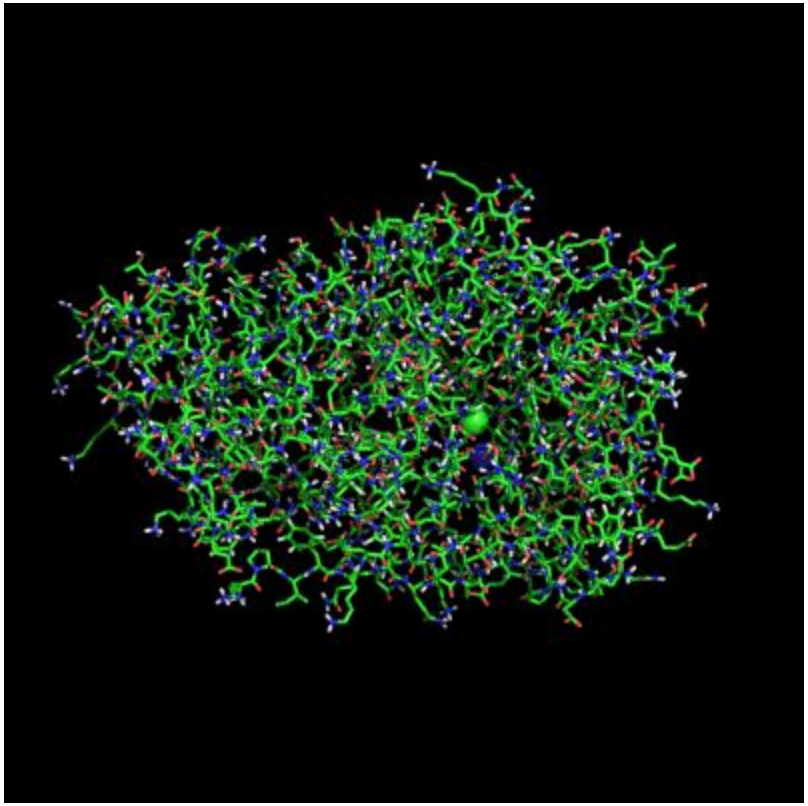
Sparse Matrices in Molecular Simulation and in Physiological Models



When will the ball escape?

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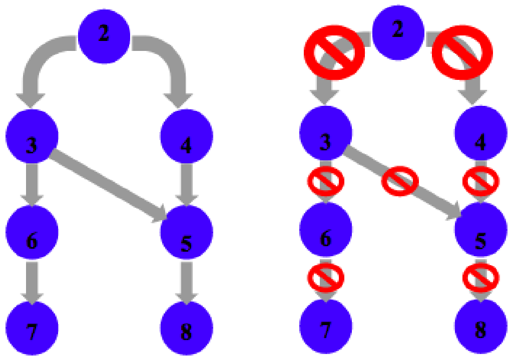
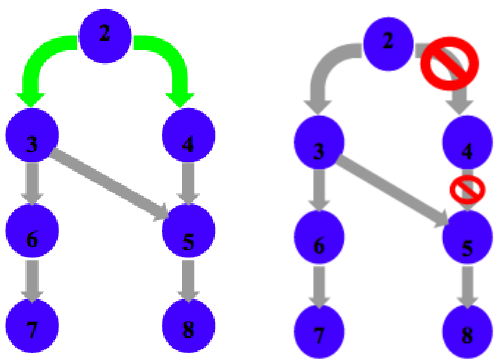
Sparse Days Toulouse, France, 2019-07-11

