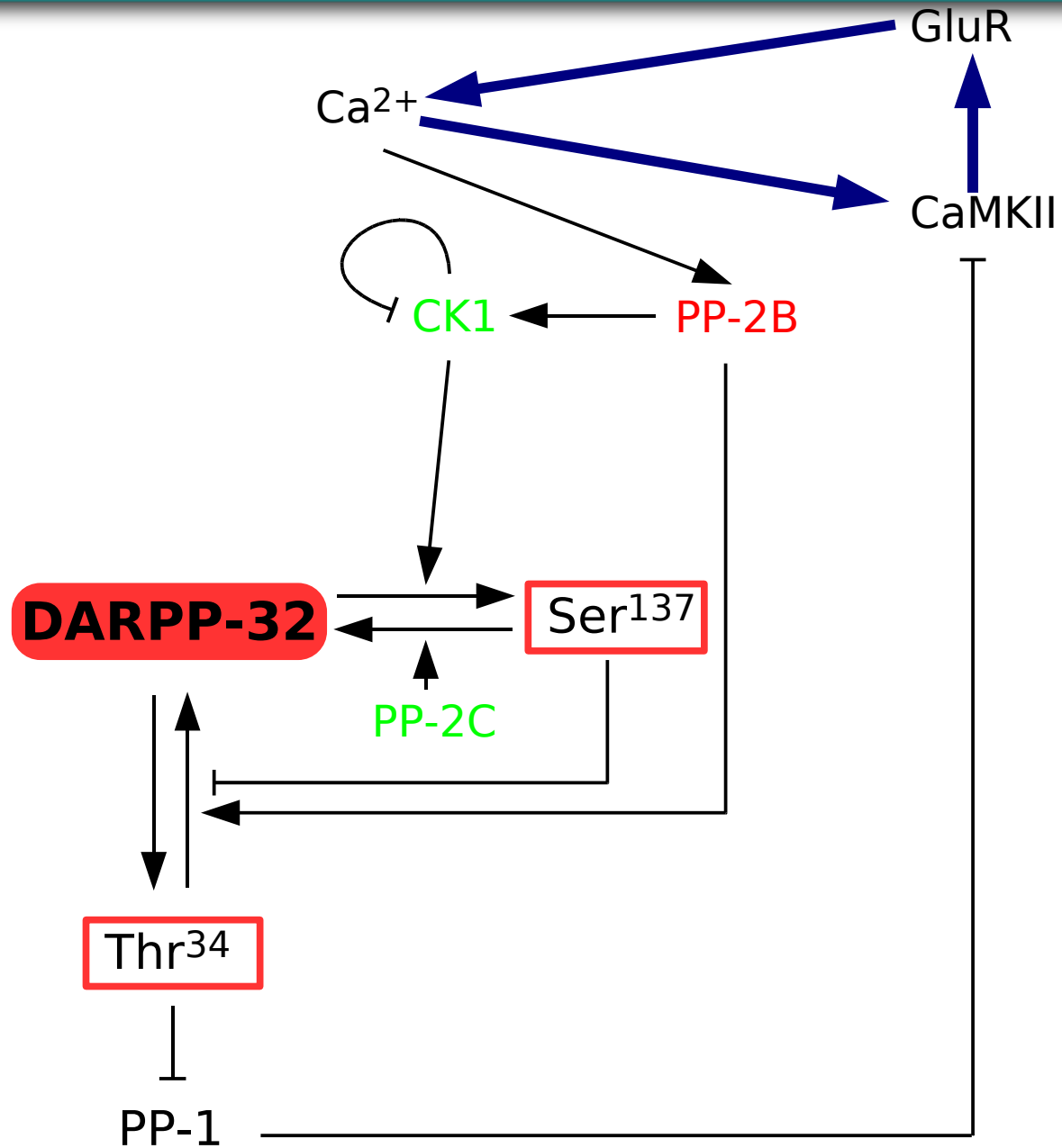
Nishi *et al.* (2002). *J Neurochem*, 82: 832-841

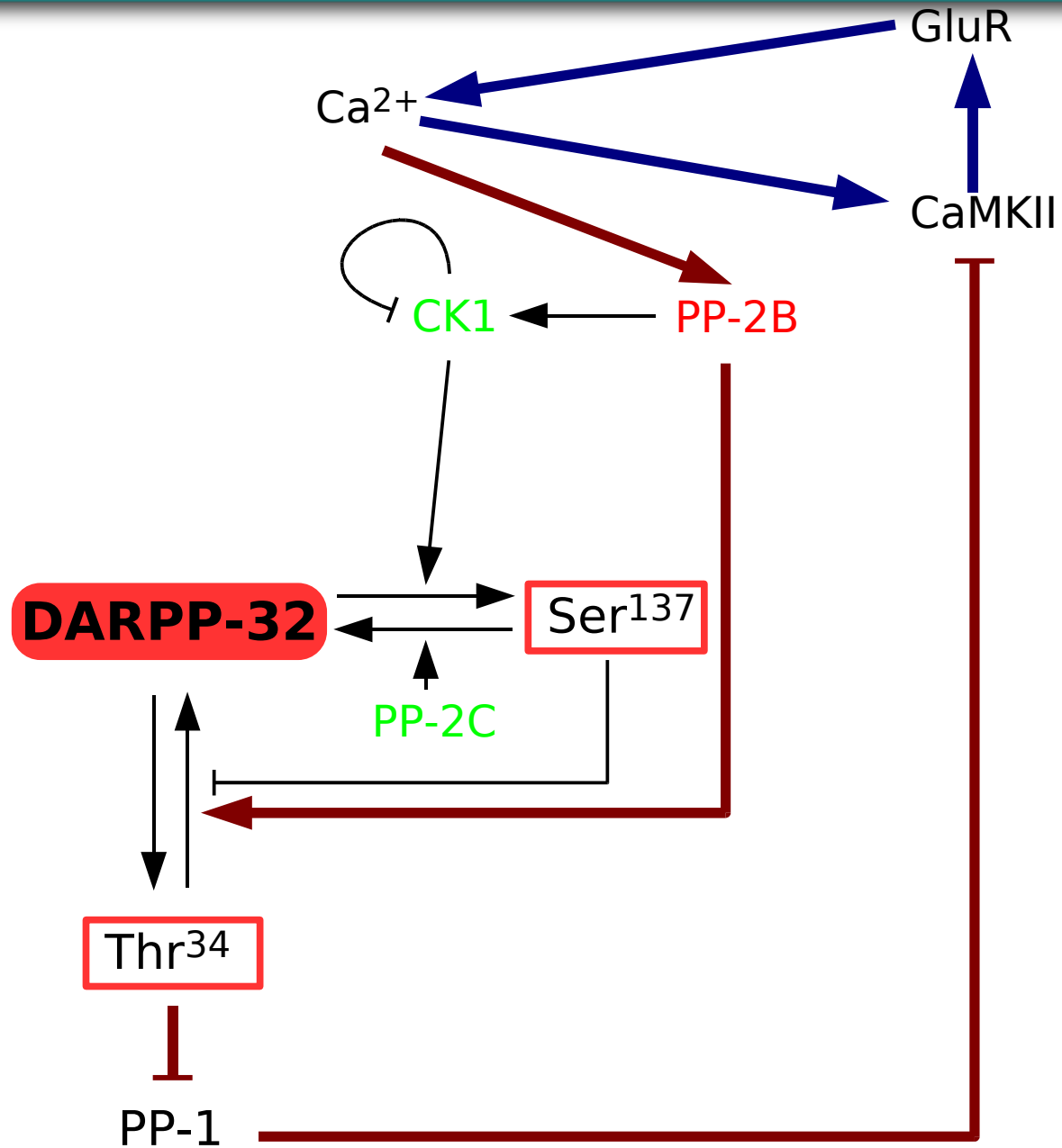


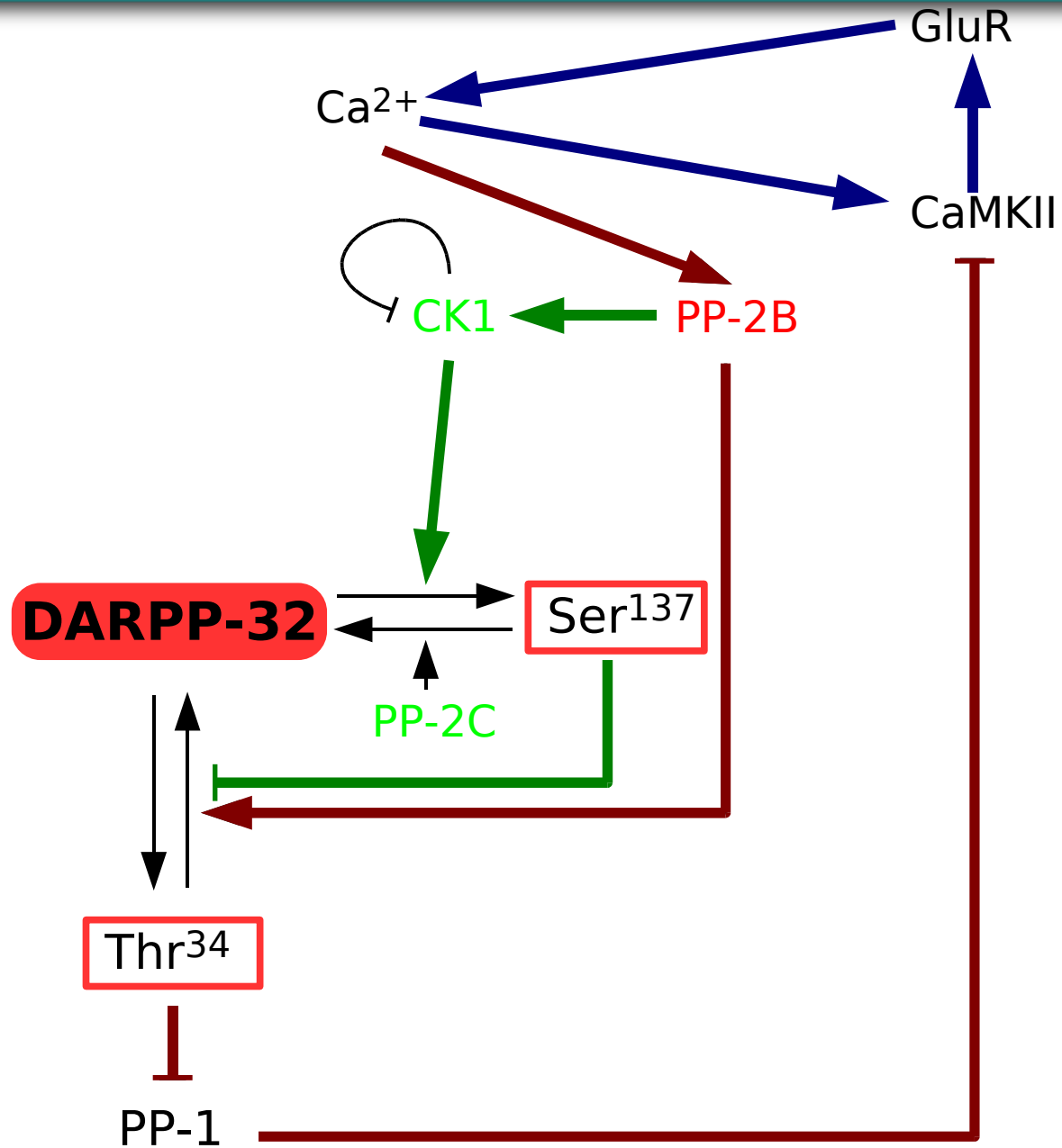


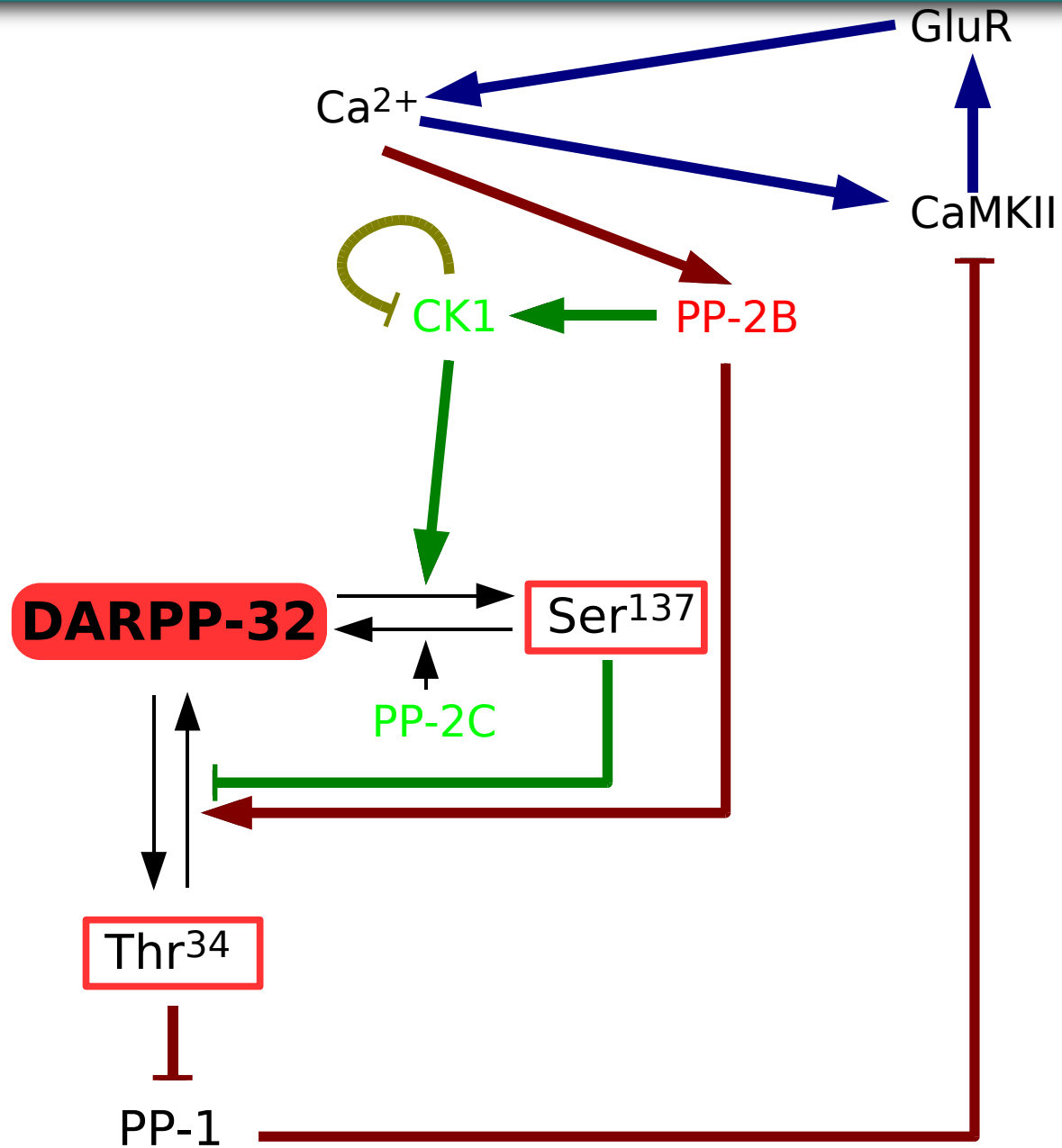
Nishi *et al.* (2002). *J Neurochem*, 82: 832-841