Sparse Transition Networks



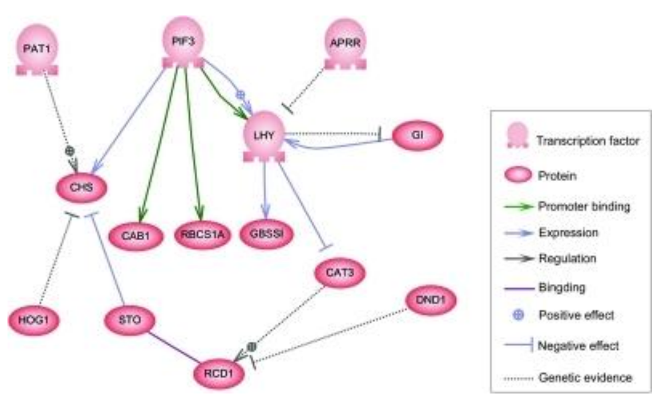
healthy



FOP

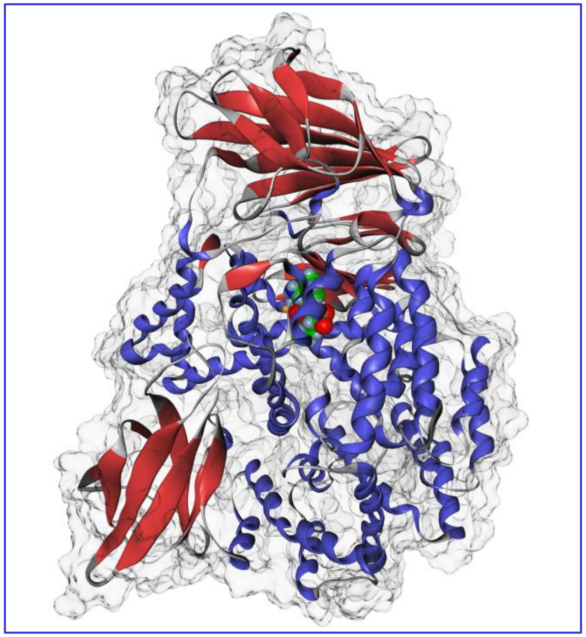
State	Description
2	Receptor activation
3	Smad1/5/8 phosphorylation
4	p38 MAPK phosphorylation
5	ID1/ID3 upregulation
6	MSX2 upregulation
7	MSX2 physiological response
8	ID1/ID3 physiological response

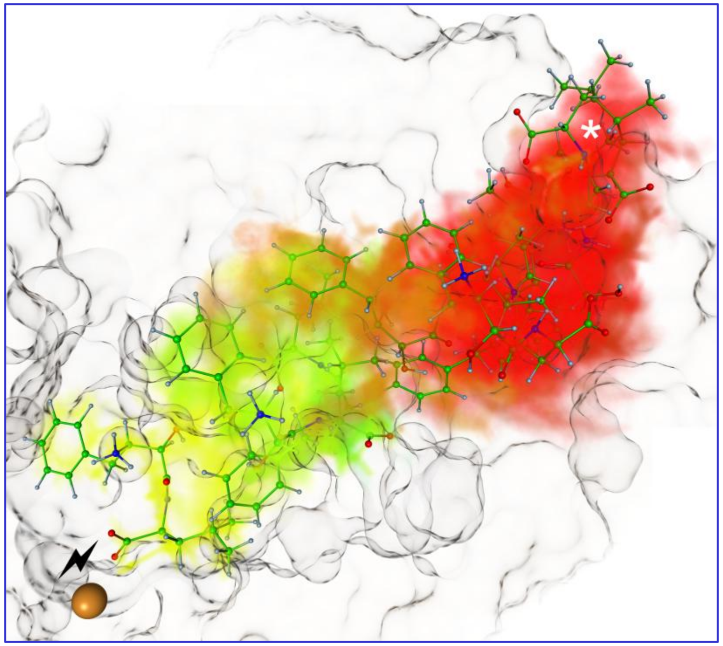
DeSouza, Quaranto, Weber (unpublished 2019)



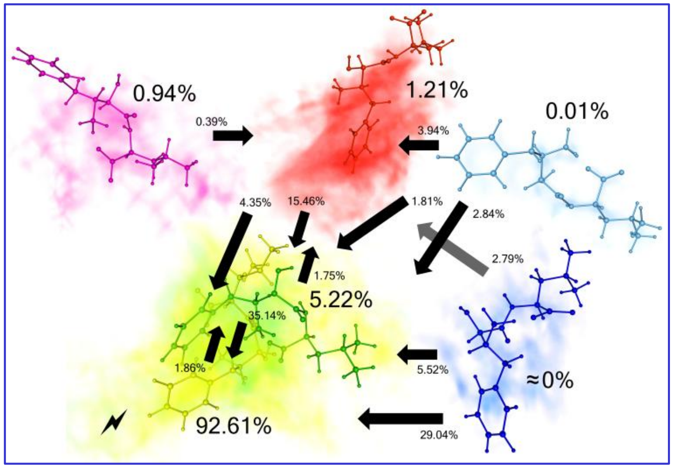
http://openi.nlm.nih.gov/detailedresult.php?img=2993235_mplantssq046f07_4c&req=4