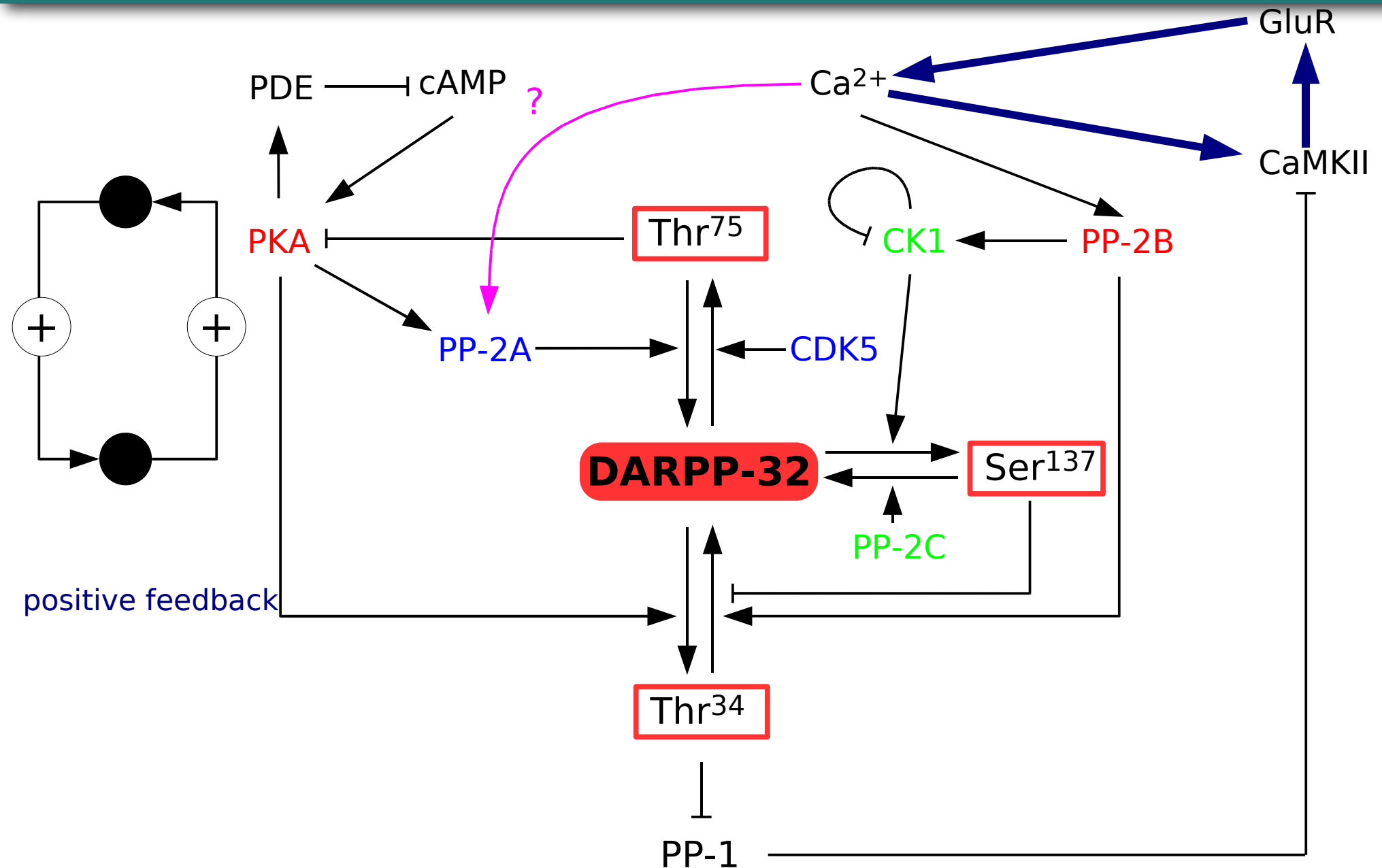


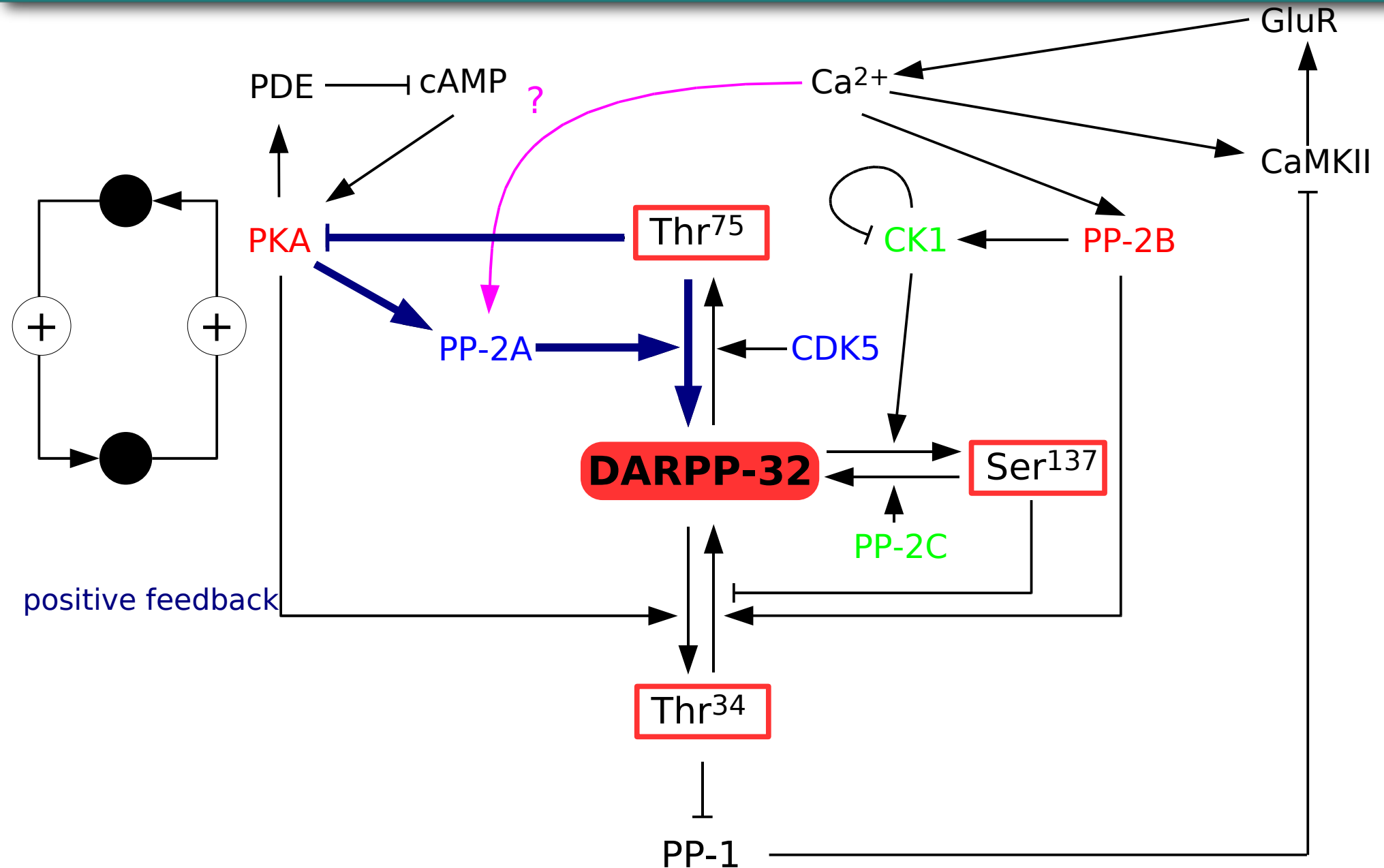


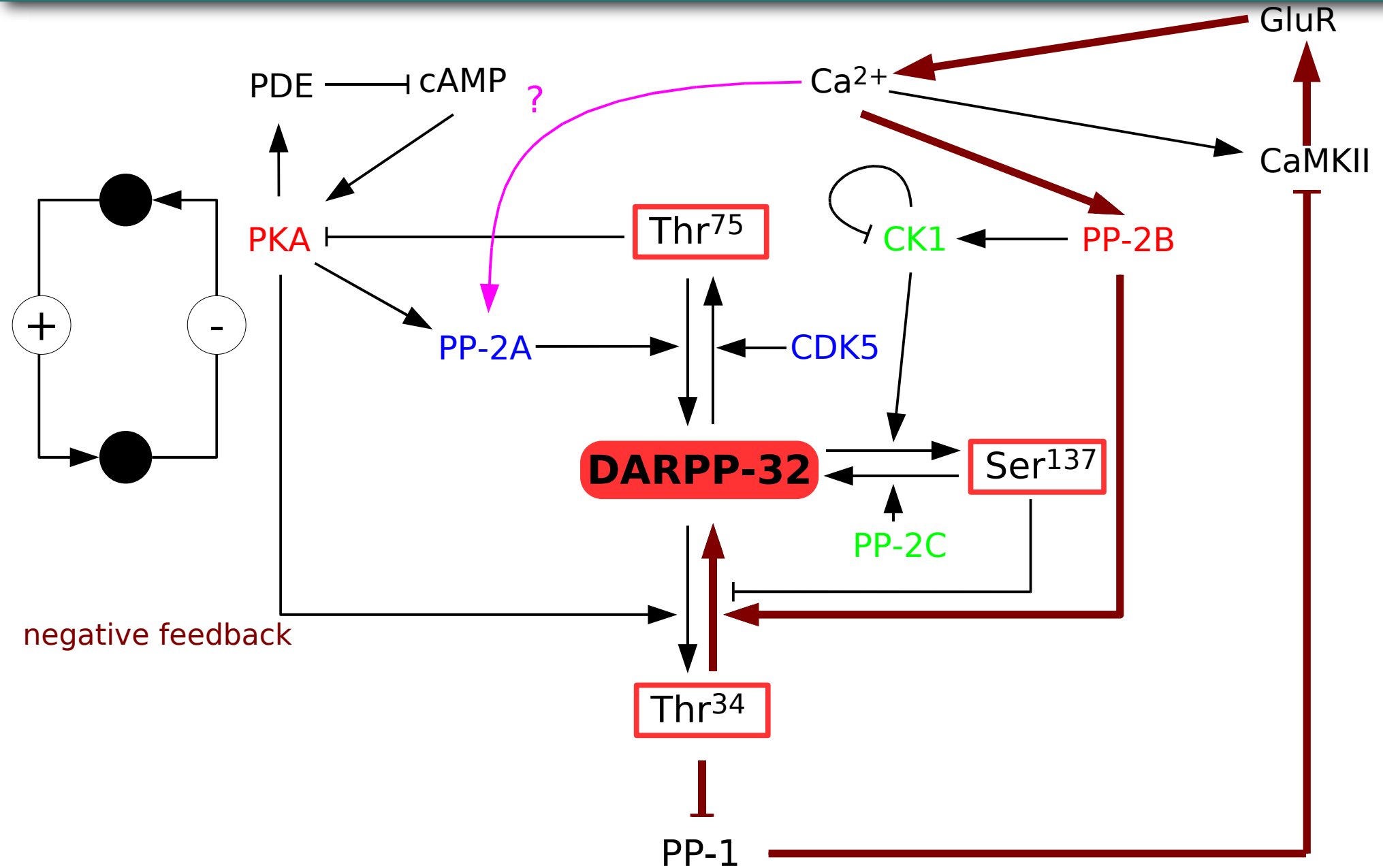


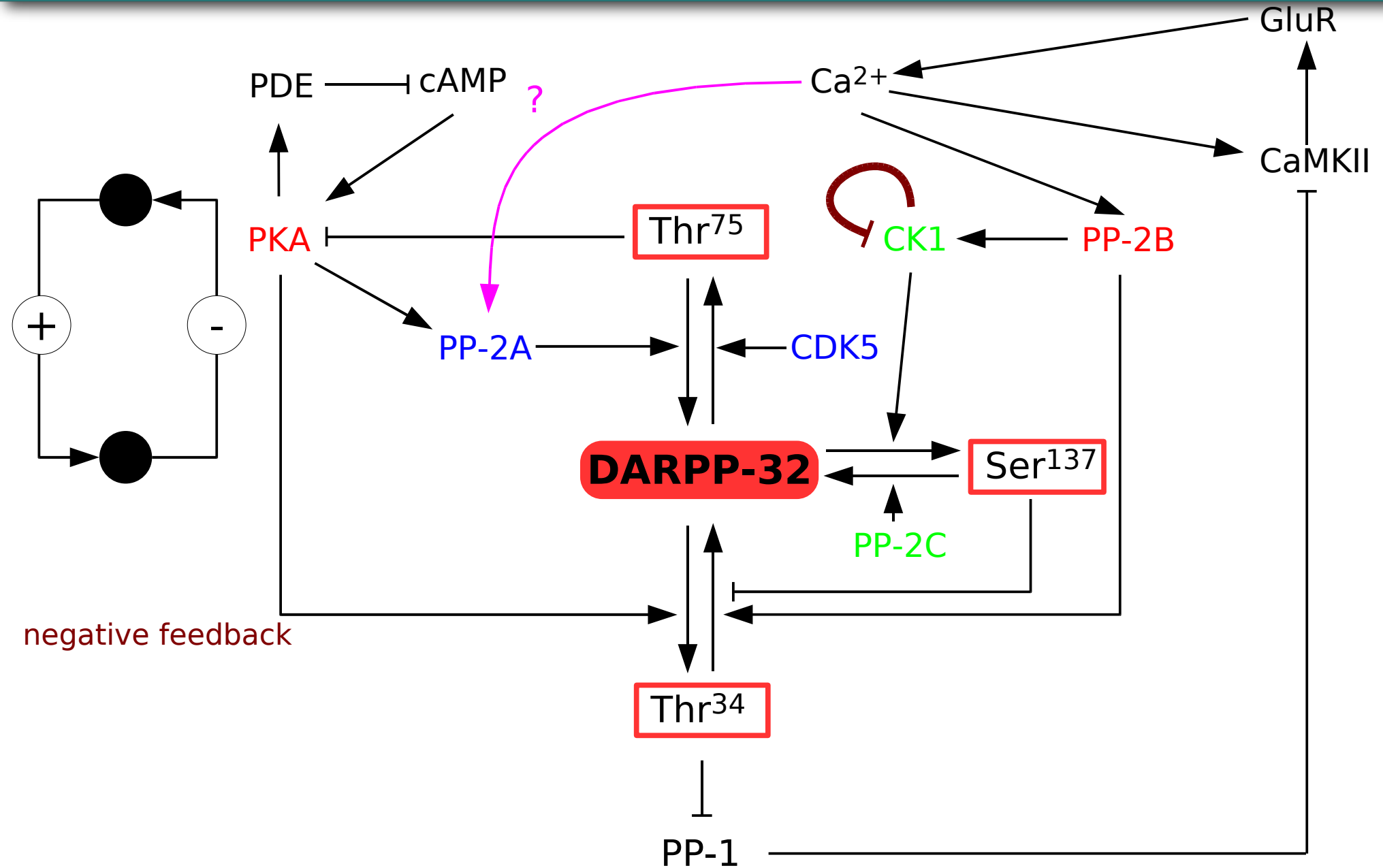


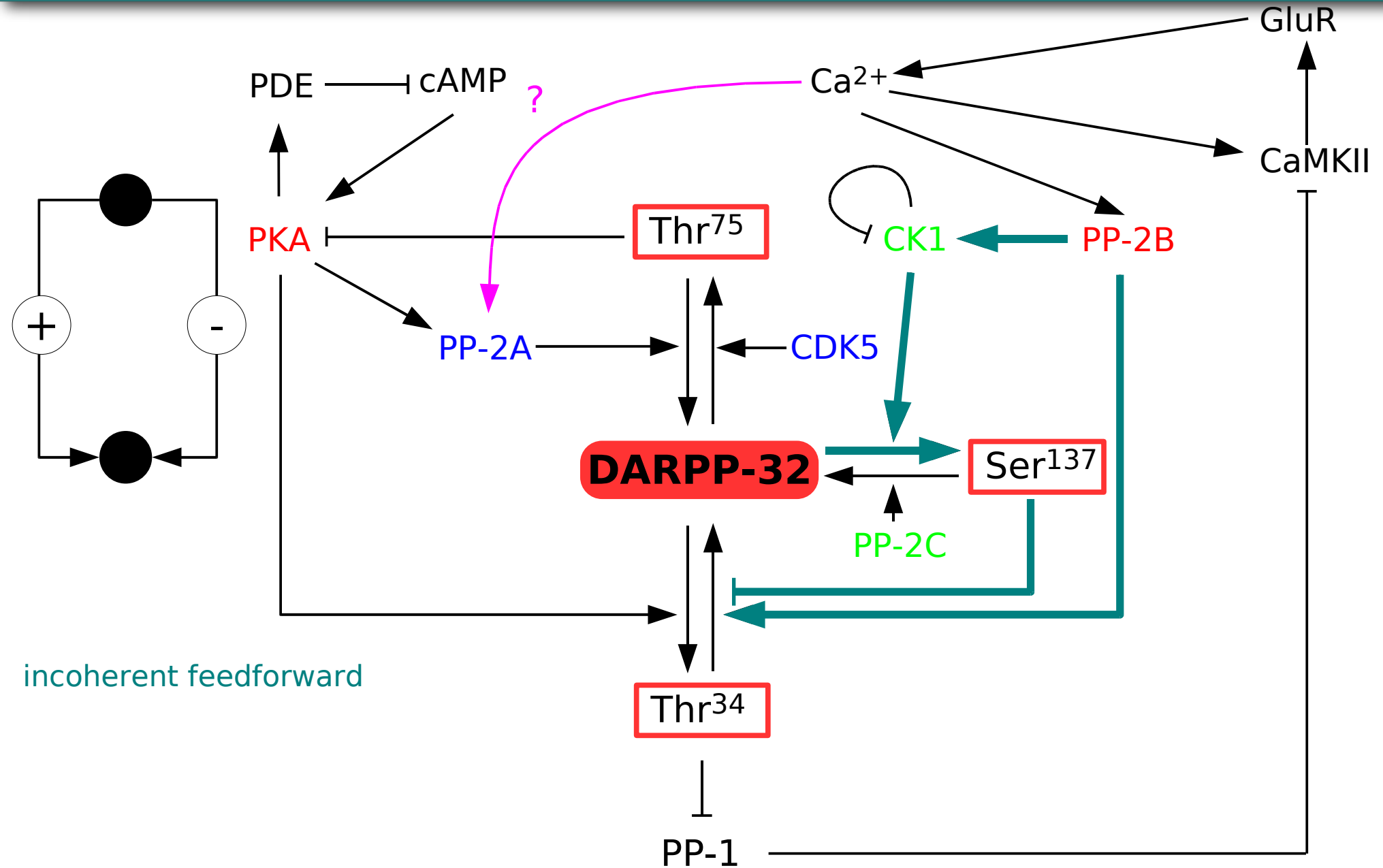


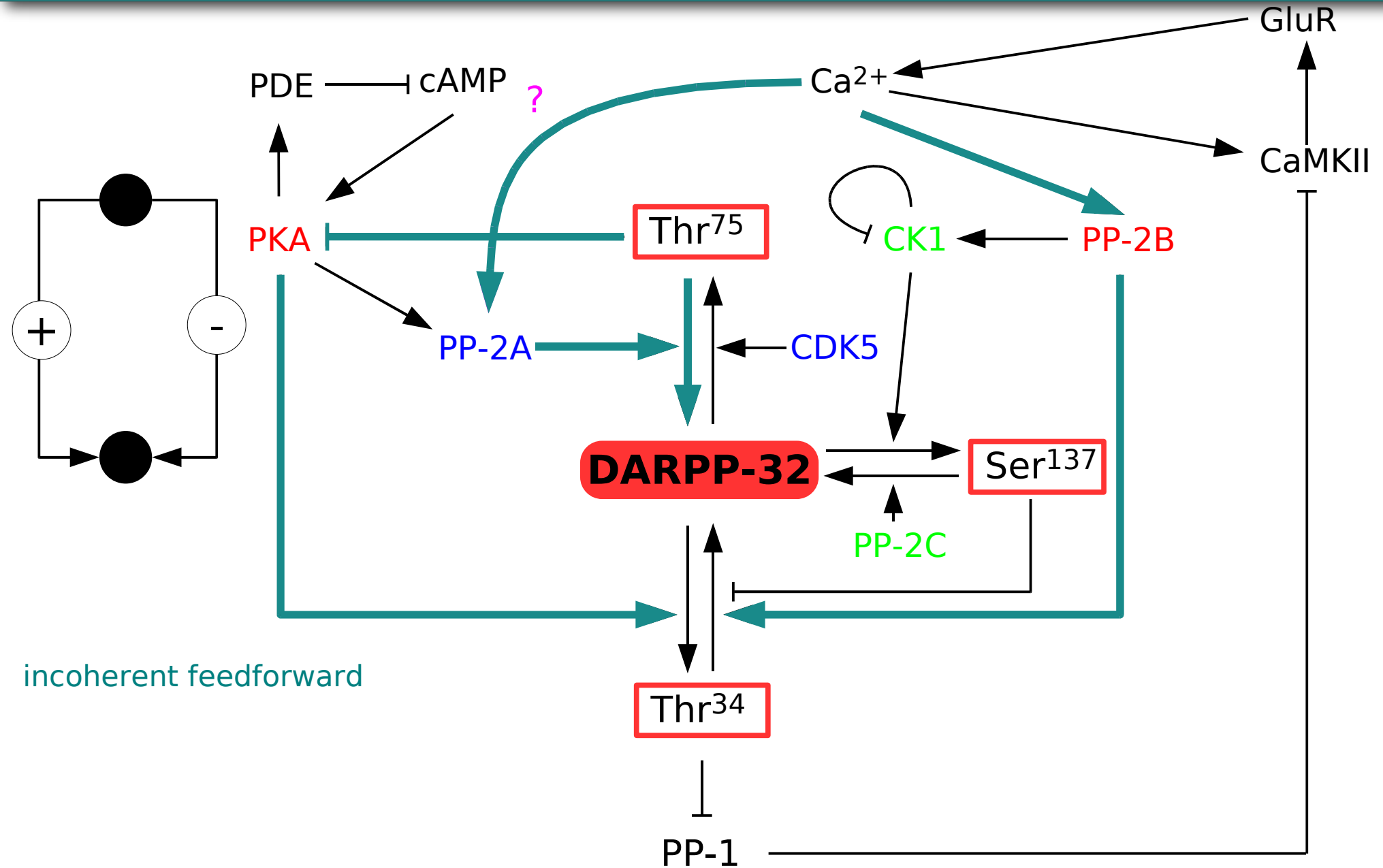


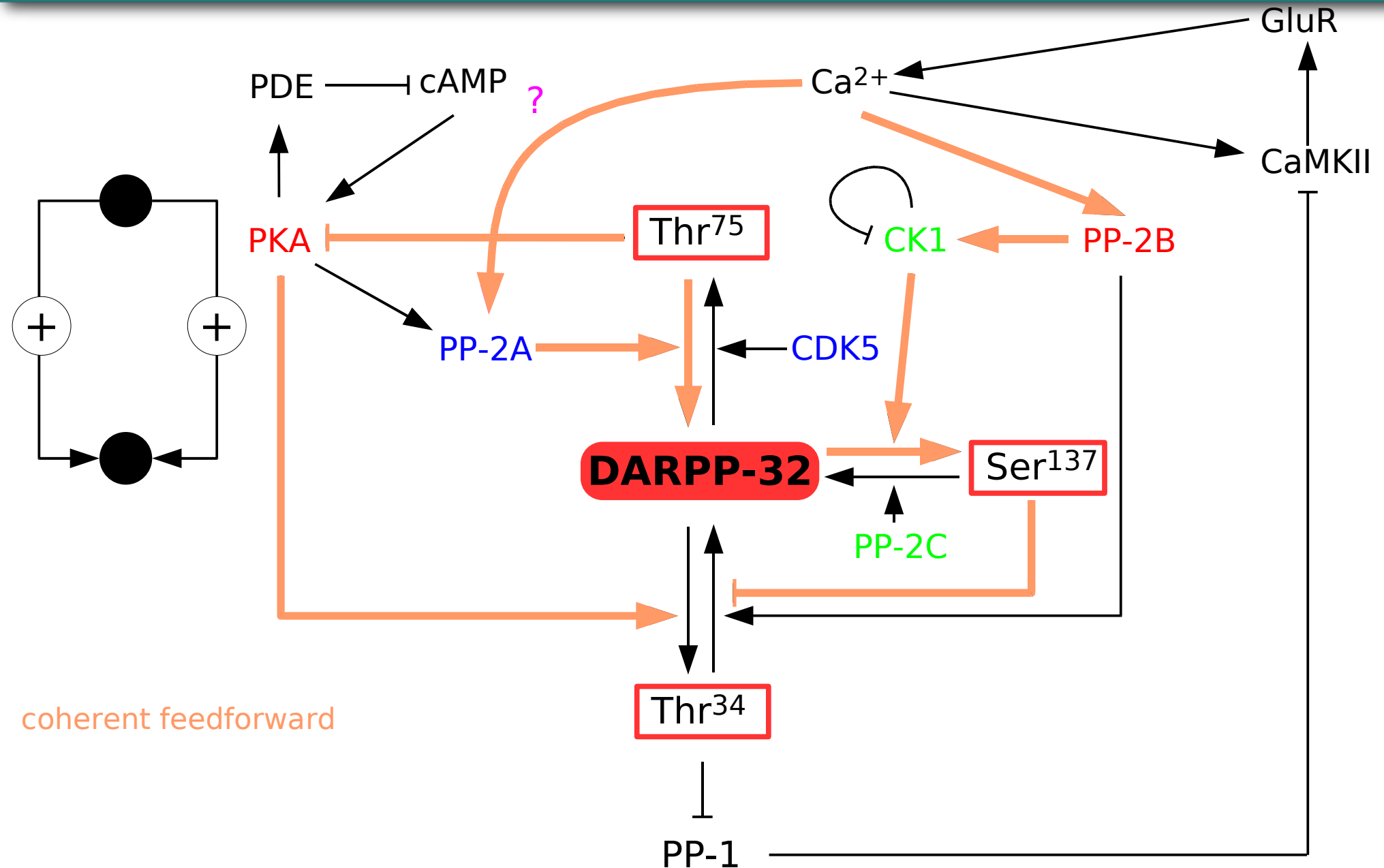


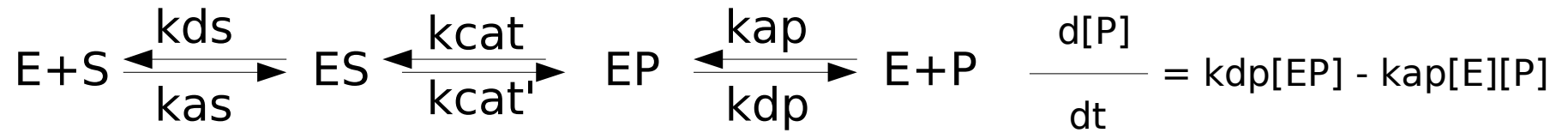


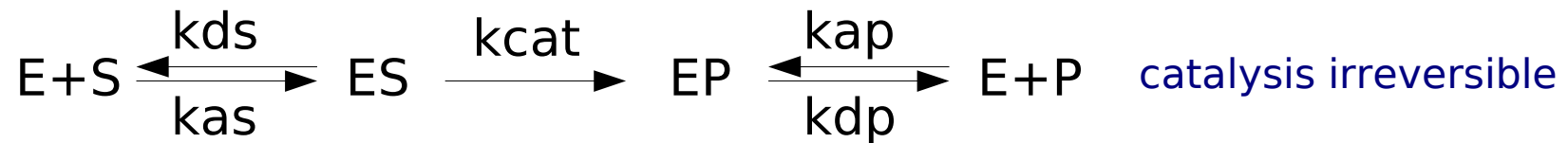
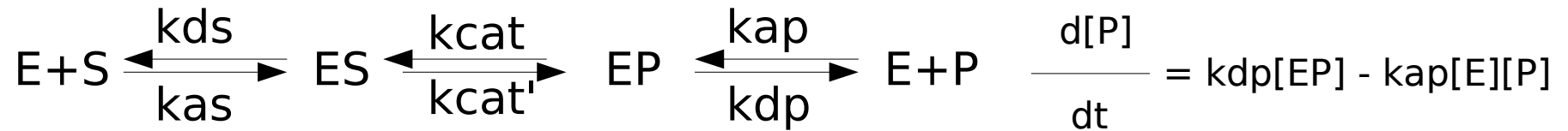


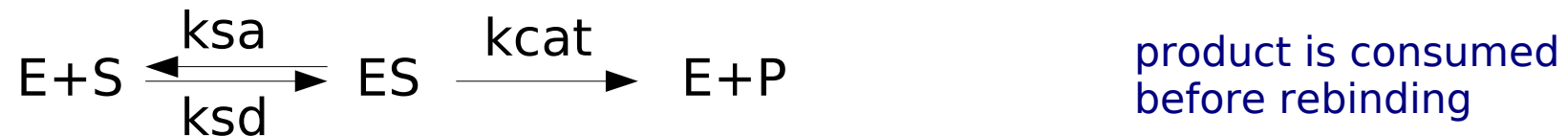
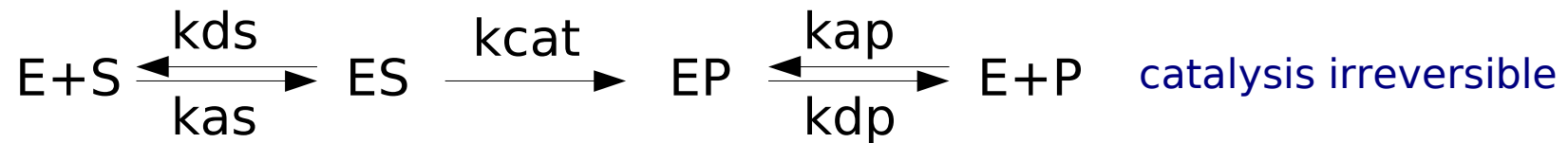
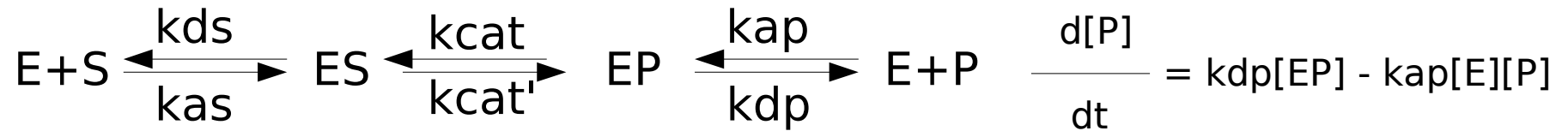


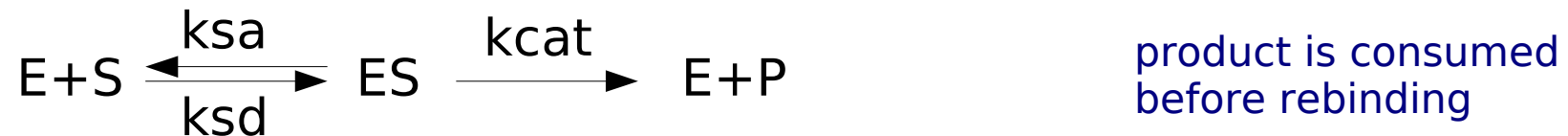
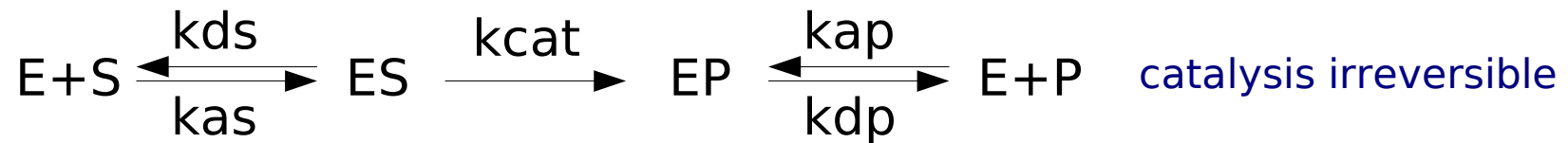
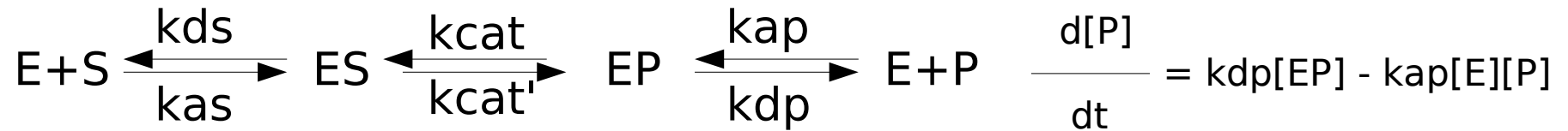






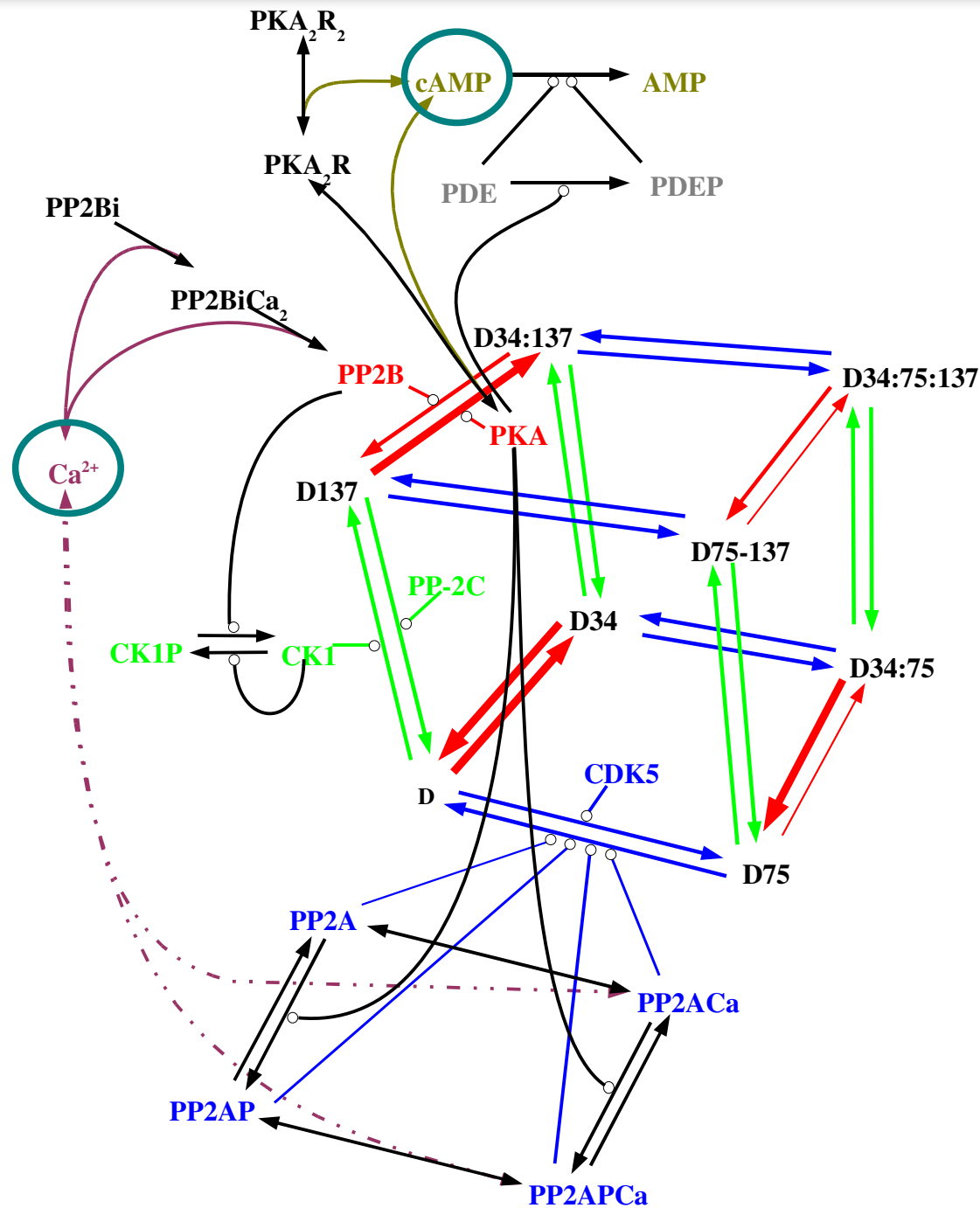






$$\frac{d[P]}{dt} = \frac{[E] k_{cat}}{1 + \frac{K_m}{[S]}}$$









$$d[\text{D}]/dt = -k_1[\text{CDK5}][\text{D}] + k_2[\text{D_CDK5}]$$

$$d[\text{D-75P}]/dt = +k_3[\text{D_CDK5}]$$

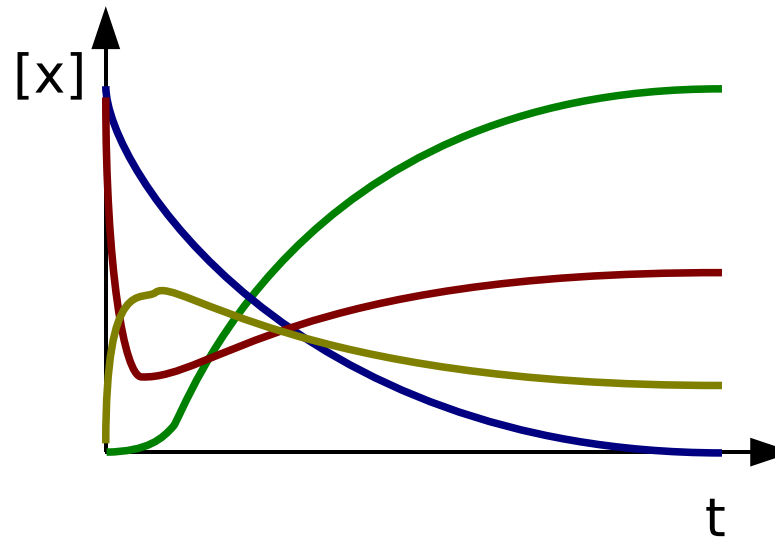
$$d[\text{CDK5}]/dt = -k_1[\text{CDK5}][\text{D}] + k_2[\text{D_CDK5}] + k_3[\text{D_CDK5}]$$

$$d[\text{D_CDK5}]/dt = +k_1[\text{CDK5}][\text{D}] - k_2[\text{D_CDK5}] - k_3[\text{D_CDK5}]$$





$$\begin{aligned} d[D]/dt &= -k_1[CDK5][D] + k_2[D_CDK5] \\ d[D-75P]/dt &= +k_3[D_CDK5] \\ d[CDK5]/dt &= -k_1[CDK5][D] + k_2[D_CDK5] + k_3[D_CDK5] \\ d[D_CDK5]/dt &= +k_1[CDK5][D] - k_2[D_CDK5] - k_3[D_CDK5] \end{aligned}$$

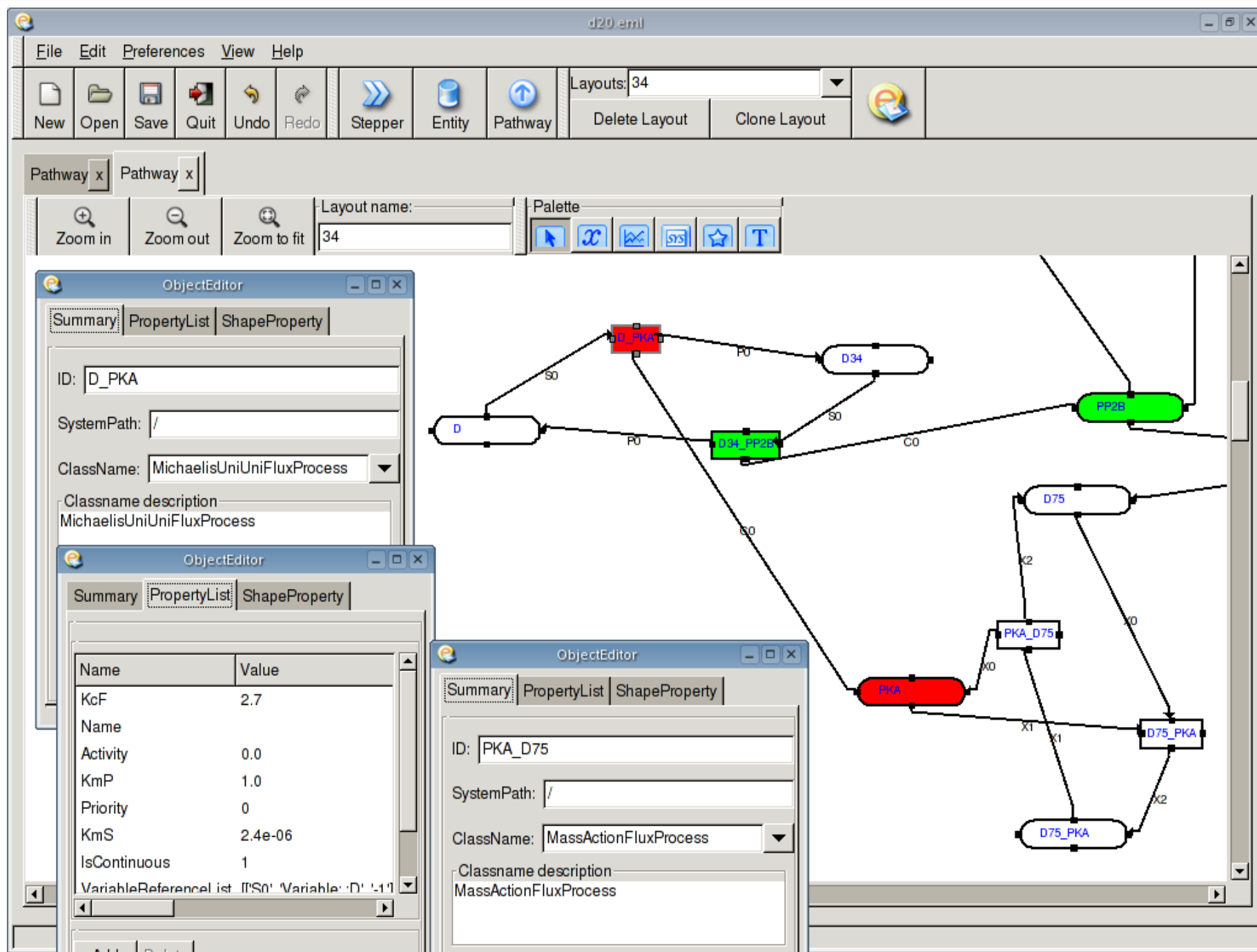


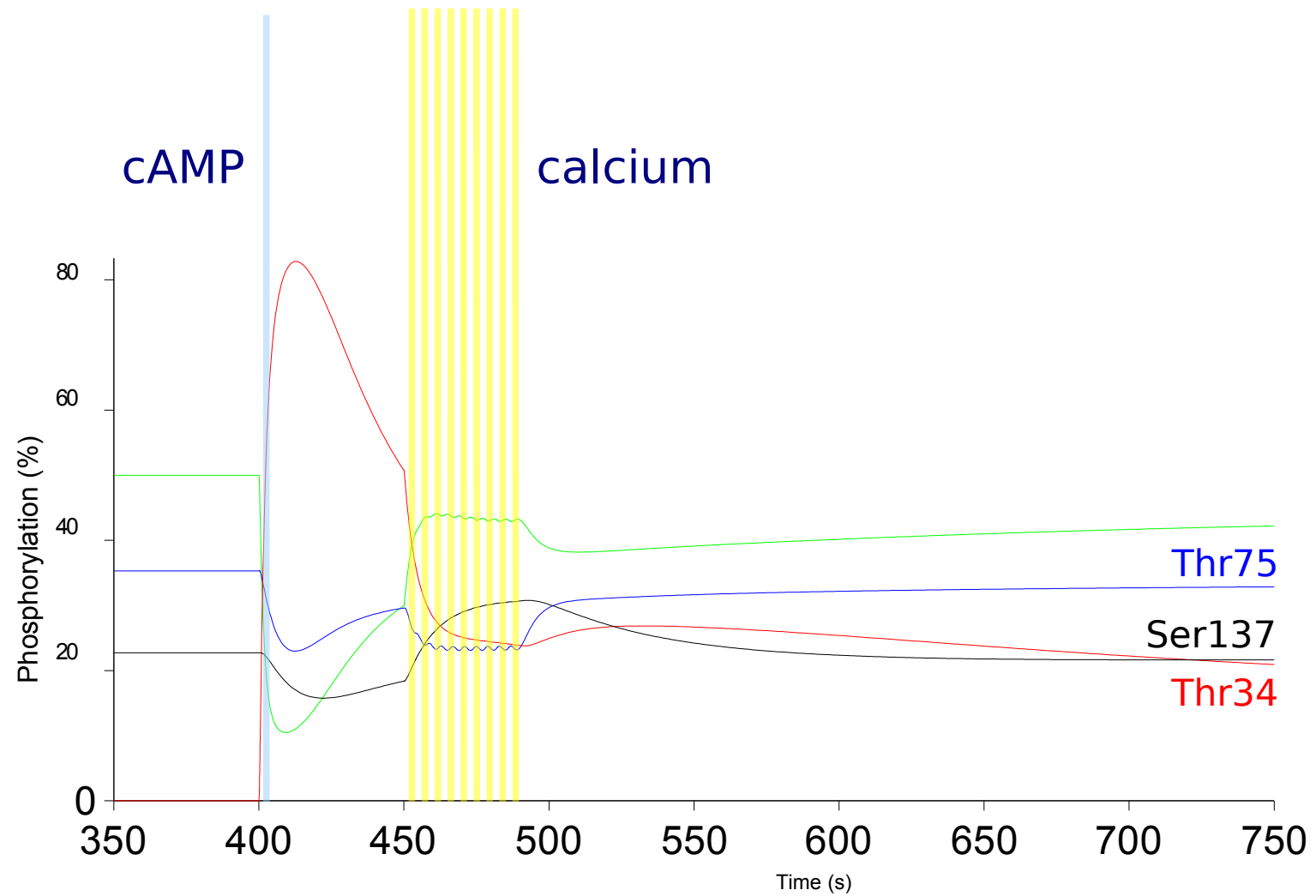
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- $D75 + PP2A \rightleftharpoons D75_PP2A \rightarrow D + PP2A$
- $D75 + PP2ACa \rightleftharpoons D75_PP2ACa \rightarrow D + PP2ACa$
- $D75 + PP2AP \rightleftharpoons D75_PP2AP \rightarrow D + PP2AP$
- $D75 + PP2APCa \rightleftharpoons D75_PP2APCa \rightarrow D + PP2APCa$
- $D137 + CDK5 \rightleftharpoons D137_CDK5 \rightarrow D75-137 + CDK5$
- $D75-137 + PP2A \rightleftharpoons D75-137_PP2A \rightarrow D137 + PP2A$
- $D75-137 + PP2ACa \rightleftharpoons D75-137_PP2ACa \rightarrow D137 + PP2ACa$
- $D75-137 + PP2AP \rightleftharpoons D75-137_PP2AP \rightarrow D137 + PP2AP$
- $D75-137 + PP2APCa \rightleftharpoons D75-137_PP2APCa \rightarrow D137 + PP2APCa$
- $D34 + CDK5 \rightleftharpoons D34_CDK5 \rightarrow D34-75 + CDK5$
- $D34-75 + PP2A \rightleftharpoons D34-75_PP2A \rightarrow D34 + PP2A$
- $D34-75 + PP2ACa \rightleftharpoons D34-75_PP2ACa \rightarrow D34 + PP2ACa$
- $D34-75 + PP2AP \rightleftharpoons D34-75_PP2AP \rightarrow D34 + PP2AP$
- $D34-75 + PP2APCa \rightleftharpoons D34-75_PP2APCa \rightarrow D34 + PP2APCa$
- $D34-137 + CDK5 \rightleftharpoons D34-137_CDK5 \rightarrow D34-75-137 + CDK5$
- $D34-75-137 + PP2A \rightleftharpoons D34-75-137_PP2A \rightarrow D34-137 + PP2A$
- $D34-75-137 + PP2ACa \rightleftharpoons D34-75-137_PP2ACa \rightarrow D34-137 + PP2ACa$
- $D34-75-137 + PP2AP \rightleftharpoons D34-75-137_PP2AP \rightarrow D34-137 + PP2AP$
- $D34-75-137 + PP2APCa \rightleftharpoons D34-75-137_PP2APCa \rightarrow D34-137 + PP2APCa$
- $D + CK1 \rightleftharpoons D_CK1 \rightarrow D137 + CK1$
- $D137 + PP2C \rightleftharpoons D137_PP2C \rightarrow D + PP2C$
- $D75 + CK1 \rightleftharpoons D75_CK1 \rightarrow D75-137 + CK1$
- $D75-137 + PP2C \rightleftharpoons D75-137_PP2C \rightarrow D75 + PP2C$
- $D34 + CK1 \rightleftharpoons D34_CK1 \rightarrow D34-137 + CK1$
- $D34-75 + PP2C \rightleftharpoons D34-75_PP2C \rightarrow D75 + PP2C$
- $D34-75 + CK1 \rightleftharpoons D34-75_CK1 \rightarrow D34-75-137 + CK1$
- $D34-75-137 + PP2C \rightleftharpoons D34-75-137_PP2C \rightarrow D34-75 + PP2C$
- $CK1 + CK1 \rightleftharpoons CK1_CK1 \rightarrow CK1P + CK1$
- $CK1P + PP2B \rightleftharpoons CK1P_PP2B \rightarrow CK1 + PP2B$

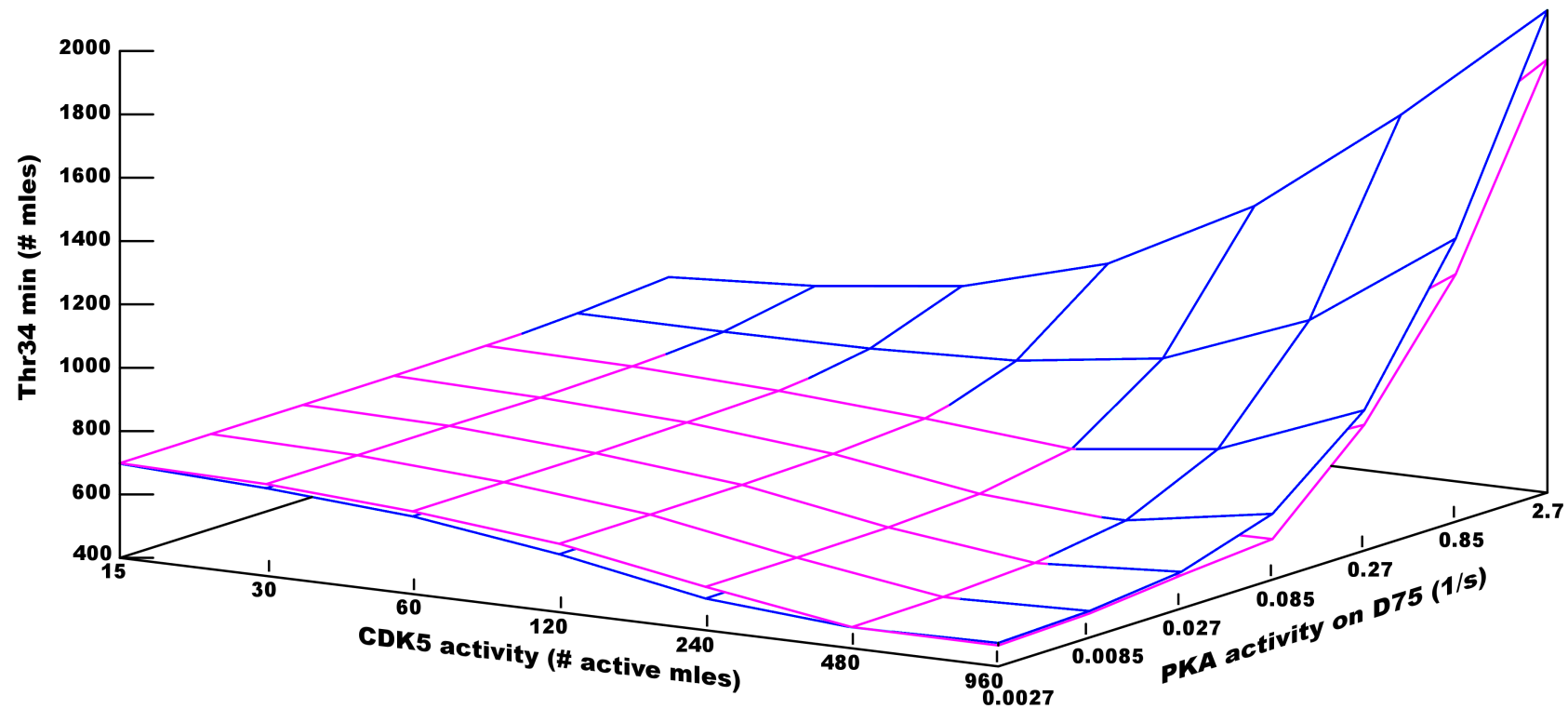
79 species, 151 reactions

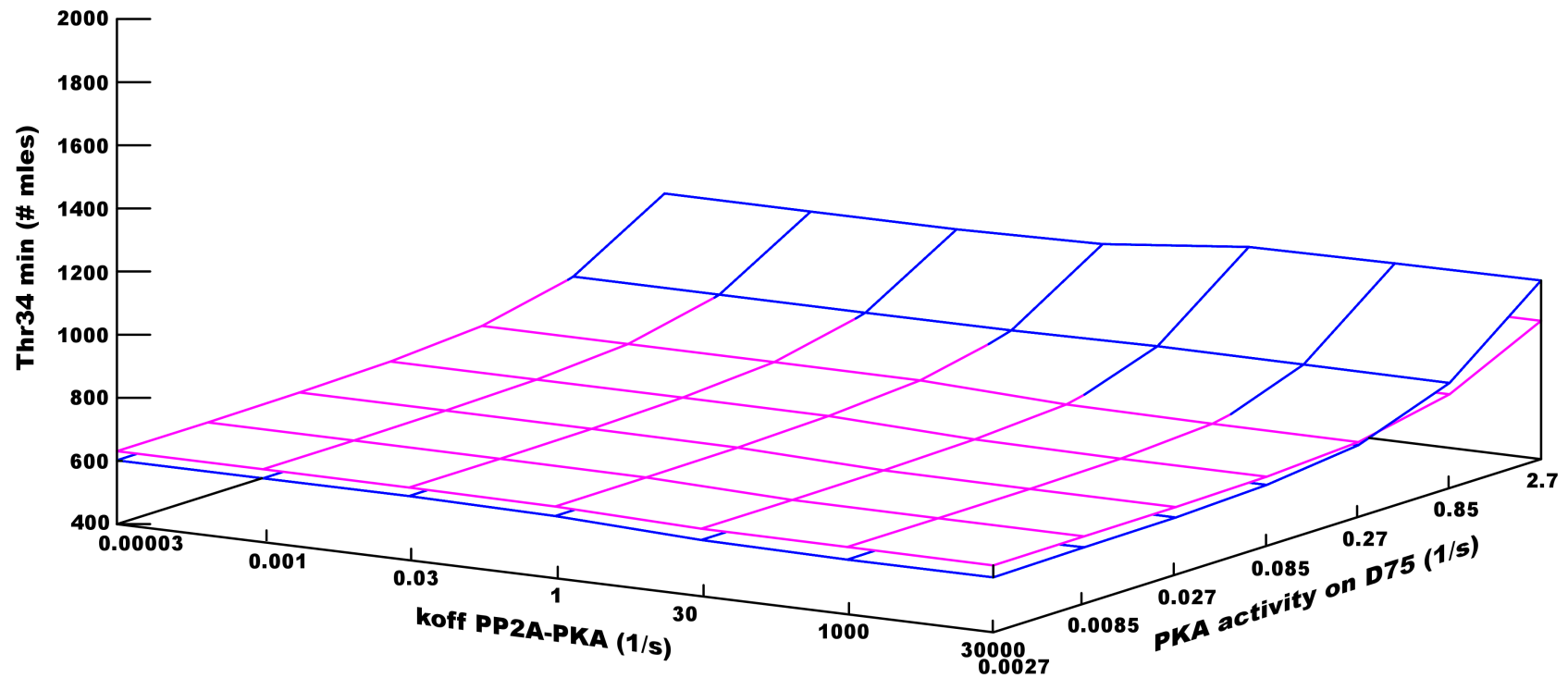
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- $D34 + PP2B \rightleftharpoons D34_PP2B \rightarrow D + PP2B$
- $D75 + PKA \rightleftharpoons D75_PKA \rightarrow D34-75 + PKA$
- $D34-75 + PP2B \rightleftharpoons D34-75_PP2B \rightarrow D75 + PP2B$
- $D137 + PKA \rightleftharpoons D137_PKA \rightarrow D34-137 + PKA$
- $D34-137 + PP2B \rightleftharpoons D34-137_PP2B \rightarrow D137 + PP2B$
- $D75-137 + PKA \rightleftharpoons D75-137_PKA \rightarrow D34-75-137 + PKA$
- $D34-75-137 + PP2B \rightleftharpoons D34-75-137_PP2B \rightarrow D75-137 + PP2B$
- $PP2A + PKA \rightleftharpoons PP2A_PKA \rightarrow PP2AP + PKA$
- $PP2ACa + PKA \rightleftharpoons PP2ACa_PKA \rightarrow PP2APCa + PKA$
- $\emptyset \rightarrow Ca^{2+}$
- $Ca^{2+} \rightarrow \emptyset$
- $PP2Bi + 2Ca \rightleftharpoons PP2Bi_Ca2$
- $PP2Bi_Ca + 2Ca \rightleftharpoons PP2B$
- $PP2A + Ca \rightleftharpoons PP2ACa$
- $PP2AP + Ca \rightleftharpoons PP2APCa$
- $R2_PKA2 + cAMP \rightleftharpoons cAMP_R2_PKA2$
- $cAMP_R2_PKA2 + cAMP \rightleftharpoons cAMP2_R2_PKA2$
- $cAMP2_R2_PKA2 + cAMP \rightleftharpoons cAMP3_R2_PKA2$
- $cAMP3_R2_PKA2 + cAMP \rightleftharpoons cAMP4_R2_PKA2$
- $cAMP4_R2_PKA2 \rightleftharpoons cAMP4_R2_PKA + PKA$
- $cAMP4_R2_PKA \rightleftharpoons cAMP4_R2 + PKA$
- $PKA + PDE \rightleftharpoons PKA_PDE \rightarrow PKA + PDEP$
- $cAMP + PDE \rightleftharpoons cAMP_PDE \rightarrow AMP + PDE$
- $cAMP + PDEP \rightleftharpoons cAMP_PDEP \rightarrow AMP + PDEP$

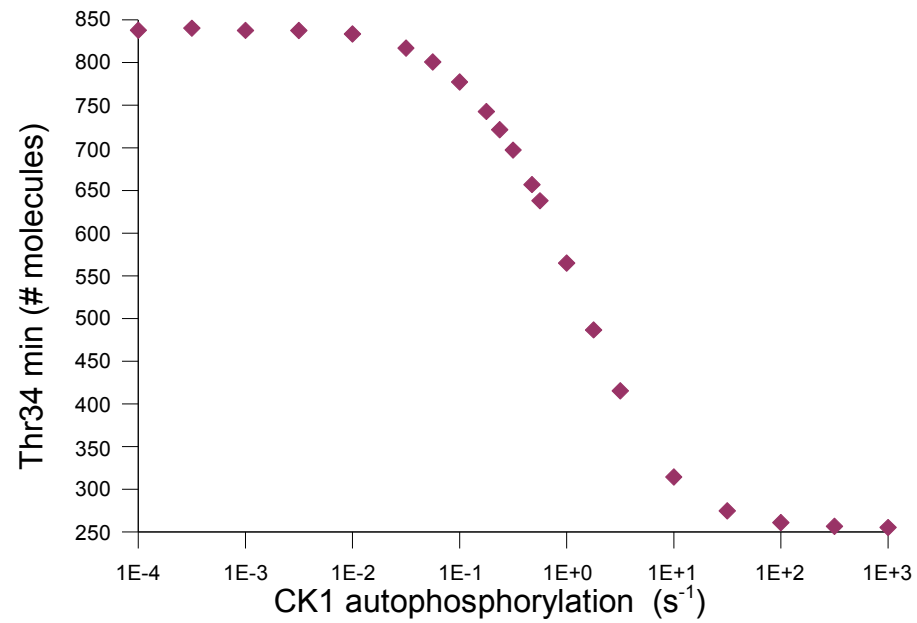
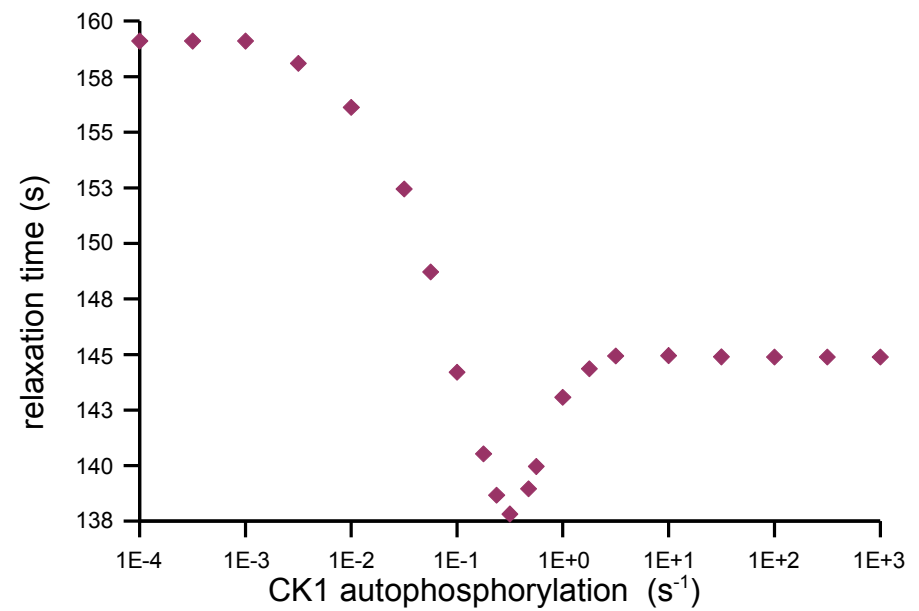


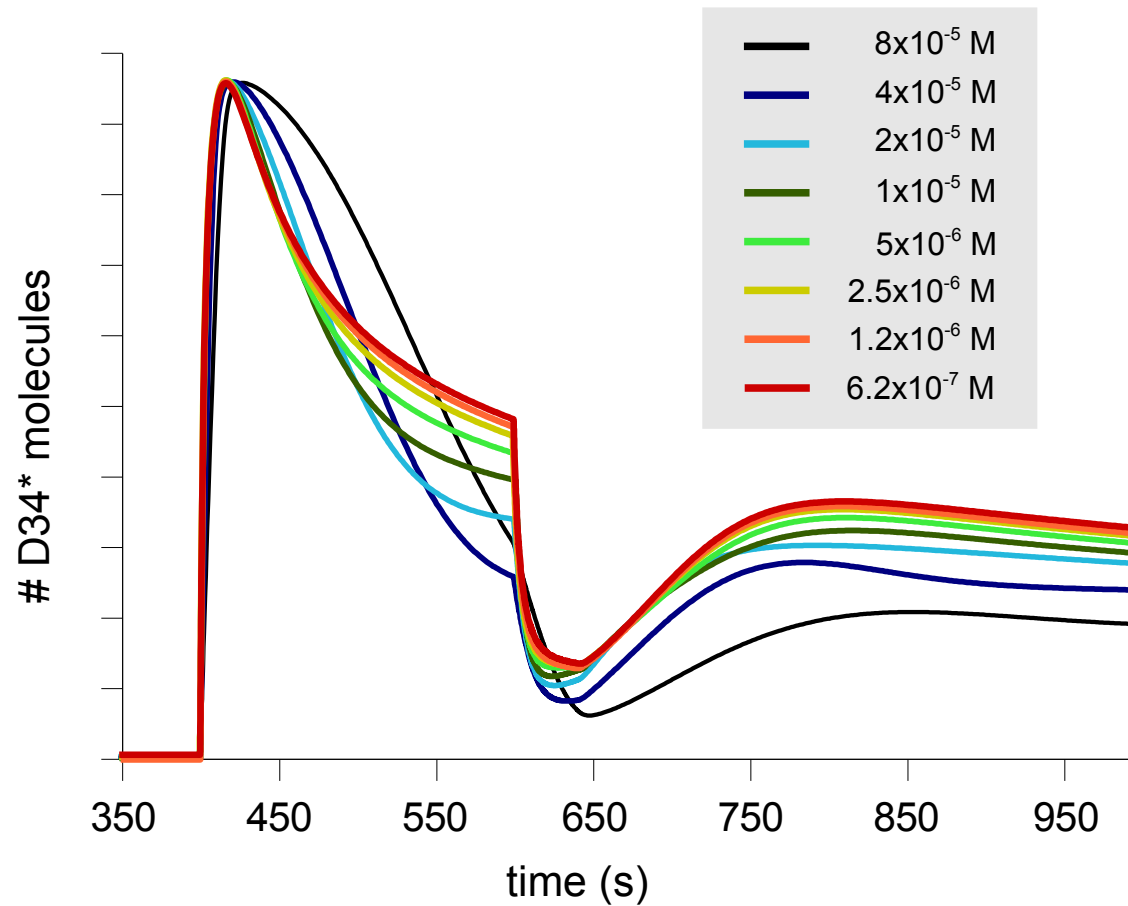


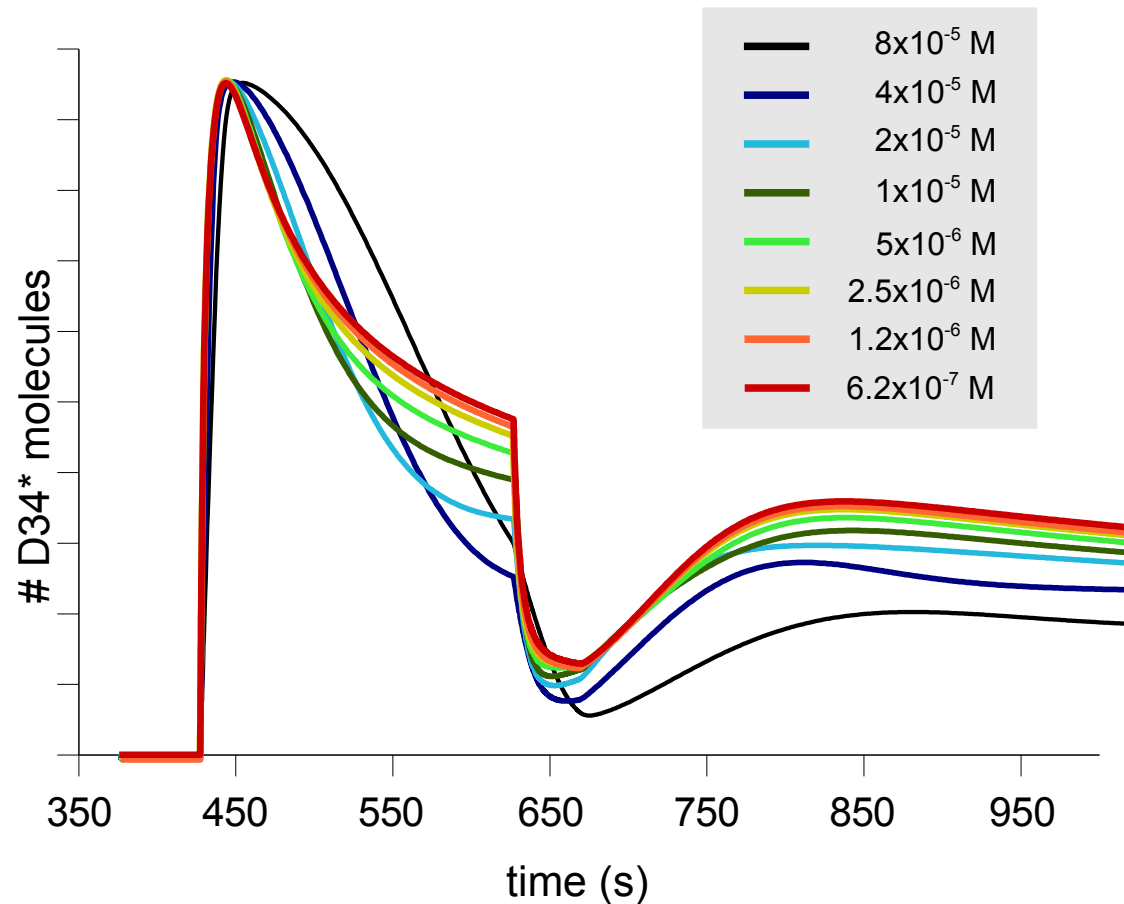






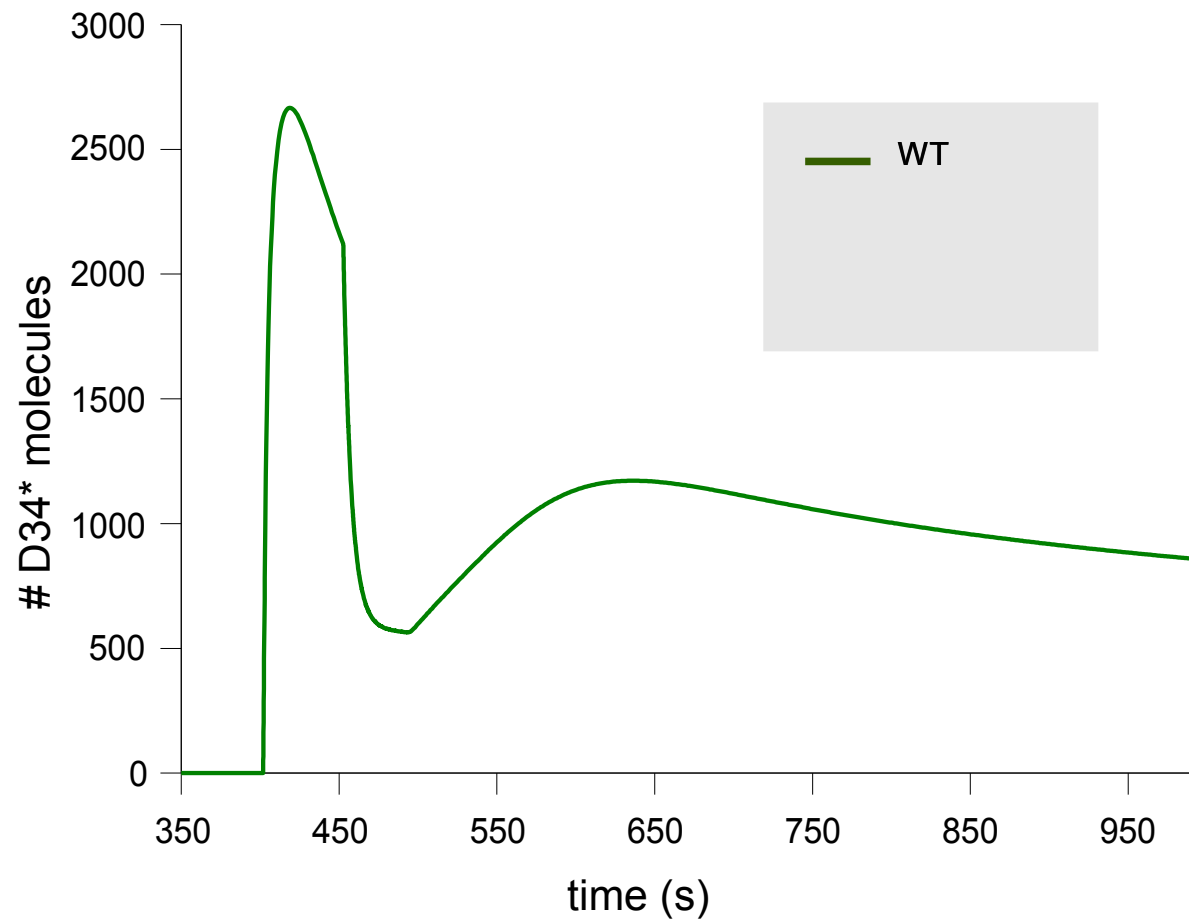
A**B**

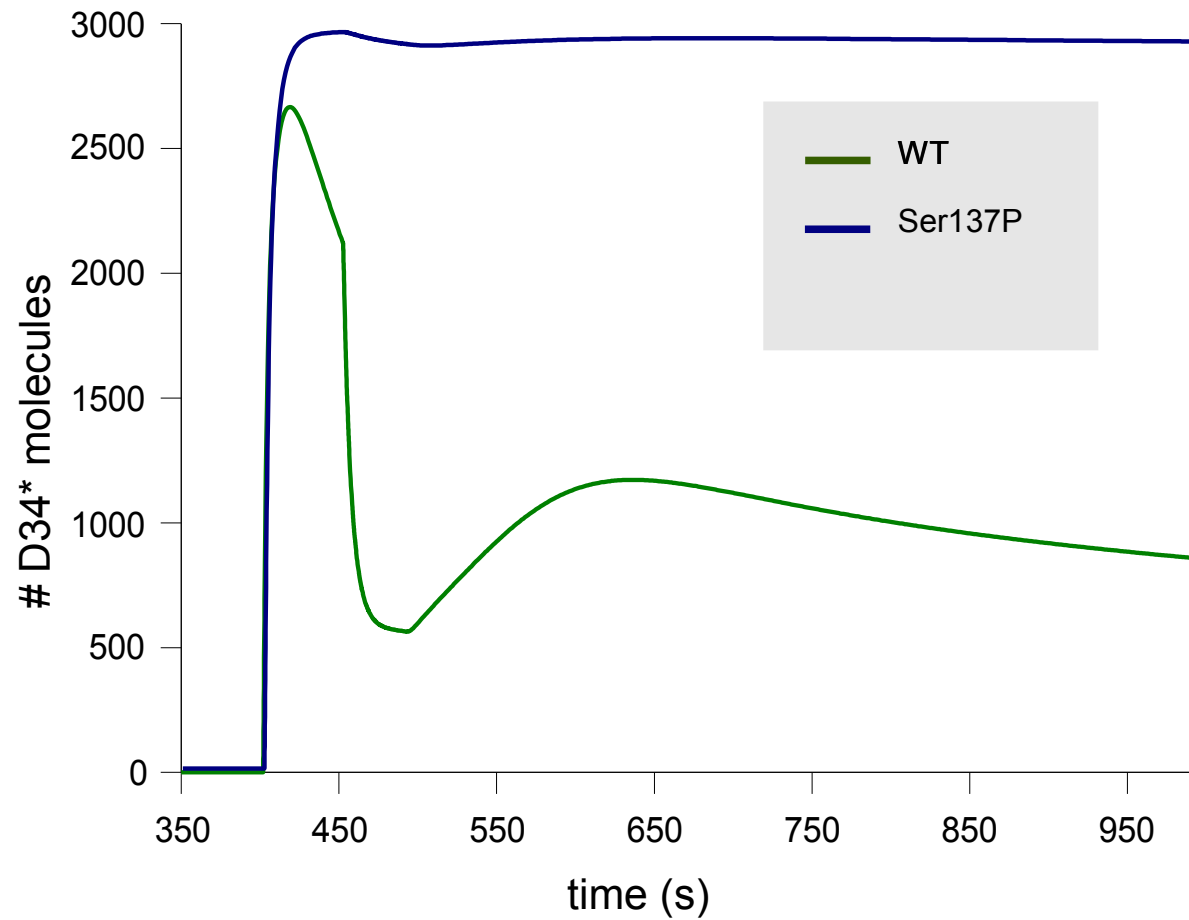


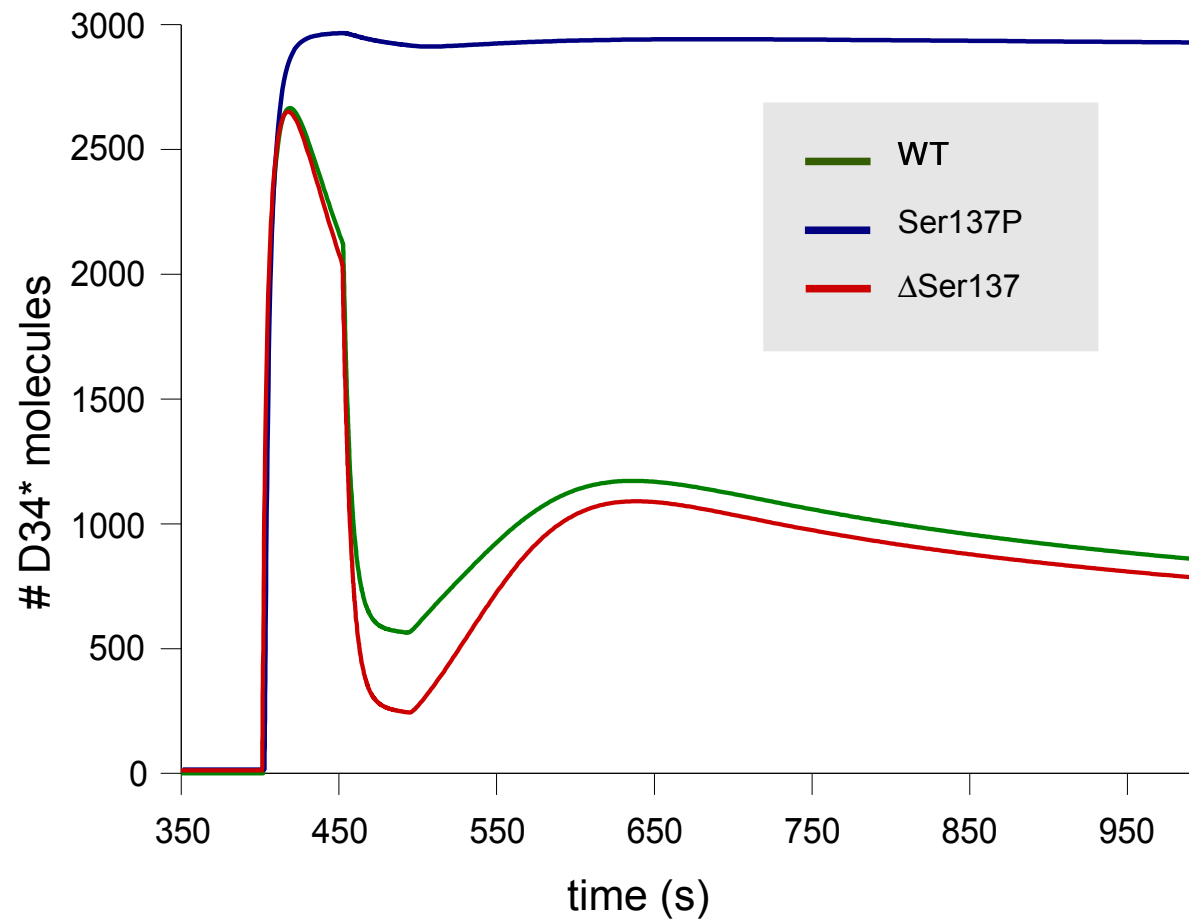


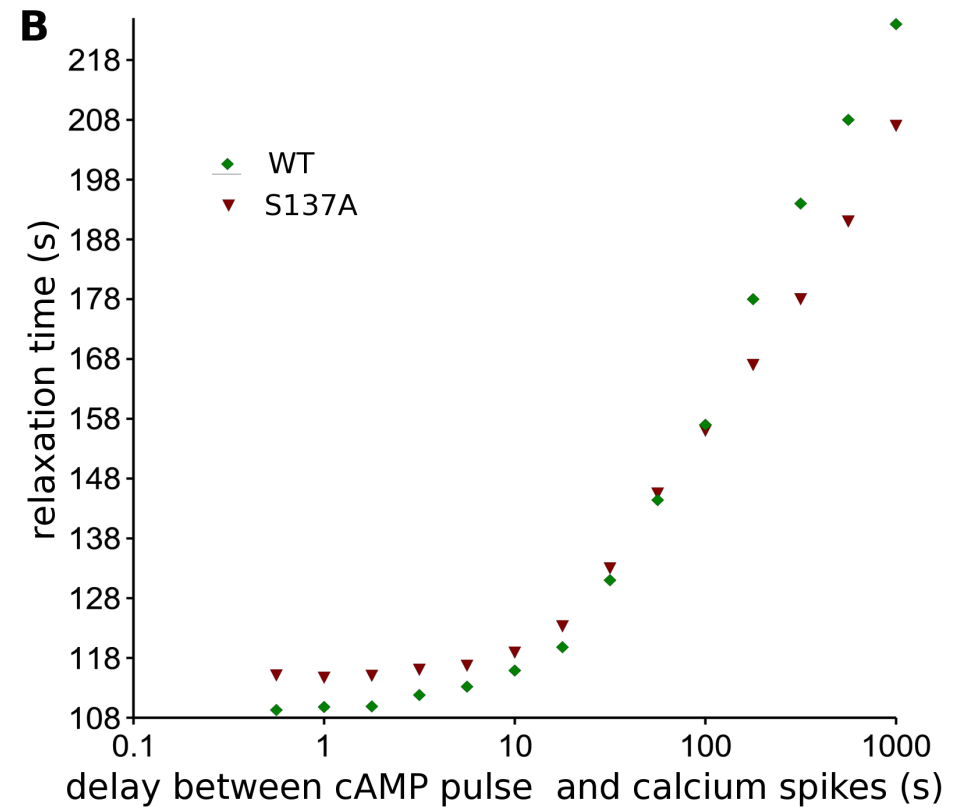
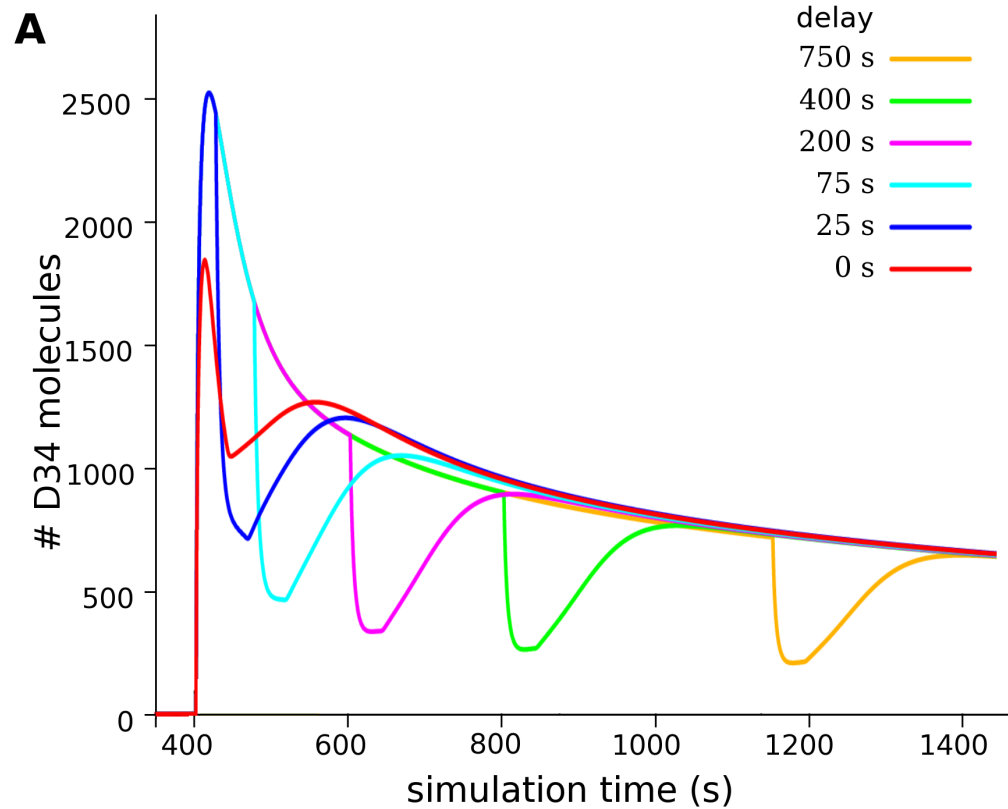
Heterozygous DARPP-32 +/- do not display phenotypes

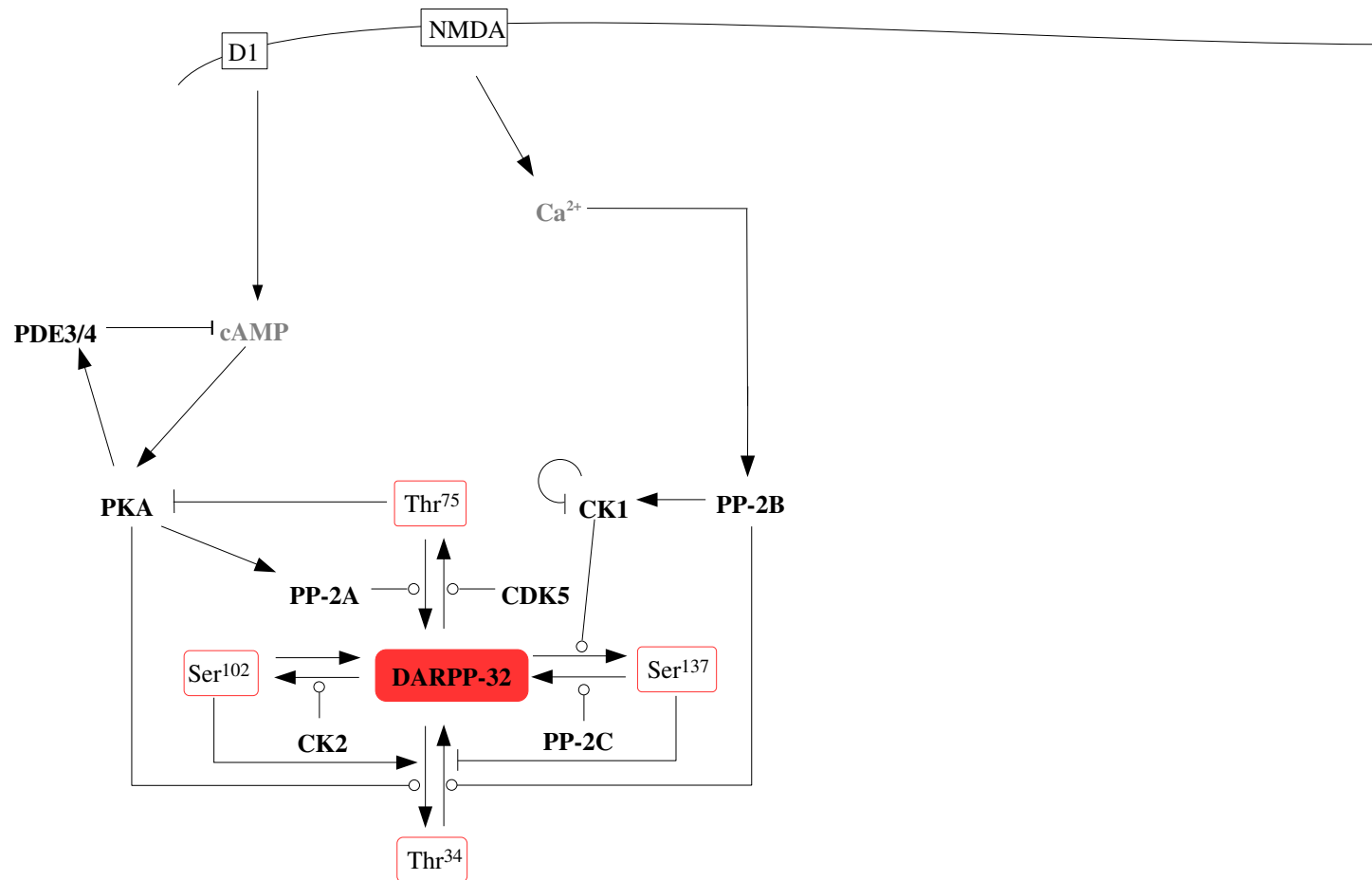


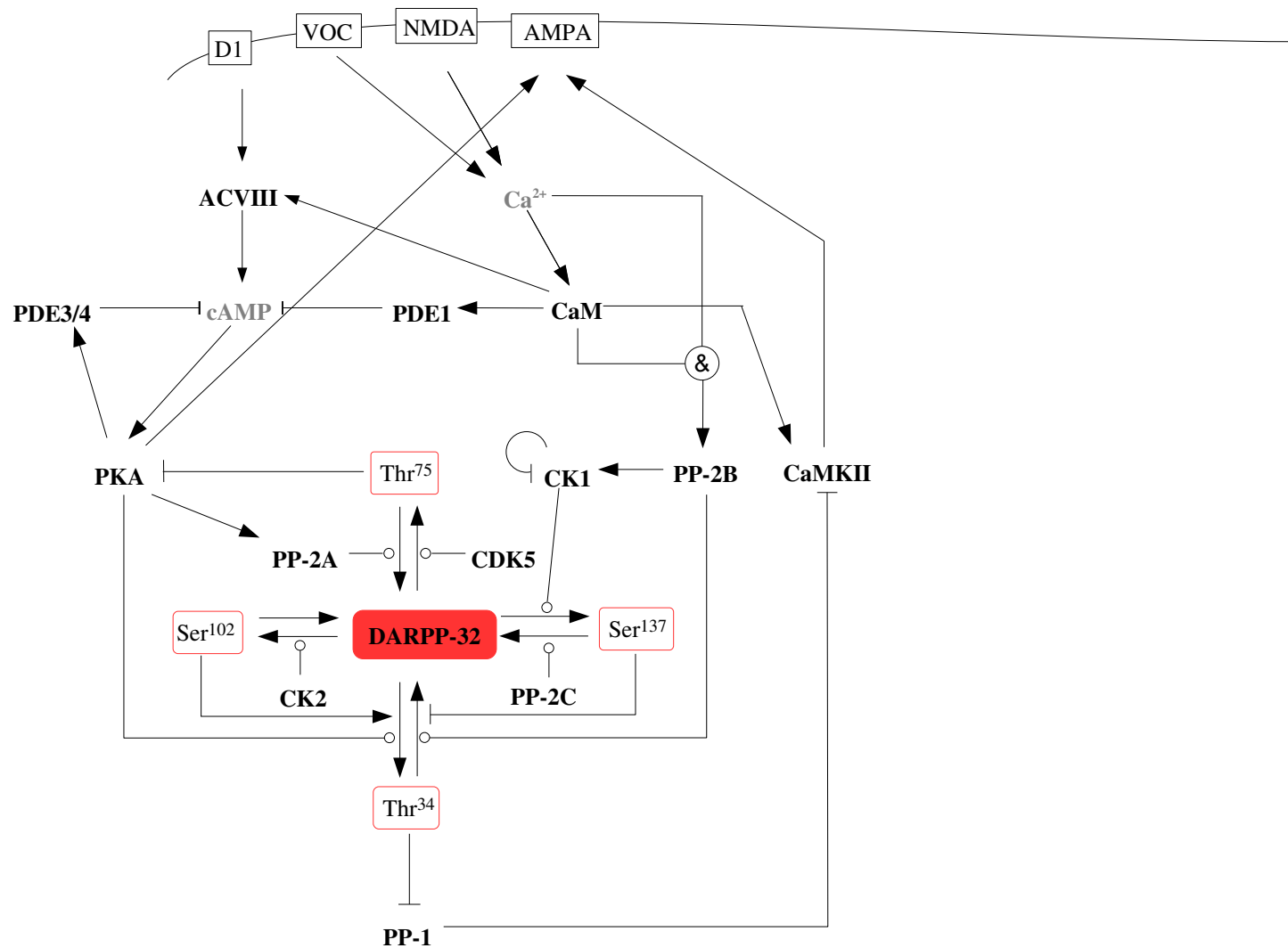


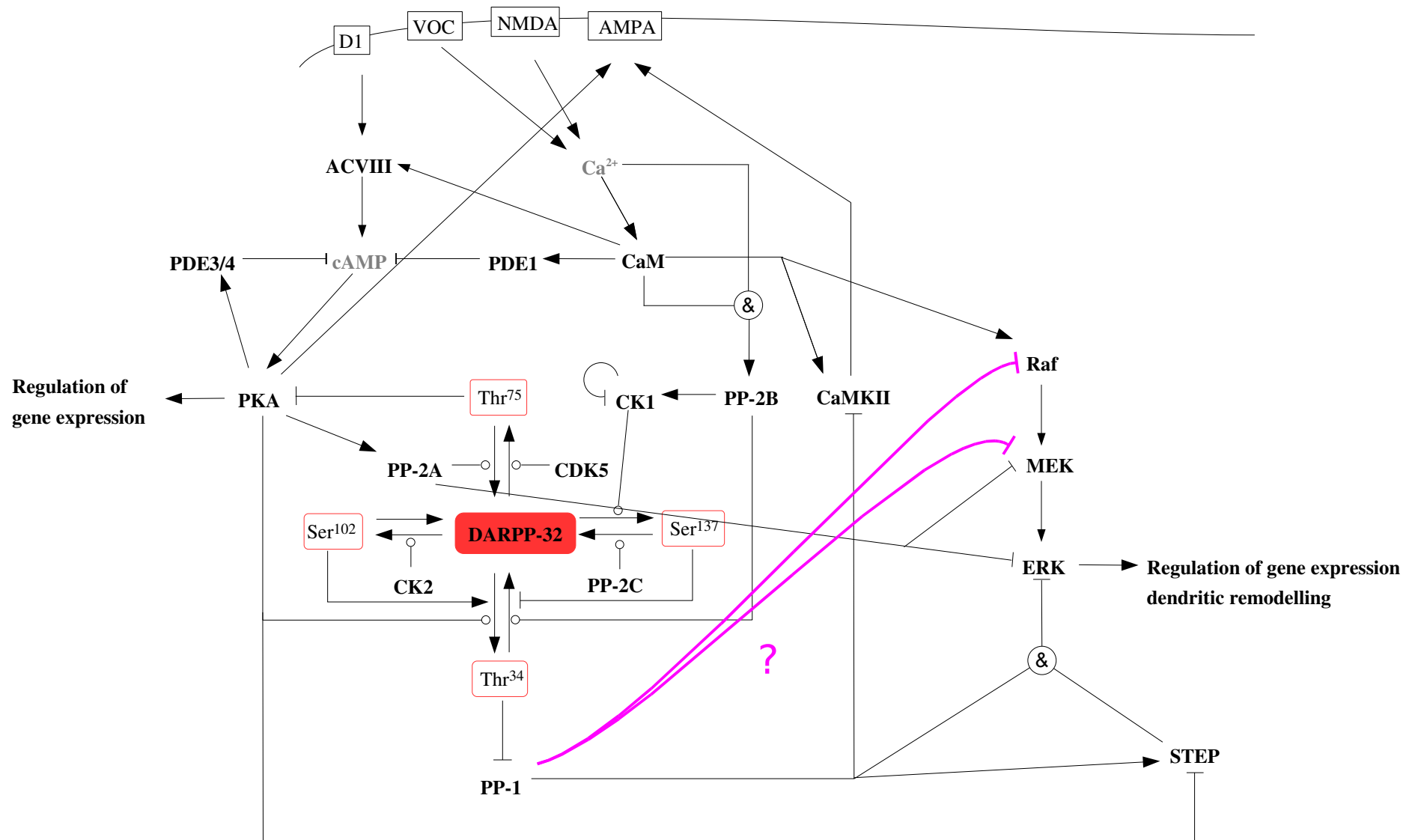






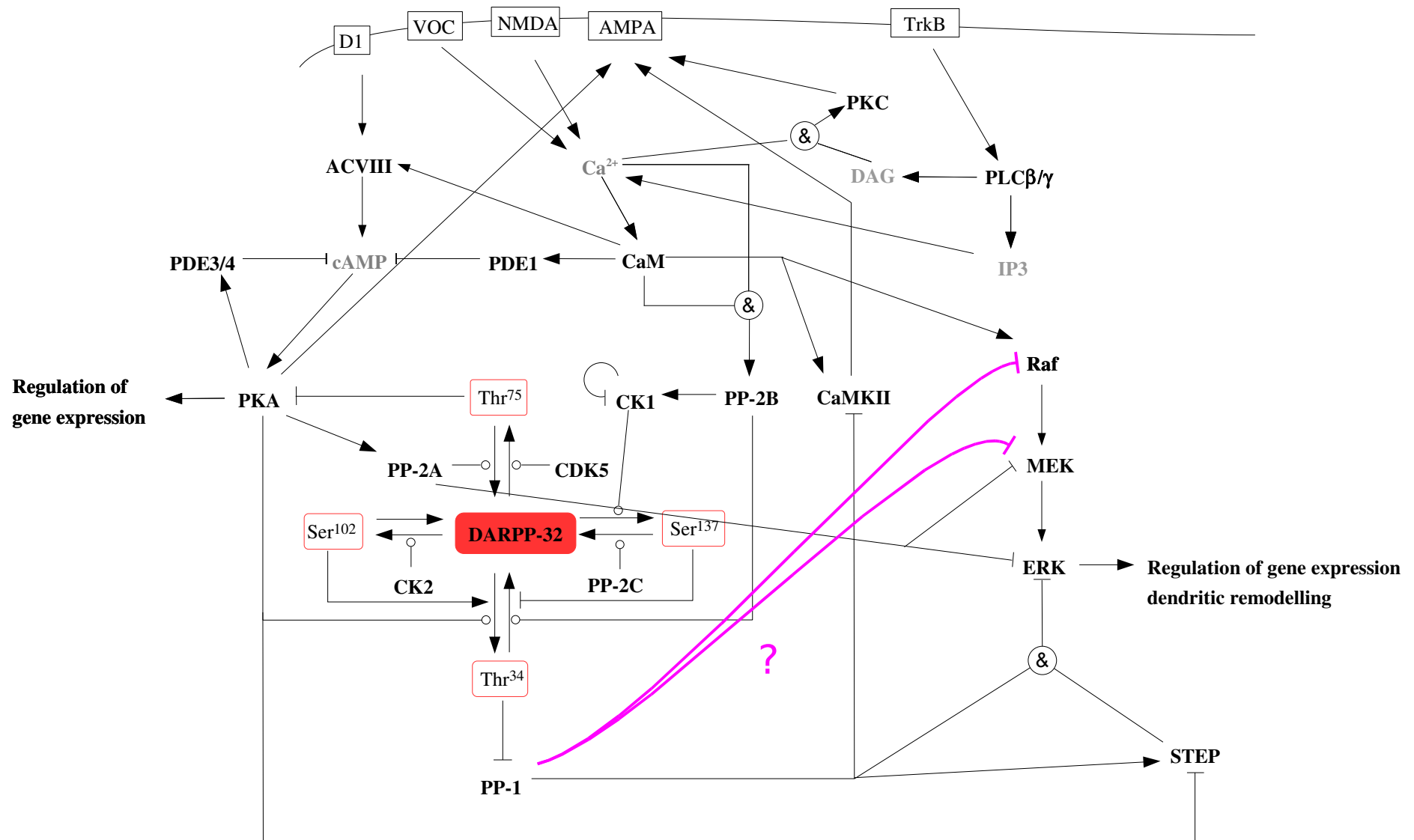






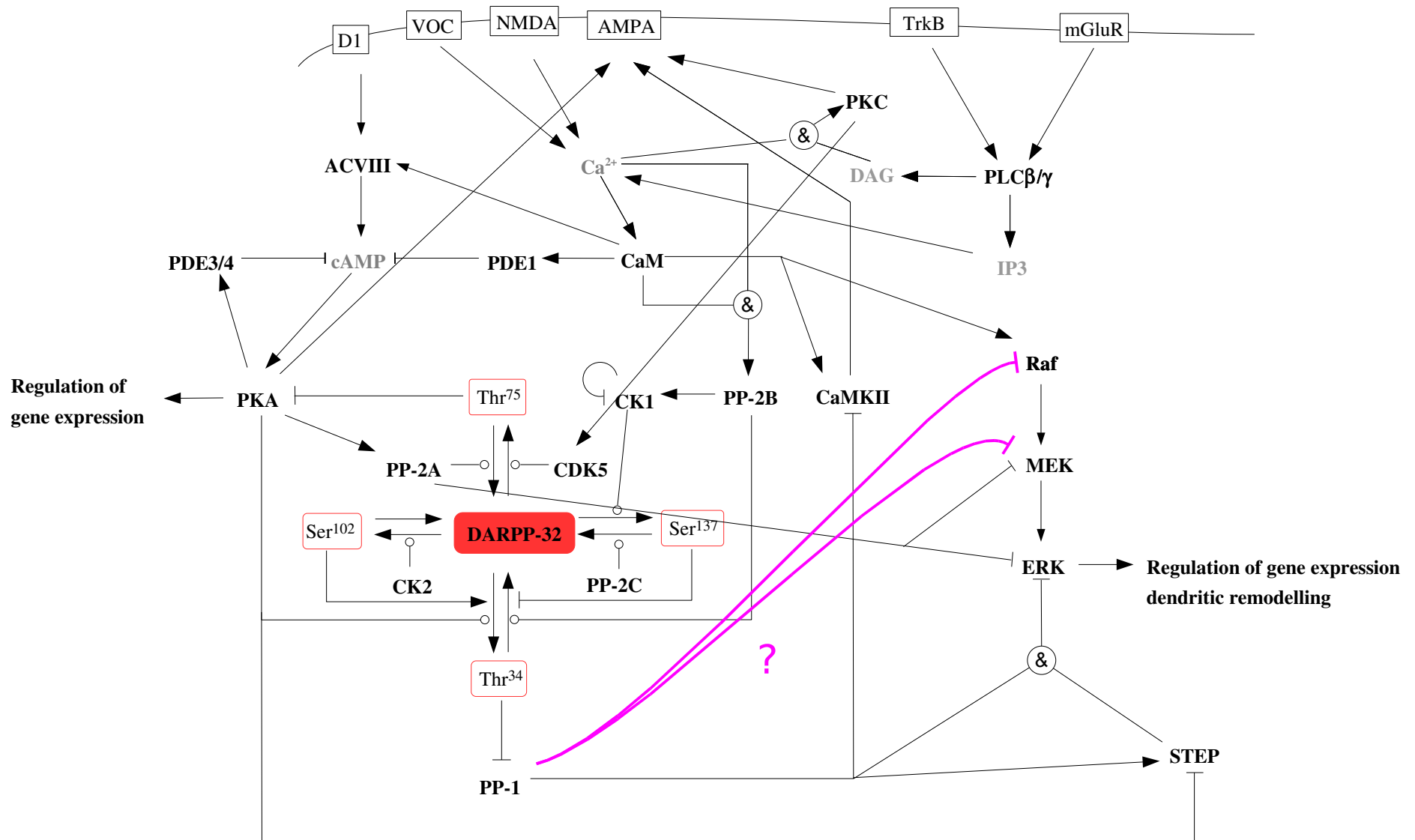
Collaboration
Jean-Antoine Girault, Paris





Collaboration
Liliana Minichiello, Monterotondo





- E-cell developers
(Institute of Advanced Biosciences,
Tsuruoka)

Kouichi Takahashi

Kazunari Kaizu

Gabor Bereczki

- Collaborators
(INSERM U536, Paris)

Jean-Antoine Girault

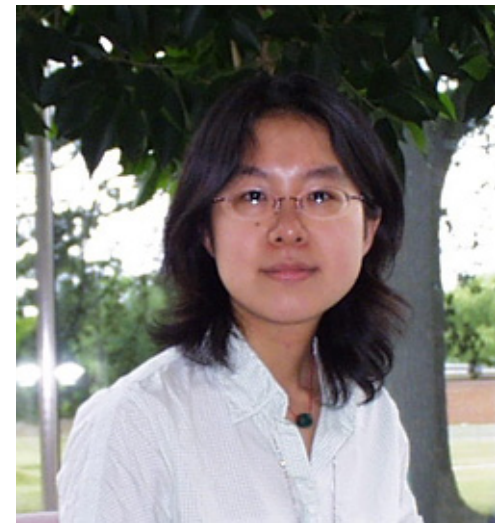
Denis Herve



Eric Fernandez

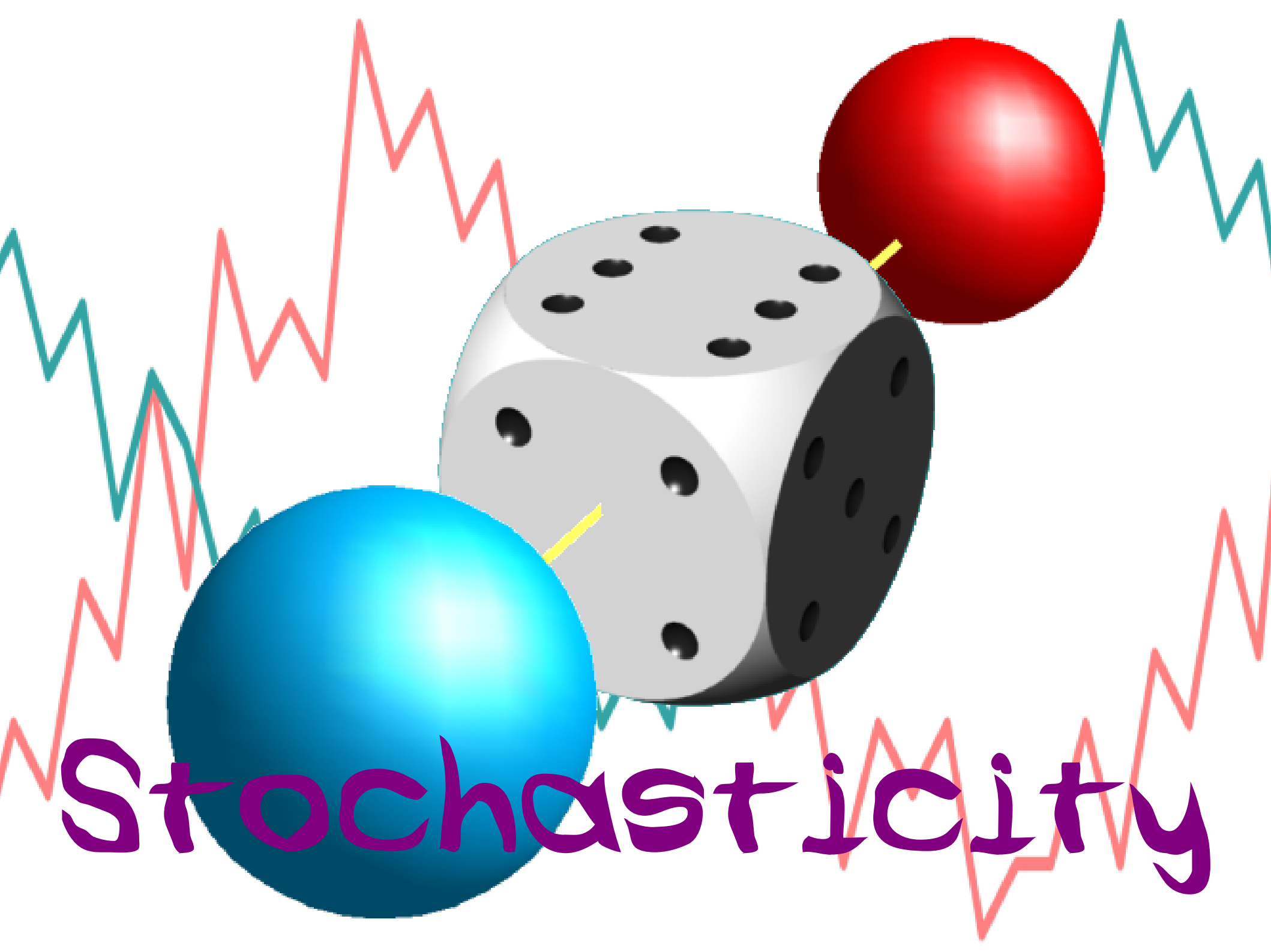


Renaud Schiappa



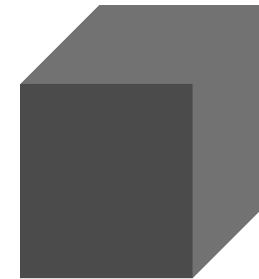
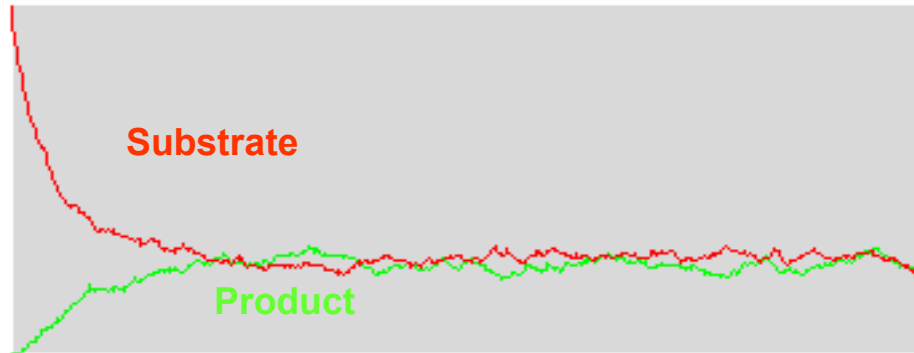
Lu Li



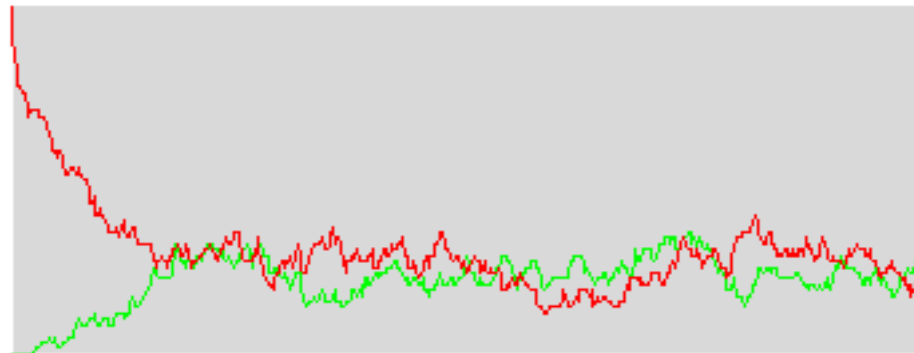


Stochasticity

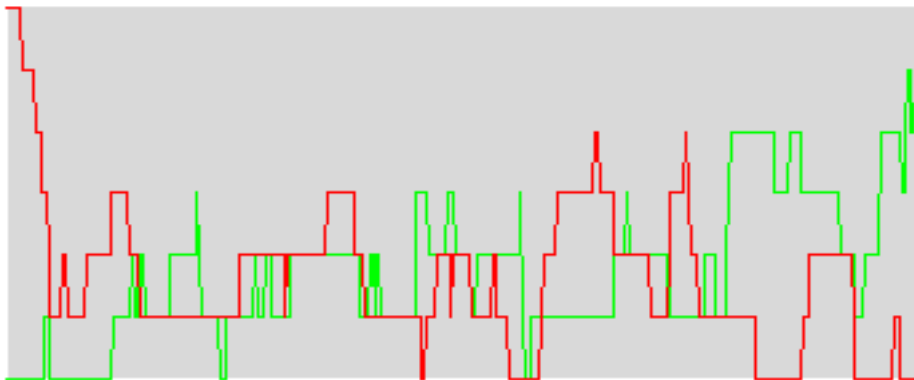
Concentration (μM)



10^{-15} litres

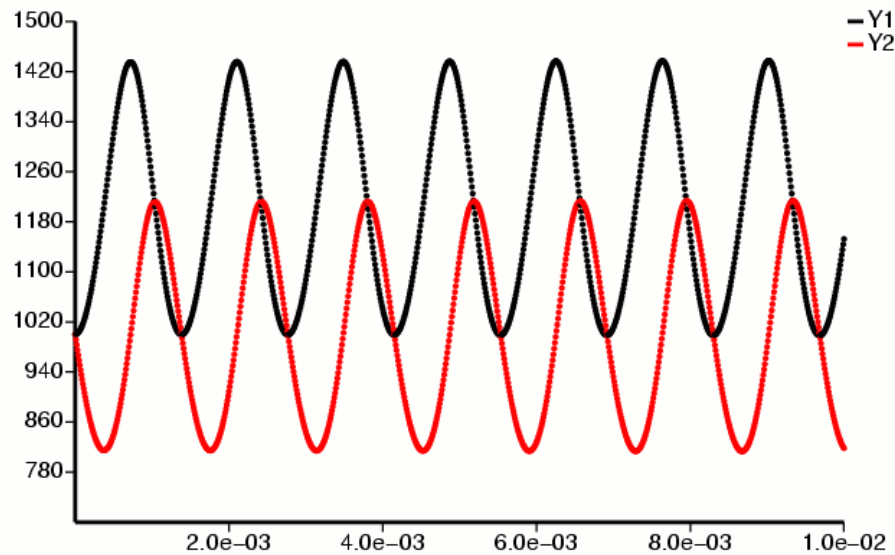


10^{-16} litres

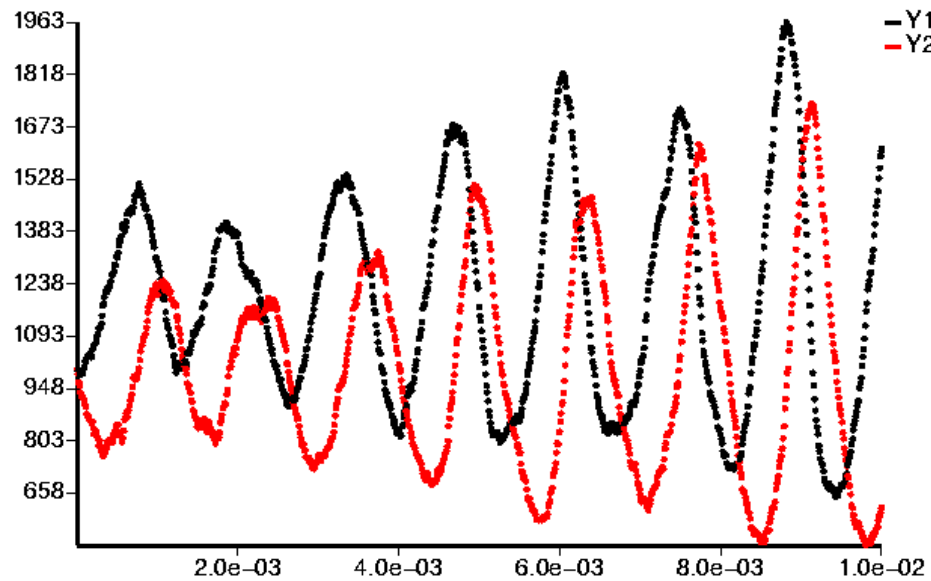


10^{-17} litres



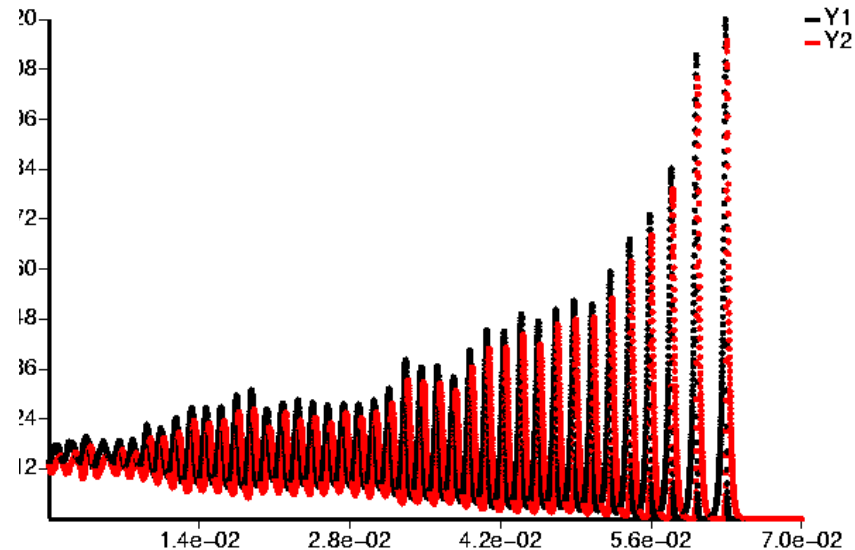
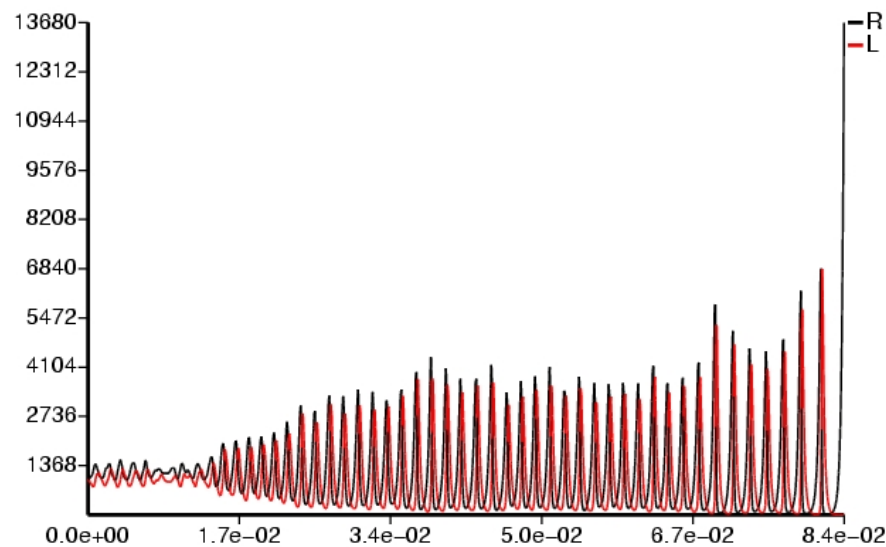
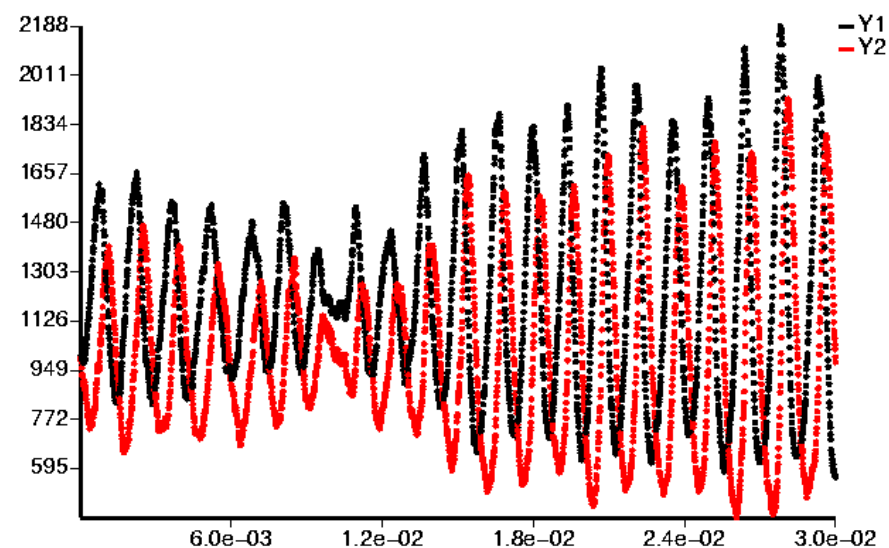
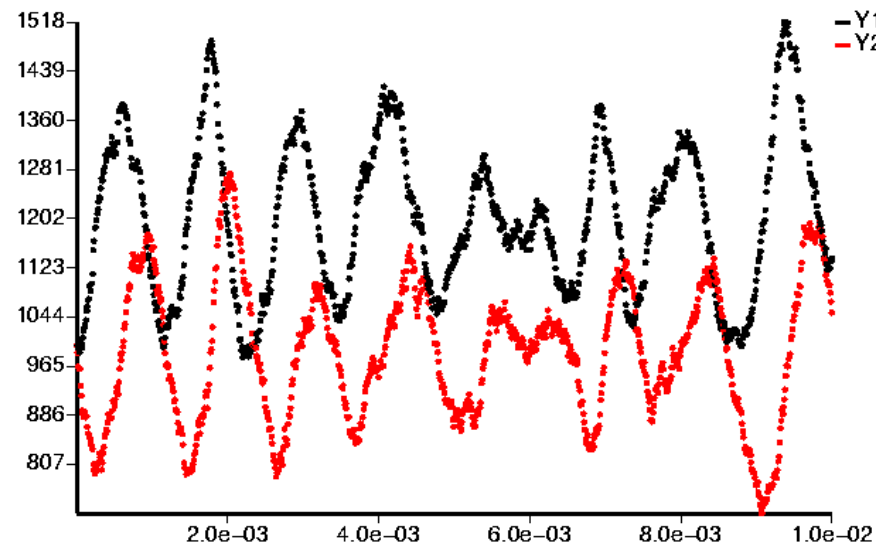


deterministic result



stochastic result





- number of AMPA receptors in a PSD: 50-100
- most kinases and phosphatases $\propto 100$
- number of free calcium ions at rest state: 3-5



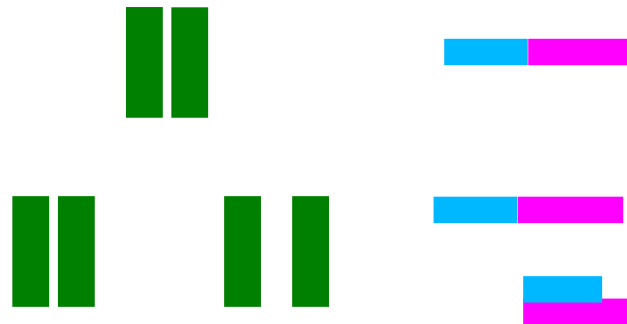


Combinatorial Explosion



NMDA + CaMKII $\rightleftharpoons$ NMDA-CaMKII





NMDA + CaMKII $\rightleftharpoons$ NMDA-CaMKII

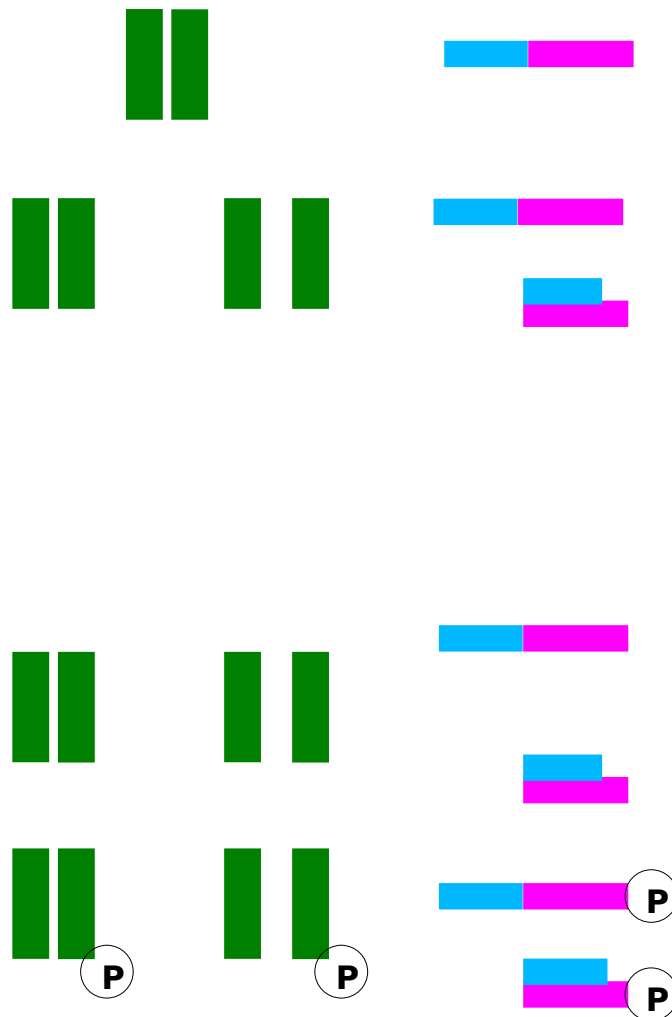
NMDAc + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAo + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAc + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo

NMDAo + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo





NMDA + CaMKII $\rightleftharpoons$ NMDA-CaMKII

NMDAc + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAo + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAc + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo

NMDAo + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo

NMDAc + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAo + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAc + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo

NMDAo + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo

pNMDAc + CaMKIIc $\rightleftharpoons$ pNMDAc-CaMKIIc

pNMDAo + CaMKIIc $\rightleftharpoons$ pNMDAc-CaMKIIc

pNMDAc + CaMKIIo $\rightleftharpoons$ pNMDAc-CaMKIIo

pNMDAo + CaMKIIo $\rightleftharpoons$ pNMDAc-CaMKIIo

NMDAc + pCaMKIIc $\rightleftharpoons$ NMDAc-pCaMKIIc

NMDAo + pCaMKIIc $\rightleftharpoons$ NMDAc-pCaMKIIc

NMDAc + pCaMKIIo $\rightleftharpoons$ NMDAc-pCaMKIIo

NMDAo + pCaMKIIo $\rightleftharpoons$ NMDAc-pCaMKIIo

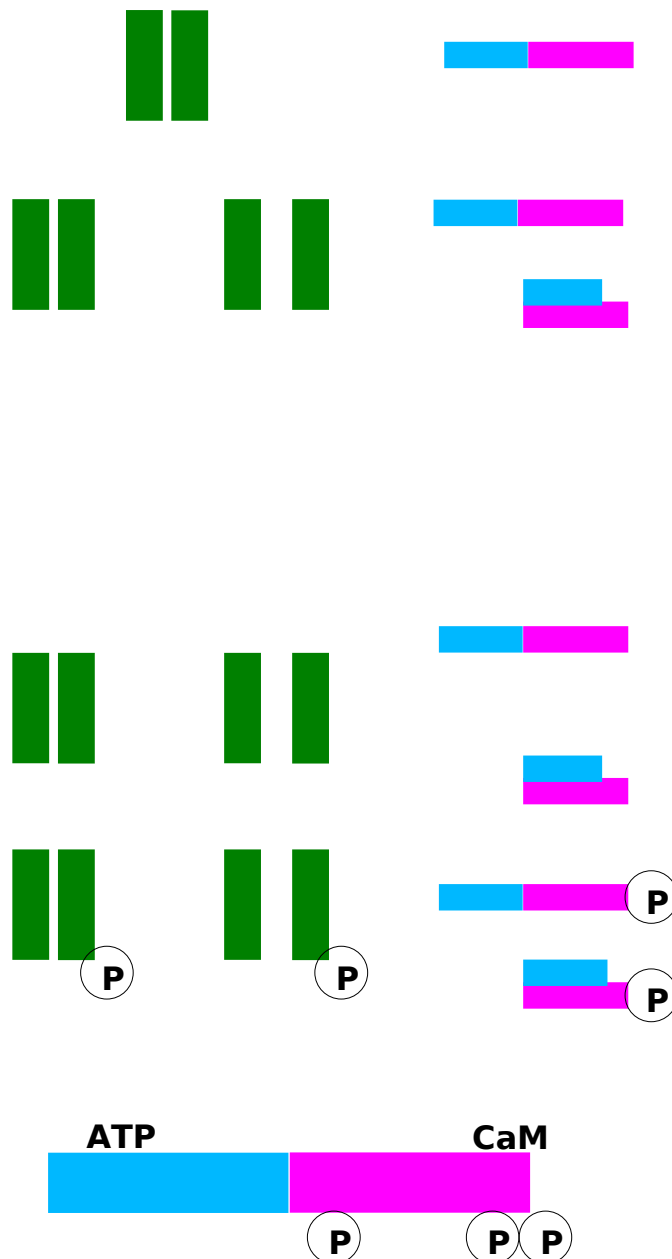
pNMDAc + pCaMKIIc $\rightleftharpoons$ pNMDAc-pCaMKIIc

pNMDAo + pCaMKIIc $\rightleftharpoons$ pNMDAc-pCaMKIIc

pNMDAc + pCaMKIIo $\rightleftharpoons$ pNMDAc-pCaMKIIo

pNMDAo + pCaMKIIo $\rightleftharpoons$ pNMDAc-pCaMKIIo





NMDA + CaMKII $\rightleftharpoons$ NMDA-CaMKII

NMDAc + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAo + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAc + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo

NMDAo + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo

NMDAc + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAo + CaMKIIc $\rightleftharpoons$ NMDAc-CaMKIIc

NMDAc + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo

NMDAo + CaMKIIo $\rightleftharpoons$ NMDAc-CaMKIIo

pNMDAc + CaMKIIc $\rightleftharpoons$ pNMDAc-CaMKIIc

pNMDAo + CaMKIIc $\rightleftharpoons$ pNMDAc-CaMKIIc

pNMDAc + CaMKIIo $\rightleftharpoons$ pNMDAc-CaMKIIo

pNMDAo + CaMKIIo $\rightleftharpoons$ pNMDAc-CaMKIIo

NMDAc + pCaMKIIc $\rightleftharpoons$ NMDAc-pCaMKIIc

NMDAo + pCaMKIIc $\rightleftharpoons$ NMDAc-pCaMKIIc

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NMDAo + pCaMKIIo $\rightleftharpoons$ NMDAc-pCaMKIIo

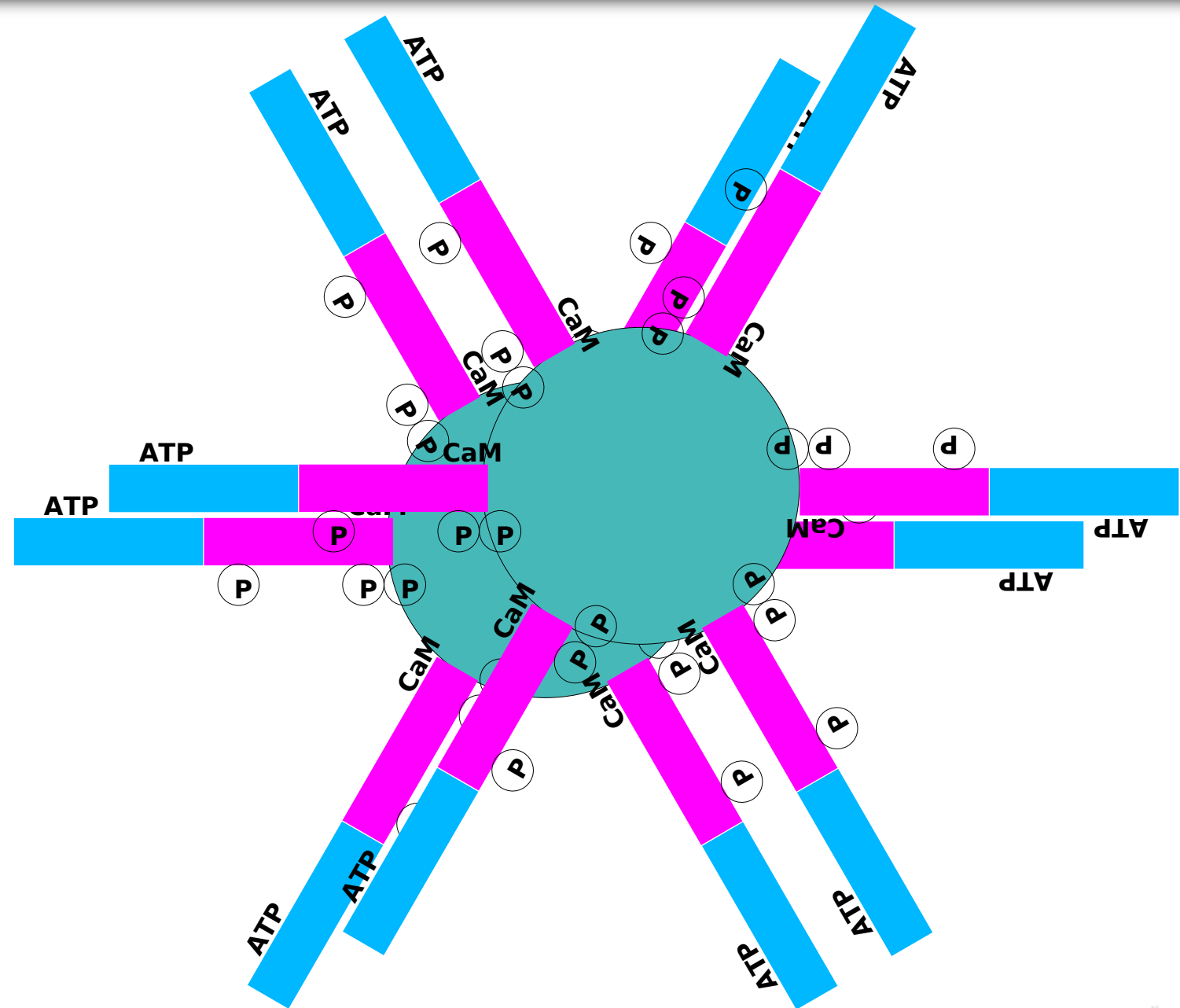
pNMDAc + pCaMKIIc $\rightleftharpoons$ pNMDAc-pCaMKIIc

pNMDAo + pCaMKIIc $\rightleftharpoons$ pNMDAc-pCaMKIIc

pNMDAc + pCaMKIIo $\rightleftharpoons$ pNMDAc-pCaMKIIo

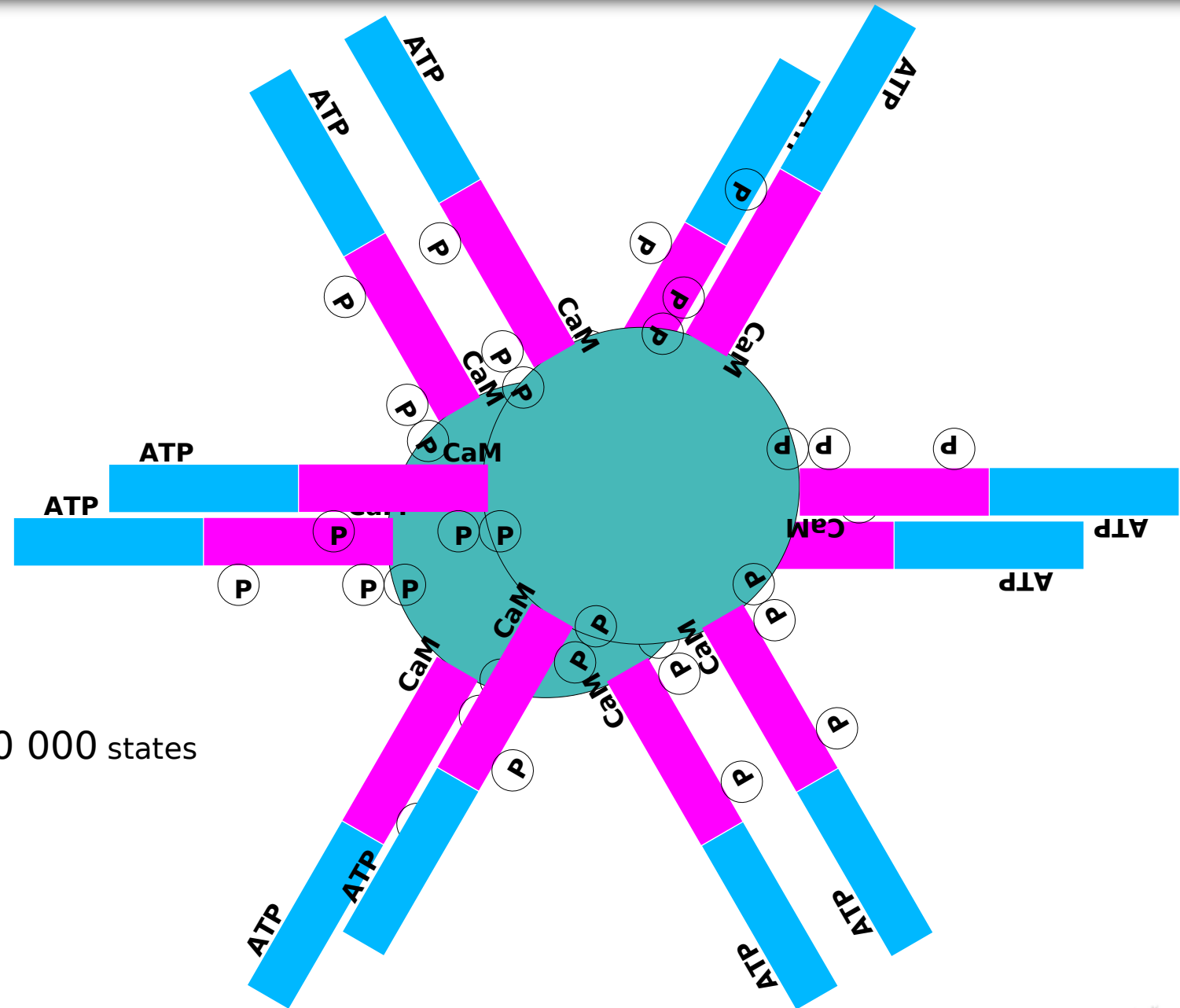
pNMDAo + pCaMKIIo $\rightleftharpoons$ pNMDAc-pCaMKIIo





5x12 state variables=



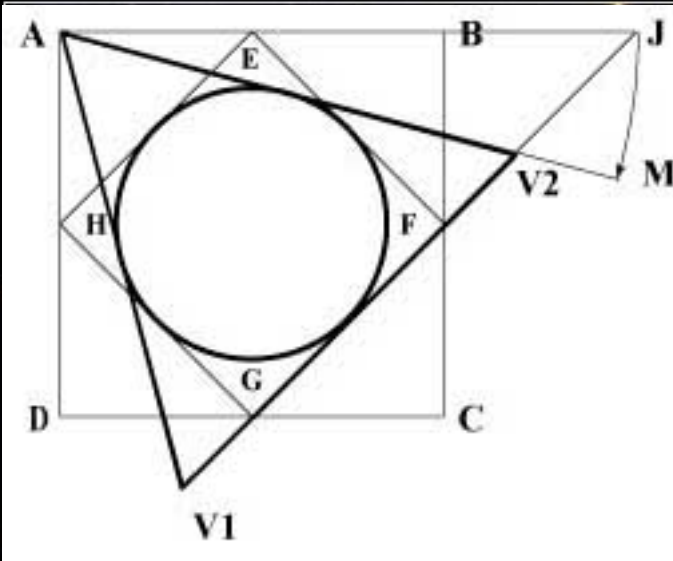


5x12 state variables=

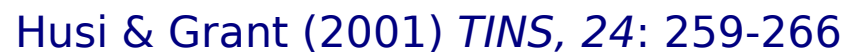
1 152 900 000 000 000 000 states

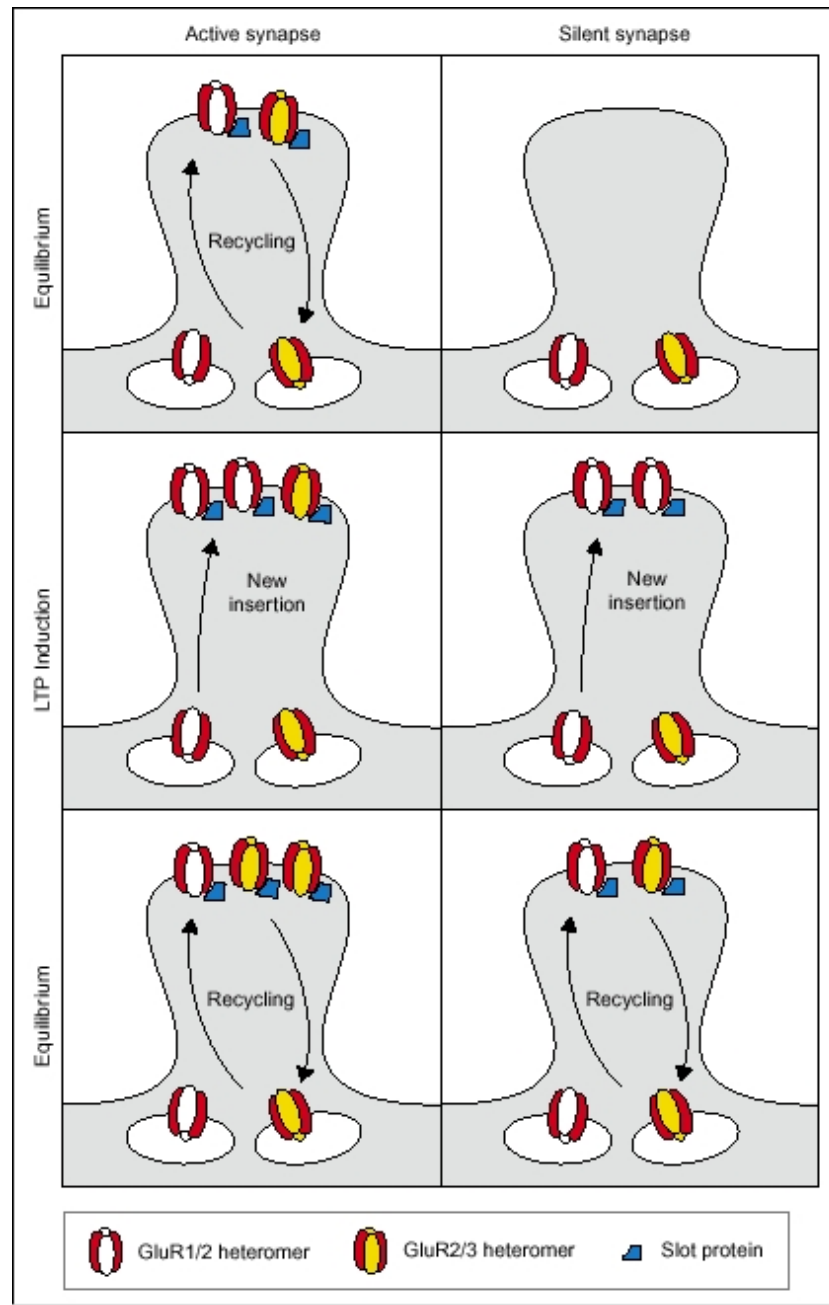
(1 billion of billion)



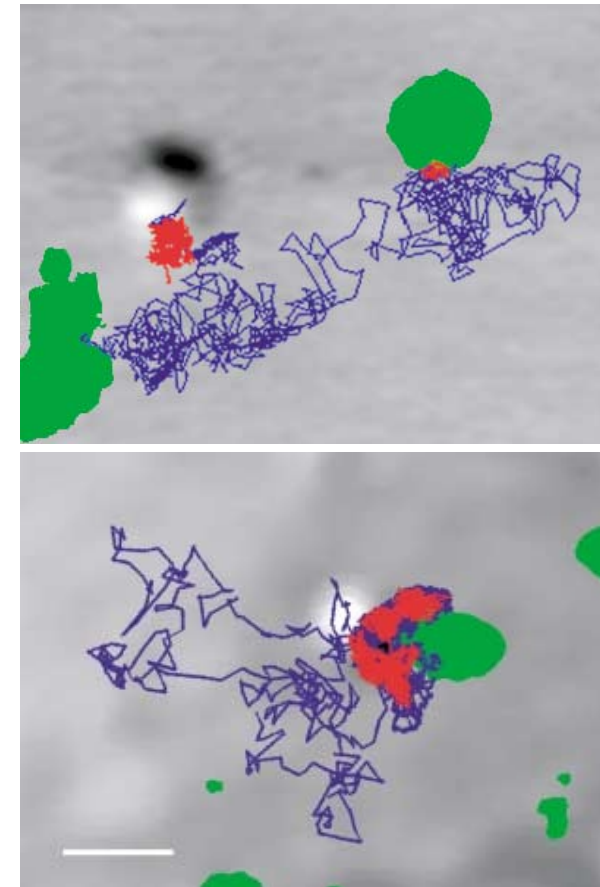


Space and geometry





Barry and Ziff. (2002)
Curr Opin Neurobiol, 12: 279-286



Choquet & Triller (2003)
Nat Rev Neurosci, 4: 251-265



Population-based simulation

- Continuous representation of populations
- Generally deterministic algorithms to simulate the evolution of populations (but not always: Gillespie)
- Generally no representation of space (but not always: finite elements)
- No movements (but not always: PDE or reaction-diffusion)
- Molecules under different states are represented by different pools

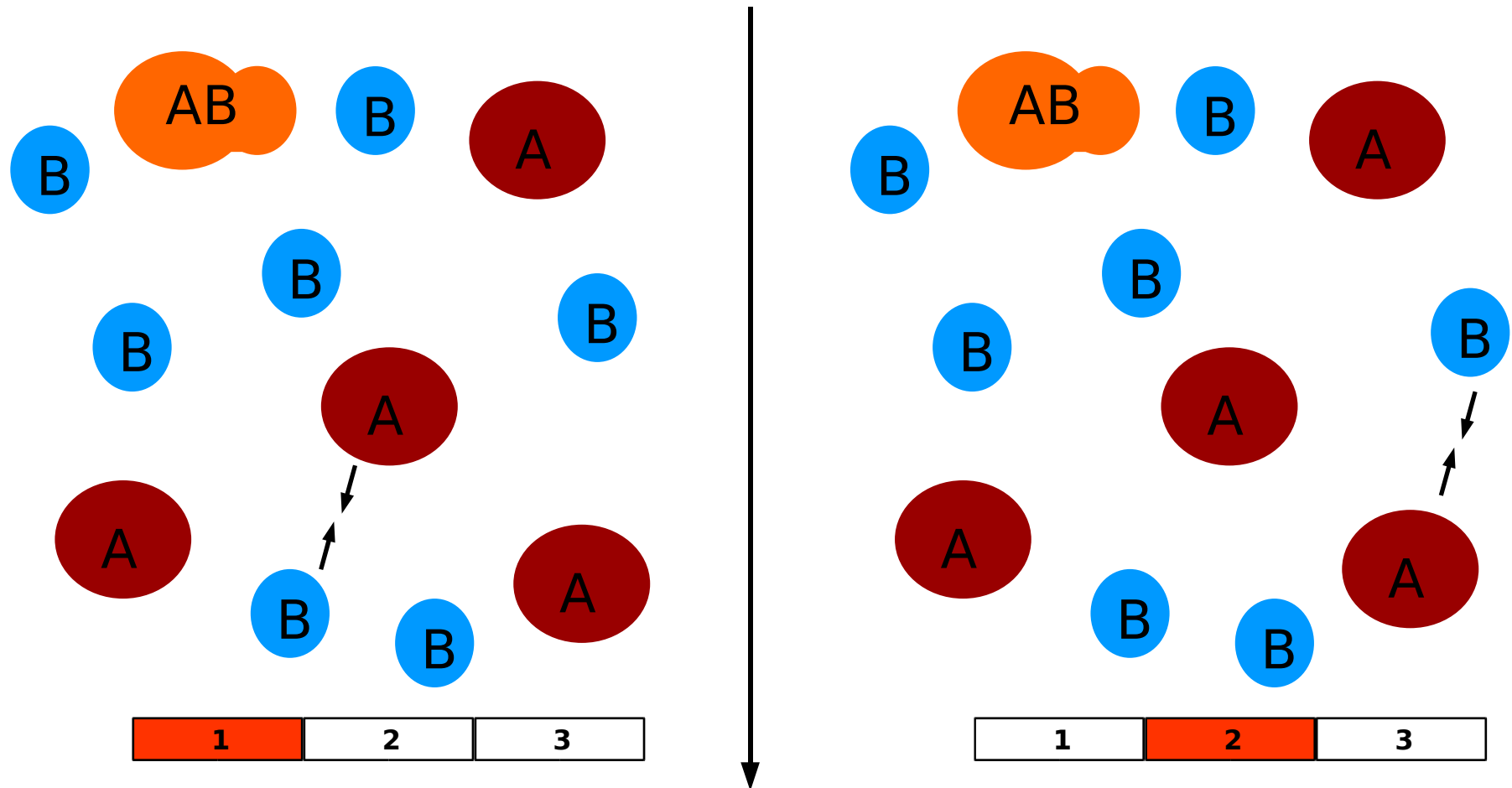
Particle-based simulation

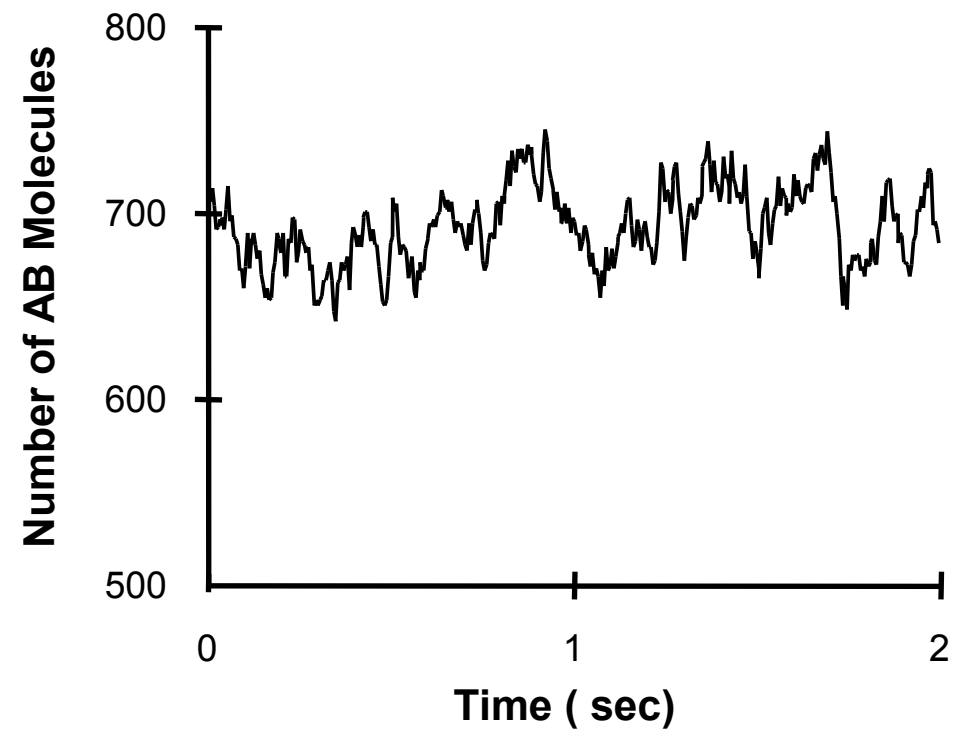
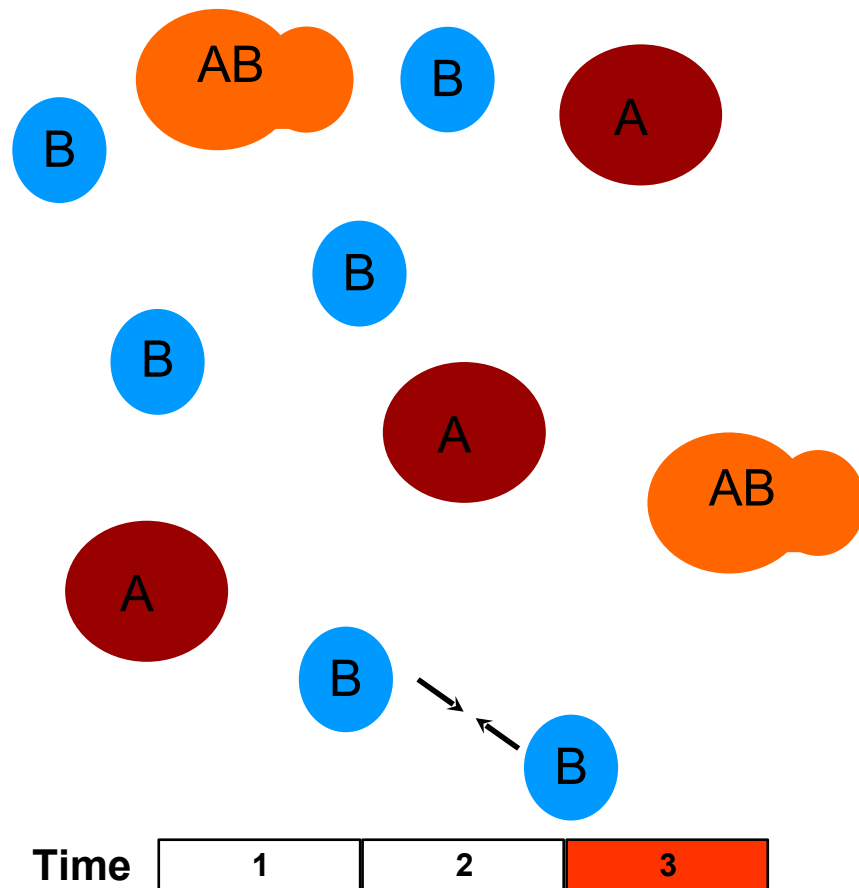
- Discrete representation of molecules
- Generally stochastic algorithms (but not always: deterministic automata)
- Generally location of molecules (but not always: StochSim v1)
- Representation of the movements of (some) molecules
- Possibility of multistates molecules

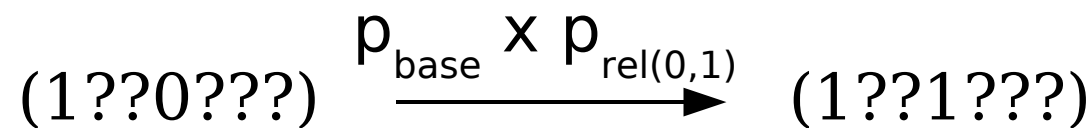
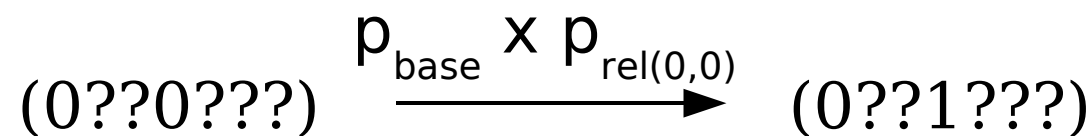
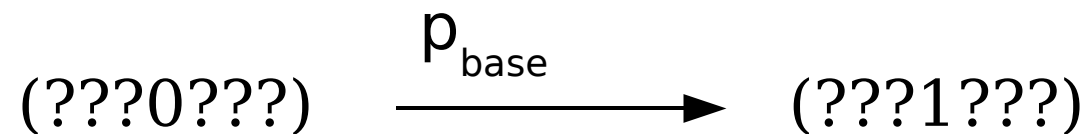


- Morton-Firth CJ, Bray D (1998) *J. Theor. Biol.* 192: 117–128.
- Le Novère N, Shimizu TS (2001) *Bioinformatics* 17: 575-576
- Particle-based stochastic simulations
- Possibility of multistate complexes
- Rapid equilibria to reduce stiffness problems
- 2D lattices of various geometry



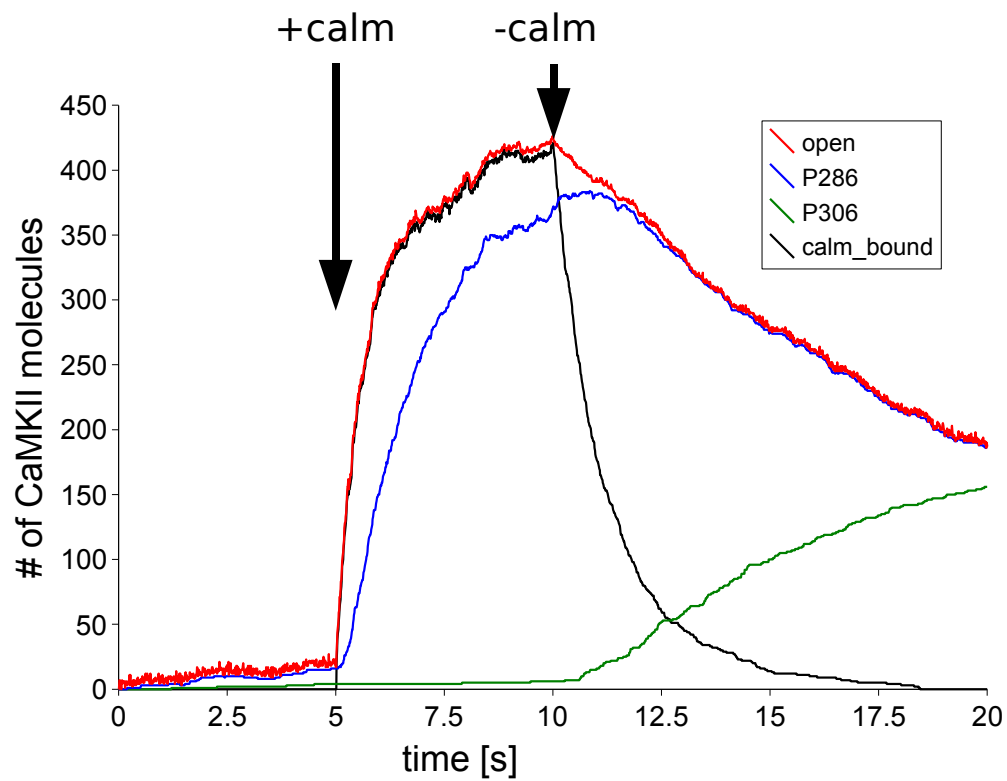
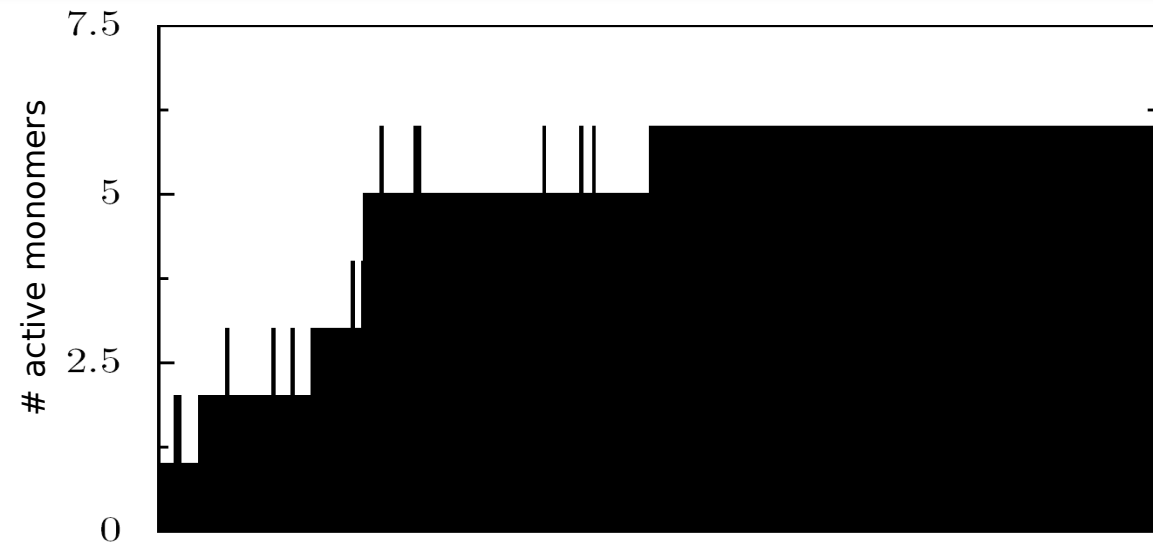


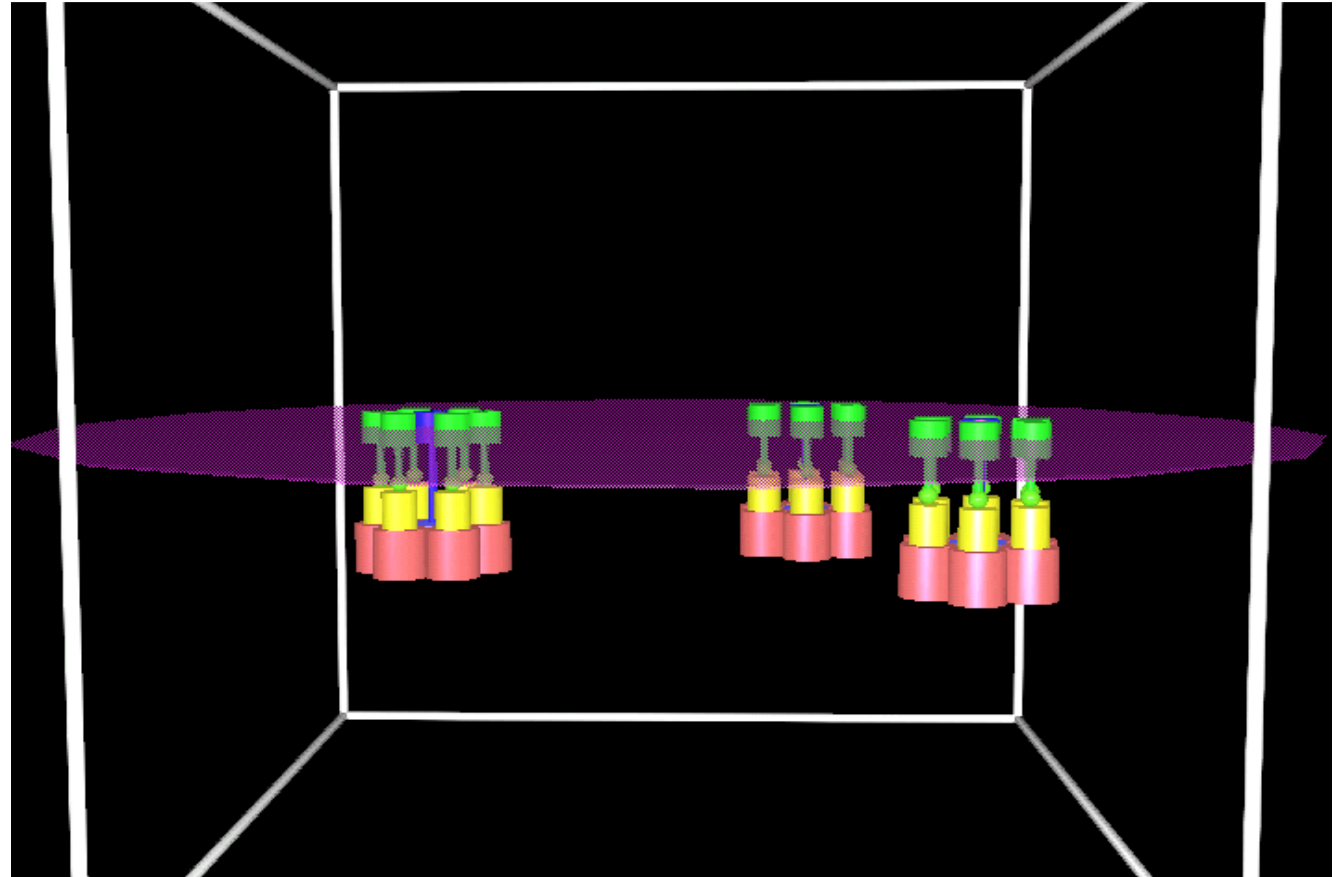
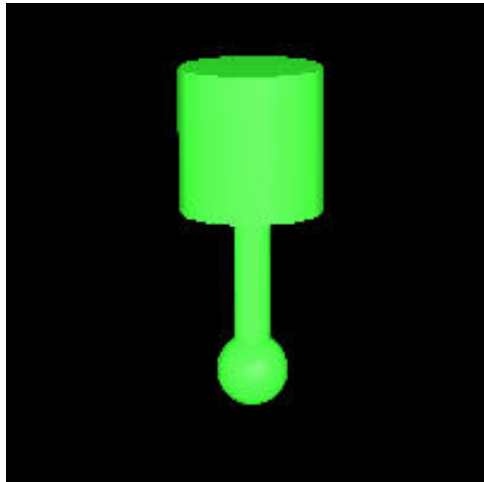
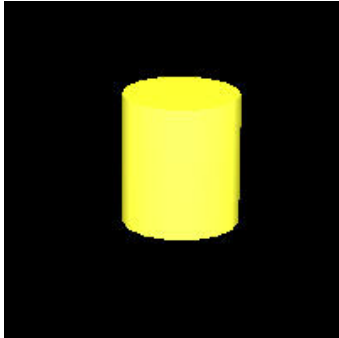




- '?' Flags do not affect the reaction
- only 4 species are needed instead of 128







Particles carry binding surfaces

Cluster and object classes allows recording of Center Of Mass, radius, RMS displacement, state

Clusters are dynamically created and destroyed – transient



- Different diffusion spaces:

- Static; Free diffusion; Membrane diffusion; Above membrane; Below membrane

- Two types of motion:

- Translational $\bar{r}^2 = 2D_T t = 2kb_T t$
 - Rotational $\bar{\theta}^2 = 2D_R t = 2kb_R t$

- random walk algorithm

$$p(x, t) = \frac{1}{\sqrt{4\pi Dt}} \exp\left(-\frac{x^2}{4Dt}\right) \quad \text{gaussian with} \quad \sigma^2 = 2Dt$$

- Translational $\Delta(x, y, z) = \sqrt{2D_T t} \times \text{gaussRand}$

- Rotational $\Delta\theta = \frac{\sqrt{2D_R t}}{r} \times \text{gaussRand}$

- Two types of diffusion equations:

- unrestricted brownian motion – Low Trans/Rot
 - intra-membrane diffusion (Saffman and Delbrück 1975) – High Trans/Rot



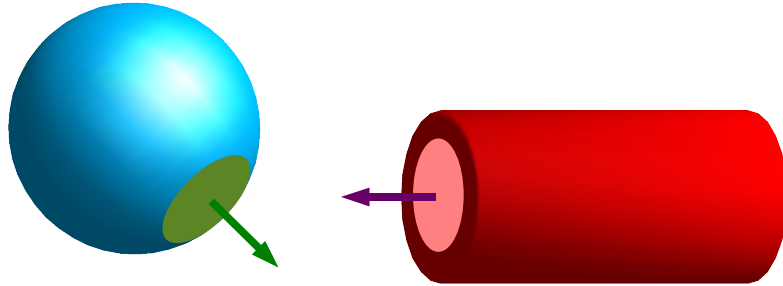
- Unrestricted brownian motion – Low Translation/Rotational

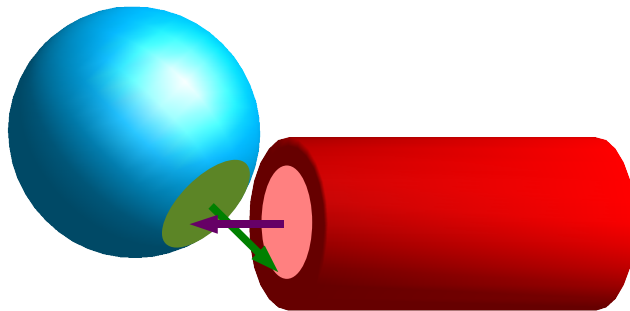
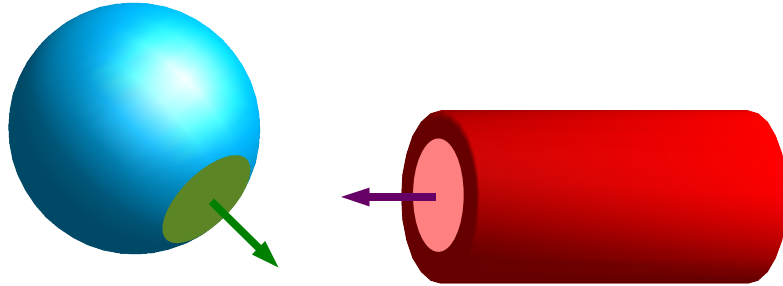
$$b_T = \frac{1}{6\pi\mu r} \quad b_R = \frac{1}{8\pi\mu r^3} \quad \frac{b_T}{b_R} = \frac{4}{3}r^2$$

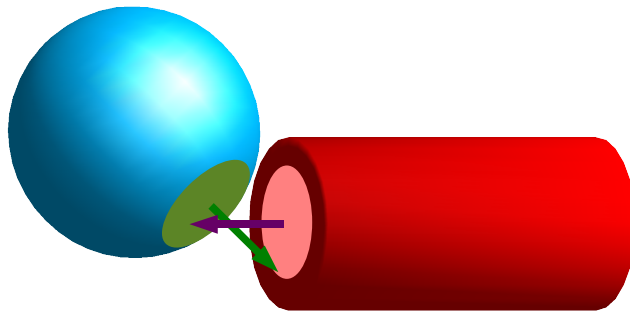
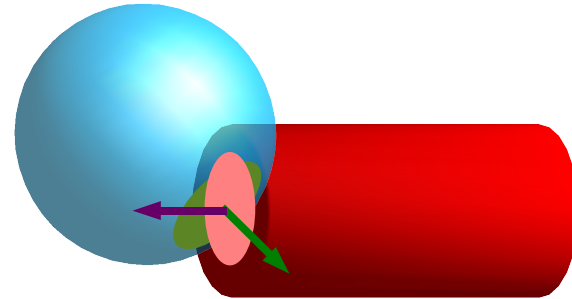
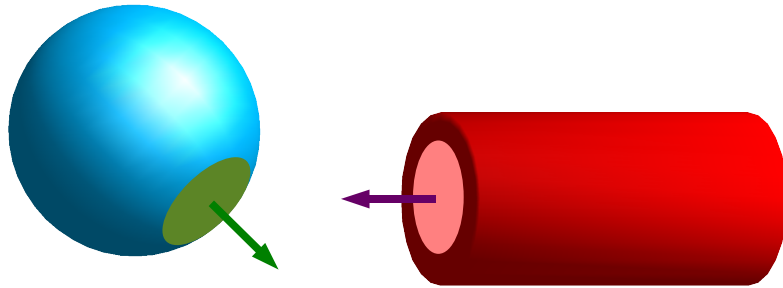
- Intra-membrane diffusion (Saffman and Delbrück 1975)
High Translational/Rotational

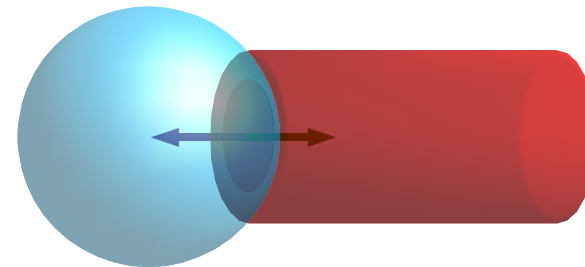
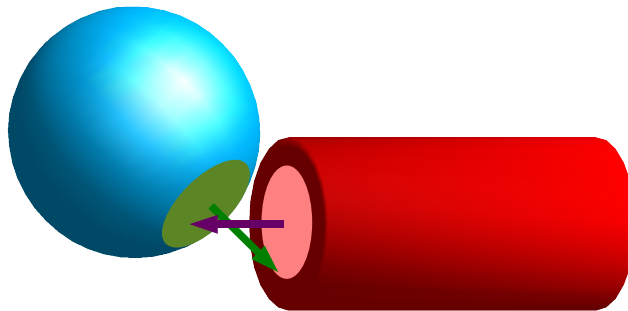
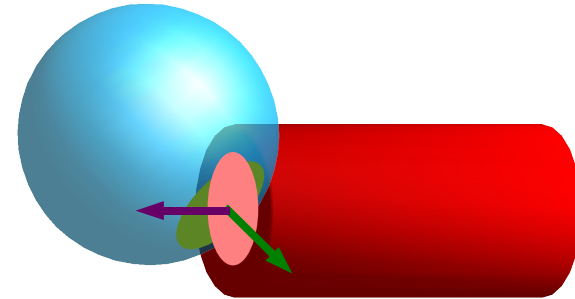
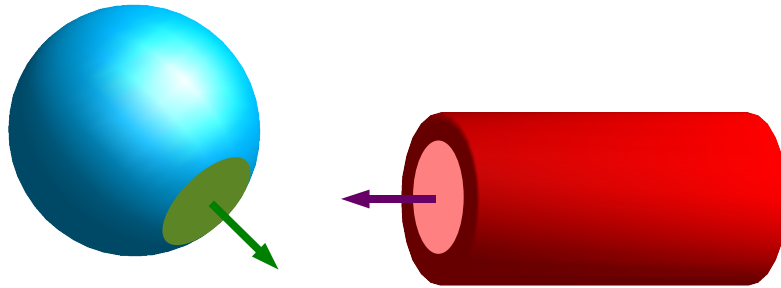
$$b_T = \frac{1}{4\pi\mu h} \left(\log\left(\frac{\mu h}{\mu' r}\right) - \gamma \right) \quad b_R = \frac{1}{4\pi\mu r^2 h} \quad \frac{b_T}{b_R} = \left(\log\left(\frac{\mu h}{\mu' r}\right) - \gamma \right) \times r^2$$

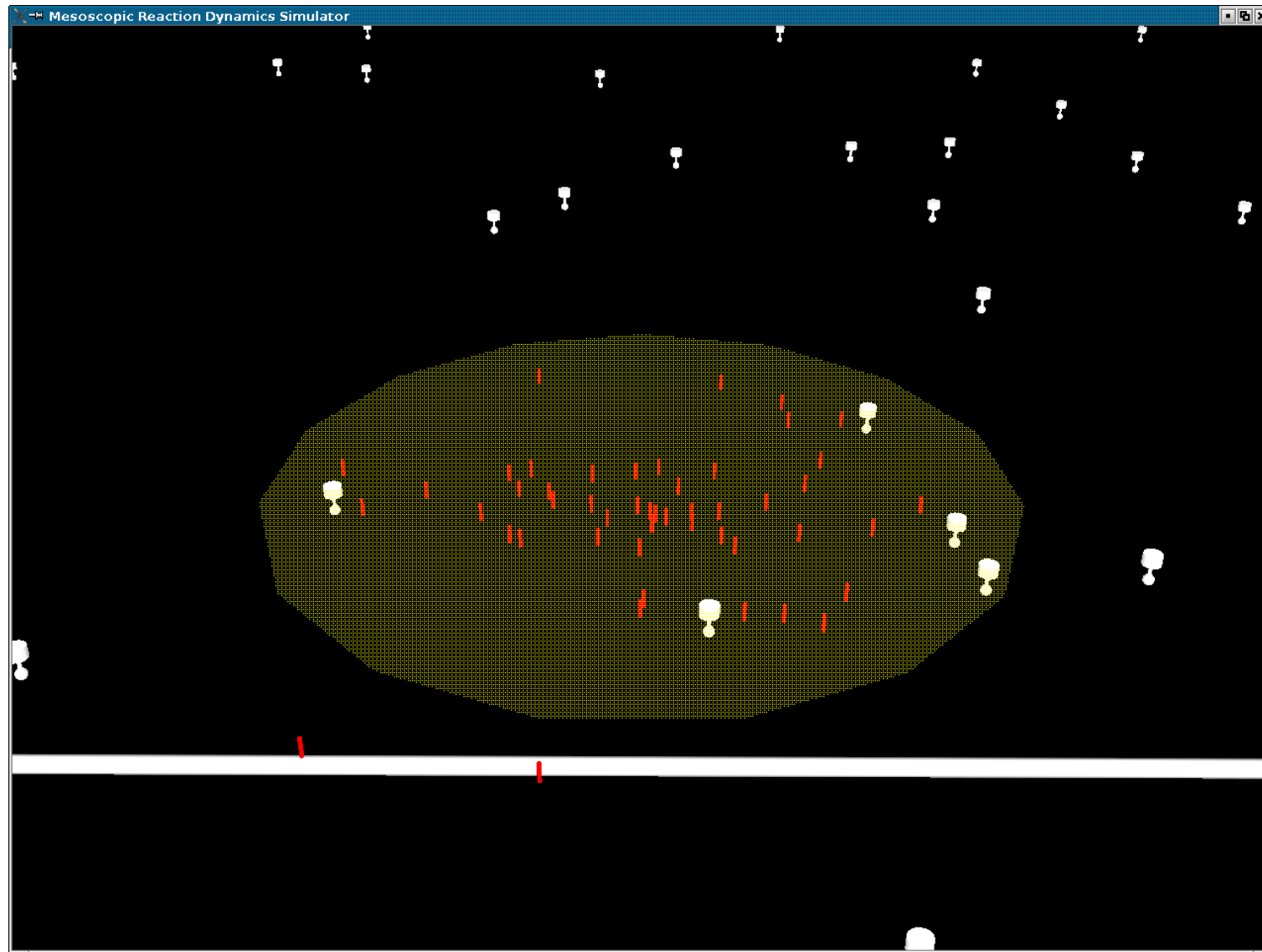


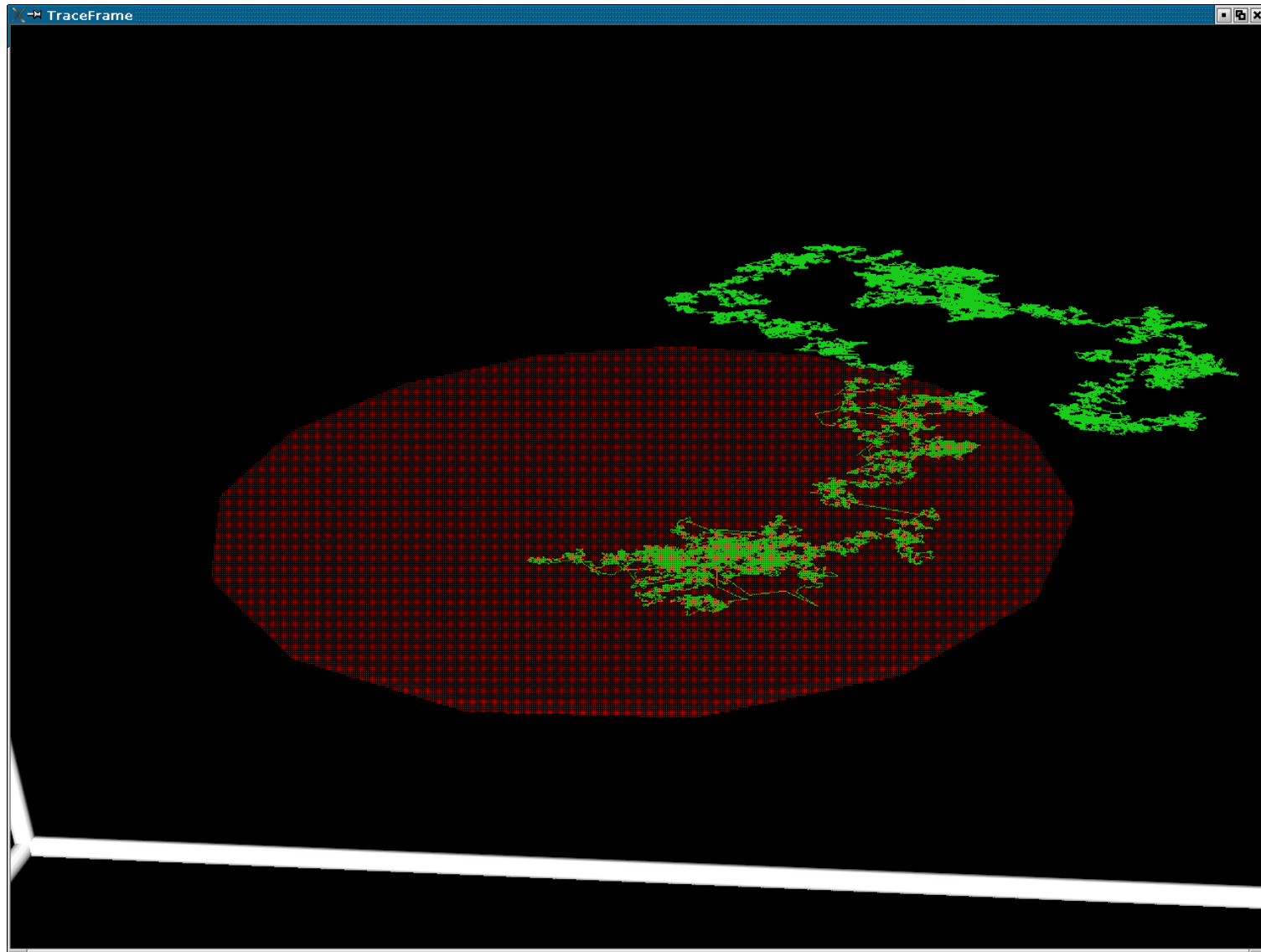










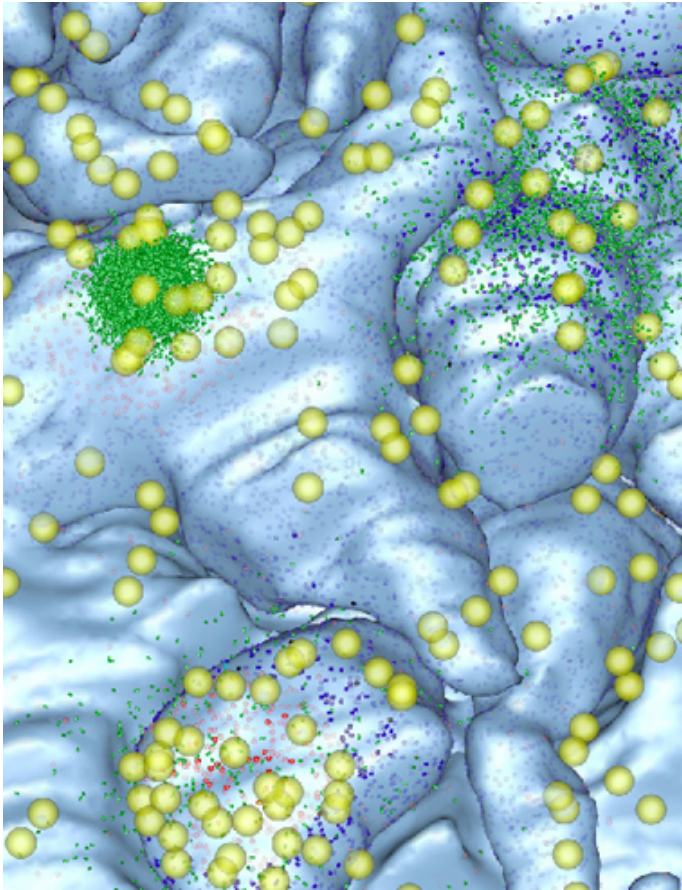


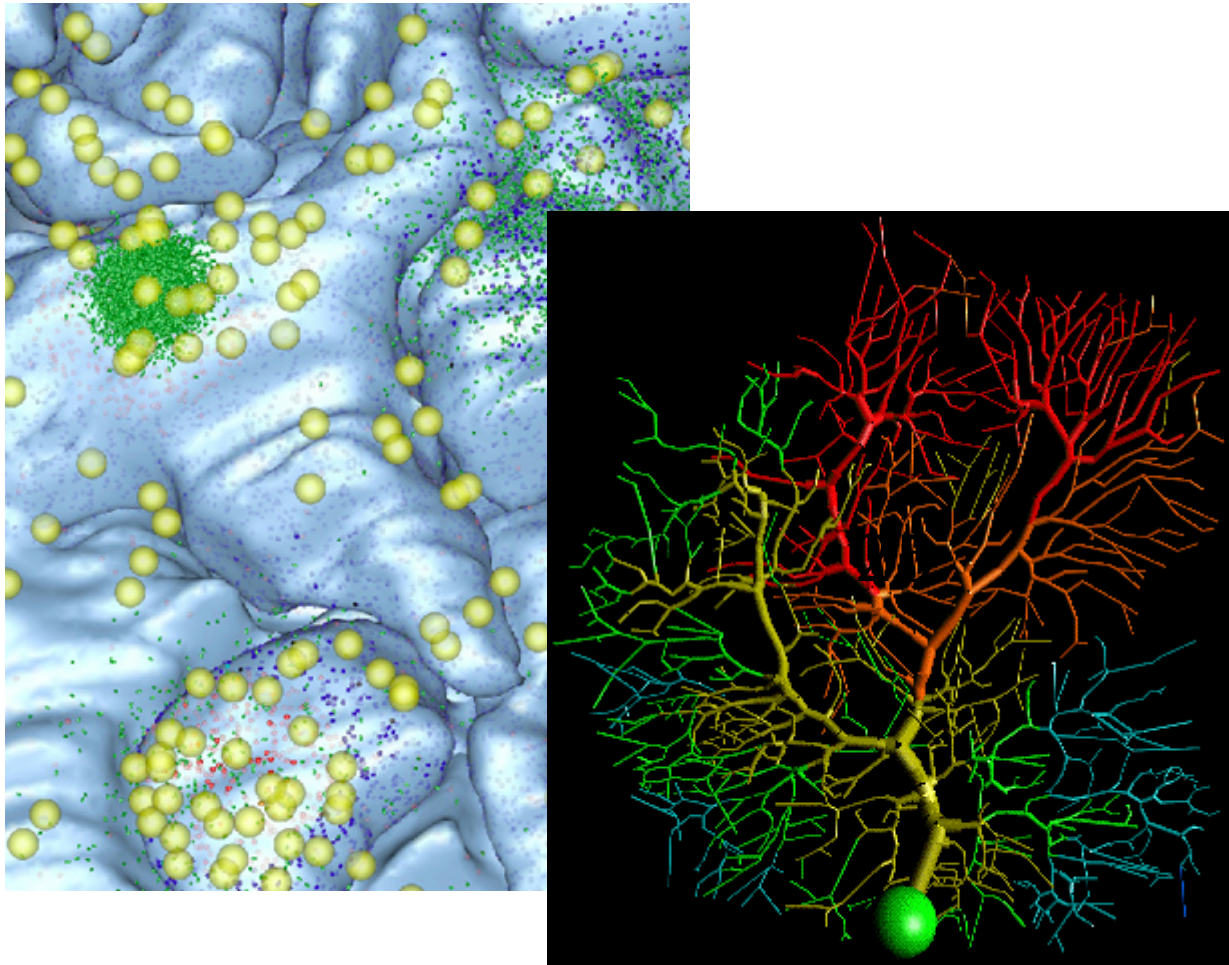
- Dopamine hypothesis
- Glutamate hypothesis
- Neuro-developmental hypothesis
- Cytoskeleton hypothesis
- Molecular, cellular and circuit levels

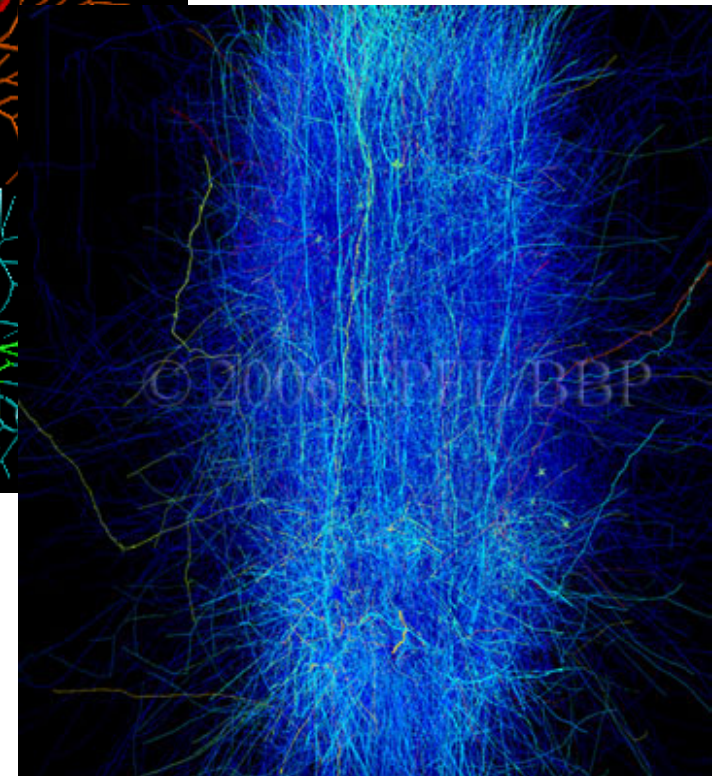
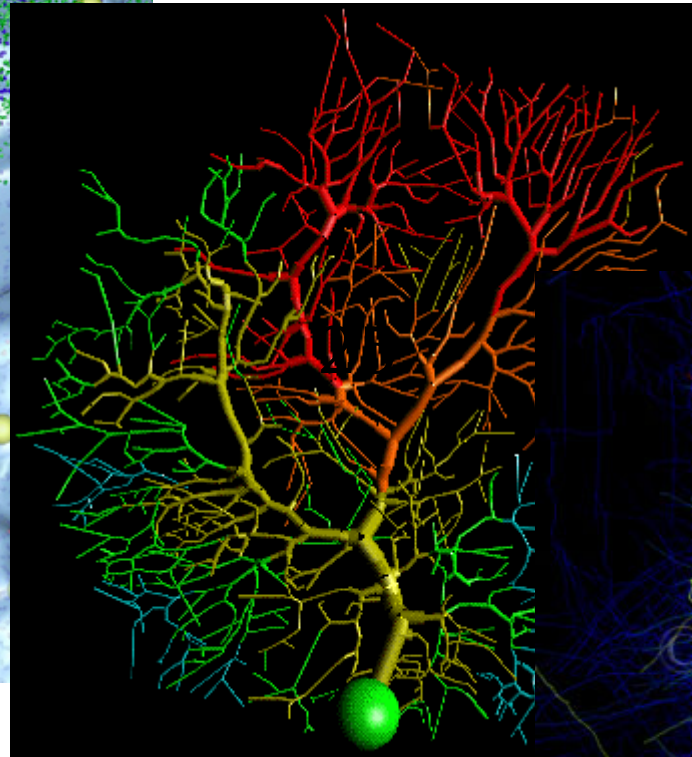
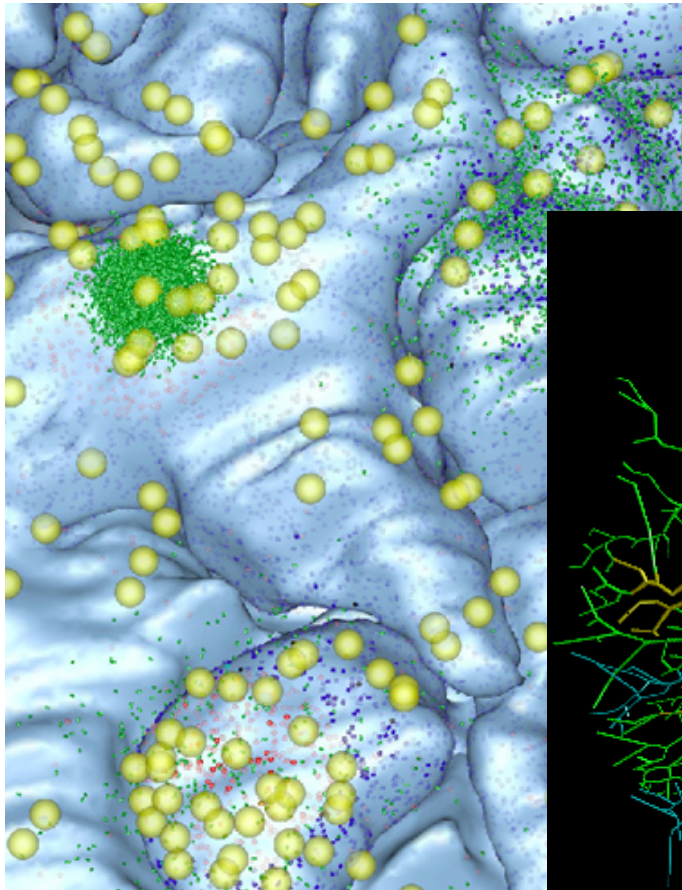


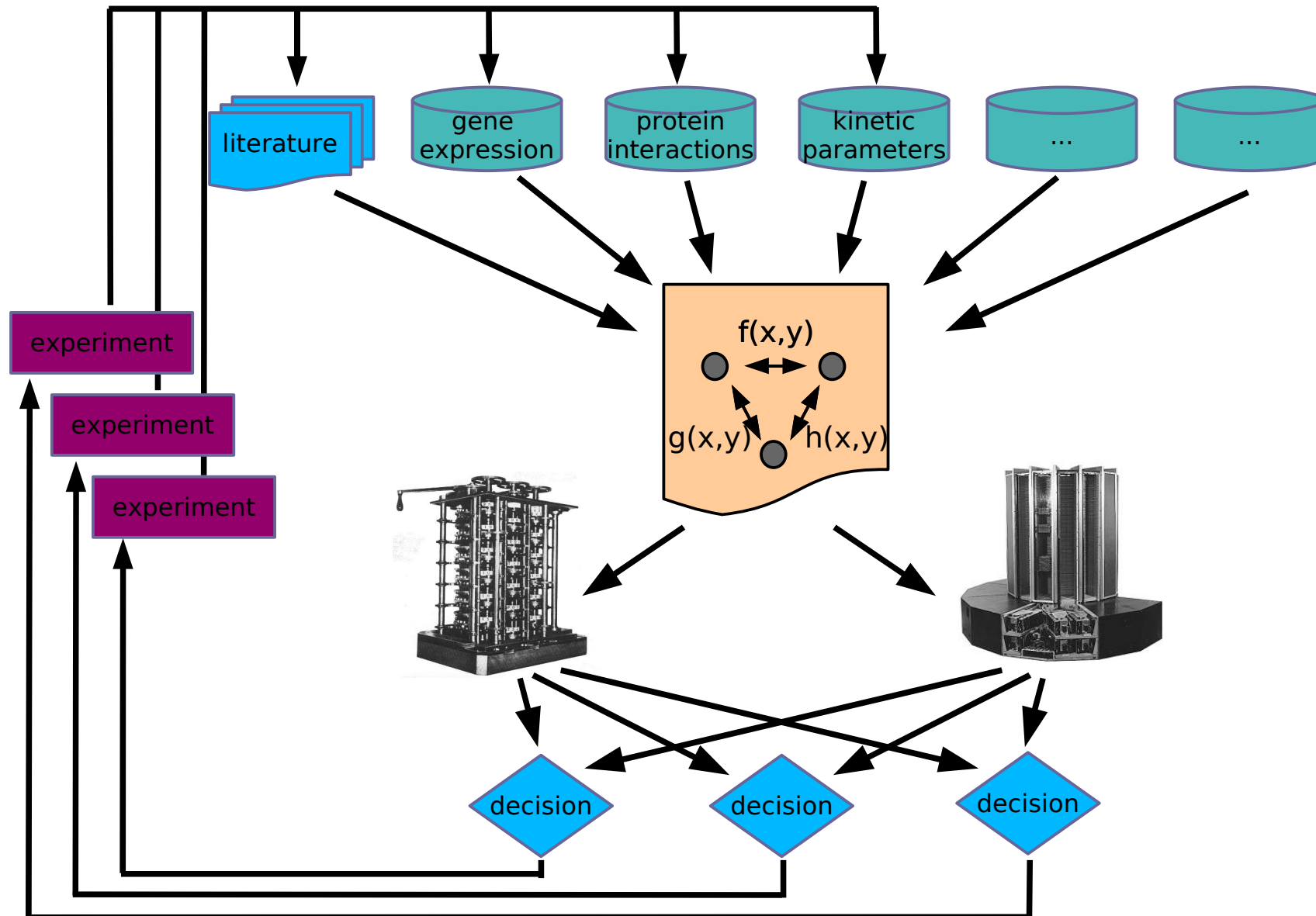
- Dopamine hypothesis
 - Glutamate hypothesis
 - Neuro-developmental hypothesis
 - Cytoskeleton hypothesis
 - Molecular, cellular and circuit levels
-
- ➔ Complex problem: numerous participants
 - ➔ Multi-scale problem: spatial, temporal
 - ➔ Multi-approach problem: biochemistry, physiology, behaviour etc.



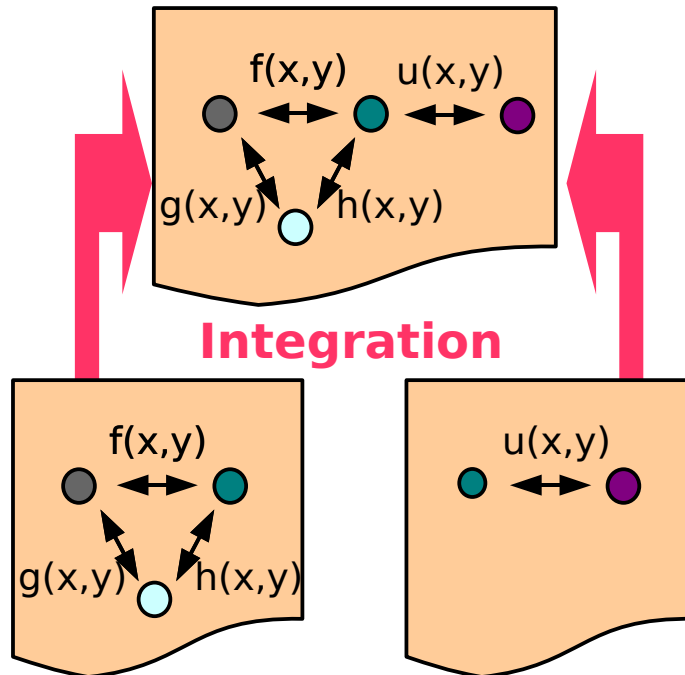


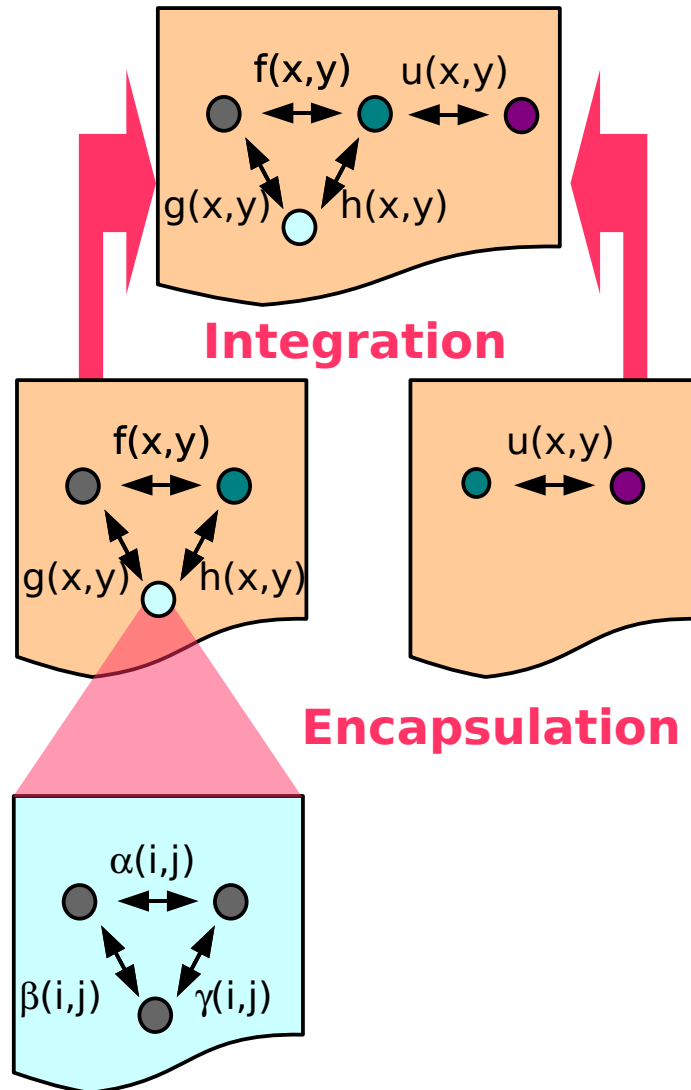


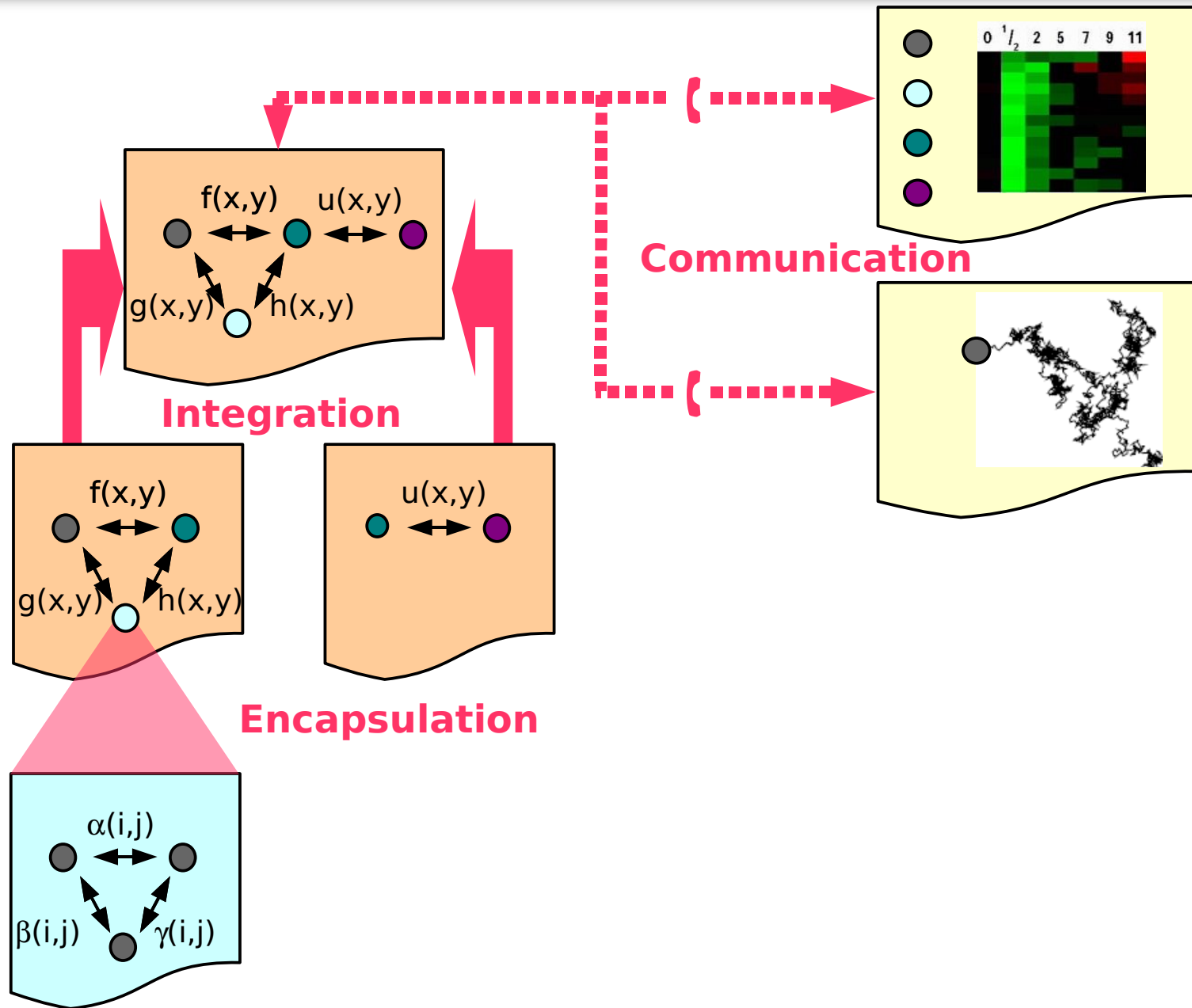


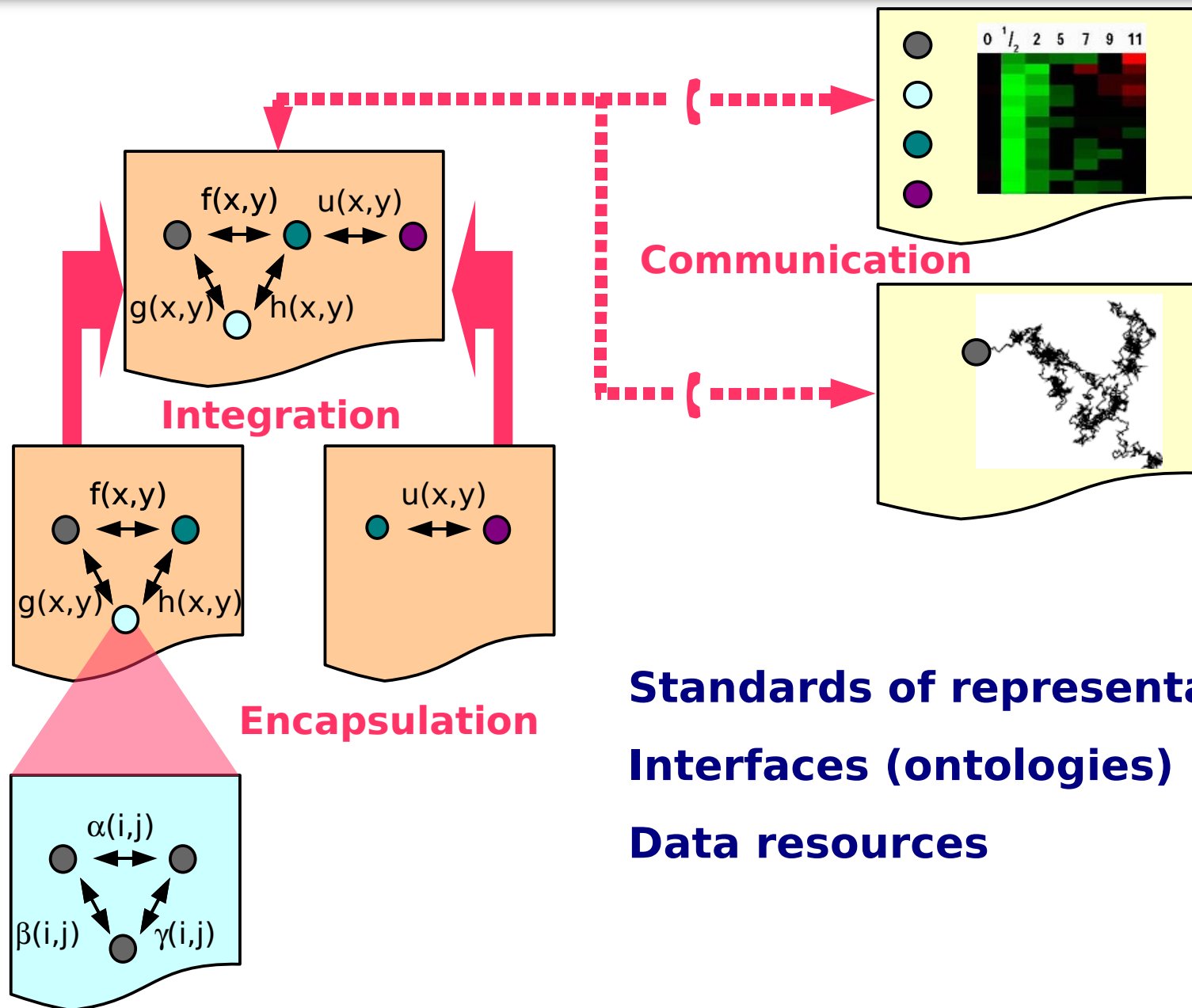












Standards of representation
Interfaces (ontologies)
Data resources



- Systems Biology Markup Language (SBML) and associated tools (e.g. SBMLeditor)

Hucka et al. (2003). The Systems Biology Markup Language (SBML): A Medium for Representation and Exchange of Biochemical Network Models. *Bioinformatics*, 19: 524-531.
Rodriguez et al. (2007) SBMLeditor: effective creation of models in the Systems Biology Markup Language (SBML). *BMC Bioinformatics*, 8:79

- Systems Biology Graphical Notation (SBGN)

- Ontologies: the Systems Biology Ontology (SBO), the Terminology to Describe Dynamics (TEDDY)

Le Novère N. (2006) Model storage, exchange and integration *BMC Neuroscience*, 7: S11.

- Minimal Information Requested In the Annotation of Models
Le Novère et al (2005) *Nature Biotechnology*,

Le Novère et al. (2005) Minimum Information Requested In the Annotation of biochemical Models (MIRIAM) *Nature Biotechnology*, 23: 1509-1515.

- BioModels Database

Le Novère et al. (2006) BioModels Database: A Free, Centralized Database of Curated, Published, Quantitative Kinetic Models of Biochemical and Cellular Systems *Nucleic Acids Research*, 34: D689-D691.

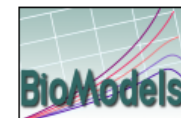


BioModels Database

<http://www.ebi.ac.uk/biomodels/>

A Database of Annotated Published Models

BioModels Database is a data resource that allows biologists to store, search and retrieve published mathematical models of biological interests. Models present in BioModels Database are annotated and linked to relevant data resources, such as publications, databases of compounds and pathways, controlled vocabularies, etc.


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[\[Search \]](#)

👉 05th January 2007 - Seventh Release! [\[More\]](#) [\[Download All Models Under SBML L2 V1 Format\]](#)

👉 4th December 2006 - BioModels Database and DOQCS join forces [\[More\]](#)

👉 July 2006 - PLoS Computational Biology supports BioModels Database [\[more\]](#)


[Acknowledgements](#)

BioModels Database is developed in collaboration by the teams of [Nicolas Le Novère](#) (EMBL-EBI, United-Kingdom), [Michael Hucka](#) (SBML Team, Caltech, USA) in collaboration with [Upinder Bhalla](#) (DOQCS, National Center for Biological Sciences, India), [Herbert Sauro](#) (Keck Graduate Institute, USA), [Hiroaki Kitano](#) (Systems Biology Institute, Japan), [Hans Westerhoff](#) and [Jacky Snoep](#) (JWS Online, Stellenbosch (ZA) and Manchester (UK) Universities and Stellenbosch University, ZA), as part of the [BioModels.net](#) initiative. BioModels Database development has benefitted from funds of the [European Molecular Biology Laboratory](#) (Le Novère team) and the [National Institute of General Medical Sciences](#) (SBML team).

Developers: Mélanie Courtot, Arnaud Henry, Camille Laibe, Chen Li (main developer), Lu Li, Nicolas Rodriguez (Alumni: Marco Donizelli)

Model curators and annotators: Harish Dharuri, Enuo He, Nicolas Le Novère, Lu Li, Rainer Machne, Bruce Shapiro (Alumni: Maria Schilstra)

External contributors: BioModels Database would not exist without the continuous support of many people, whether by their contribution of models, of software, or by their constructive comments and criticisms. It is unfortunately impossible to keep track and to acknowledge all of them here, without risking to be unfair. Therefore, a big collective thank-you all.

BioModels Database is built thanks to many third-party free software such as [libSBML](#), [Jakarta Tomcat](#), [Xindice](#), [Xalan](#), [Xerces](#), [Jena](#) and [MySQL](#).

Main software used to curate models: [CellDesigner](#), [COPASI](#), [Jarnac](#), [MathSBML](#), [XPP-Aut](#), [SBMLdeSolver](#), [SBMLeditor](#) and [SBMLmerge](#).

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Model of the month

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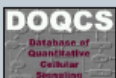
Related Software

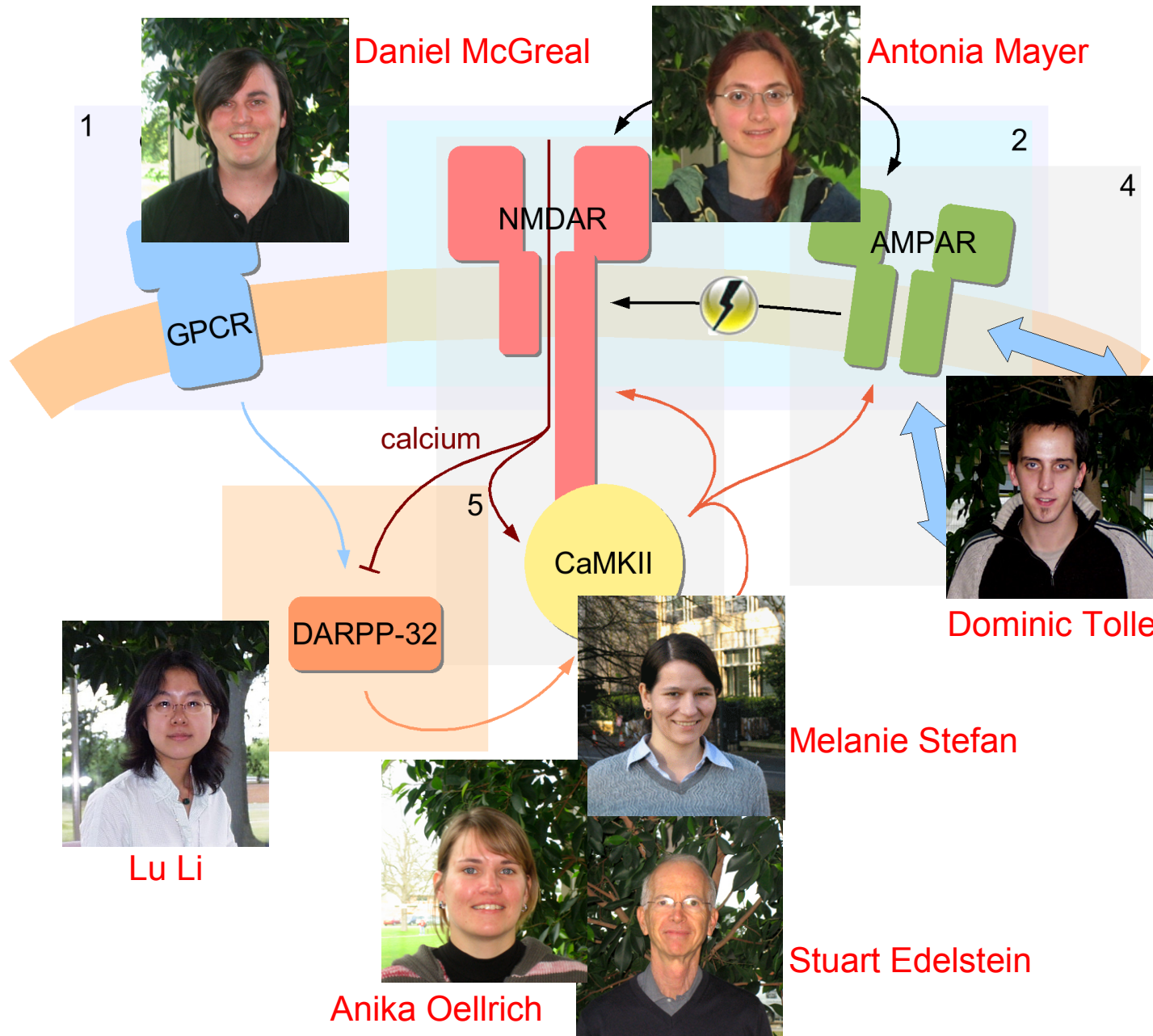
Meetings

Contact

Quote

BIO MODELS.NET





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 - Herbert Sauro
- Vienna TBI
 - Rainer Machne
- Systems Biology Institute
 - Hiroaki Kitano
 - Akira Funahashi
- JWS Online
 - Jacky Snoep
 - Hans Westerhoff
- Journals supporting BioModels Database
 - Molecular Systems Biology
 - PLoS Computational Biology
 - BMC Systems Biology
- Programs used for curation
 - CellDesigner/SBMLodeSolver
 - COPASI
 - Jarnac/JDesigner
 - MathSBML
 - SBMLEditor
 - XPP-Aut

The community of Systems Biology for their contributions of models and comments.