Molecular Simulation

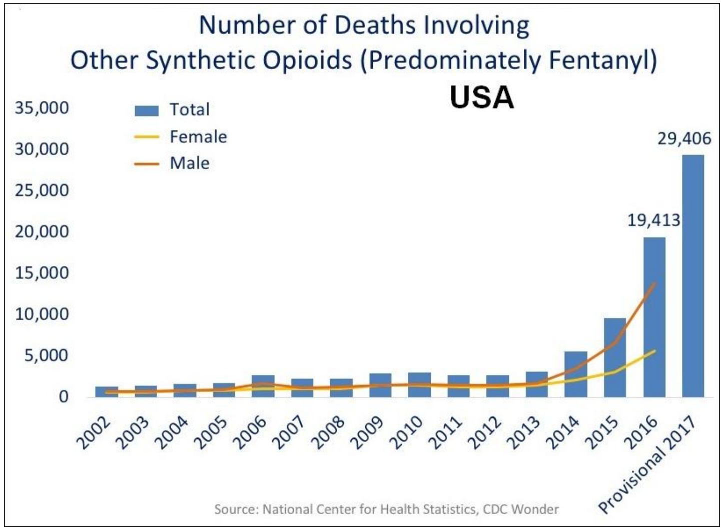




A. Bujotzek, M. Weber: Efficient Simulation of Ligand-Receptor Binding Processes Using the Conformation Dynamics Approach. *Journal of Bioinformatics and Computational Biology*, 7(5):811-831, April 2009

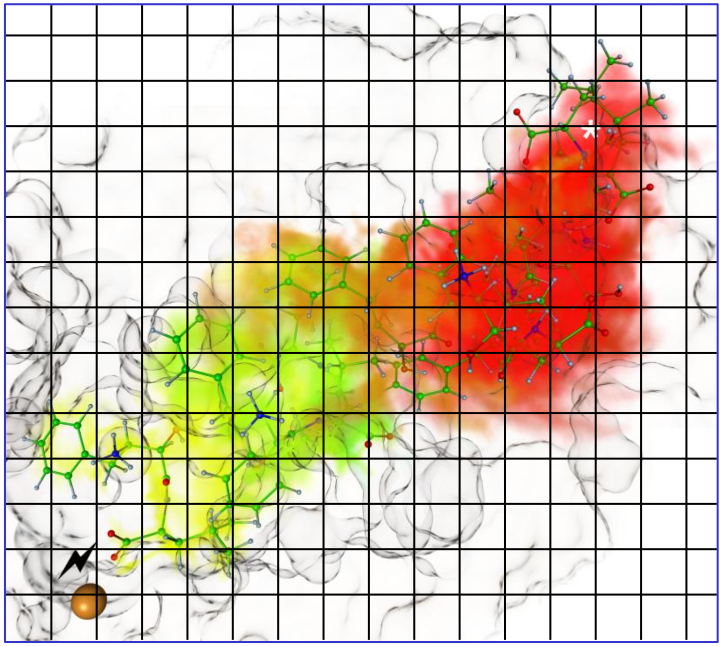


Results



V. Spahn, G. Del Vecchio, D. Labuz, A. Rodriguez-Gaztelumendi, N. Massaly, J. Temp, V. Durmaz, P. Sabri, M. Reidelbach, H. Machelska, M. Weber, C. Stein: A nontoxic pain killer designed by modeling of pathological receptor conformations. *Science*, 355(6328):966-969, March 2017

Algorithm (Sparse)



dimension: 3N

alternative: reaction coordinates

Algorithm (Sparse)

L. Donati, M. Heida, M. Weber, B. Keller: Estimation of the infinitesimal generator by square-root approximation, Weierstraß Report Nr. 2416, 2018.

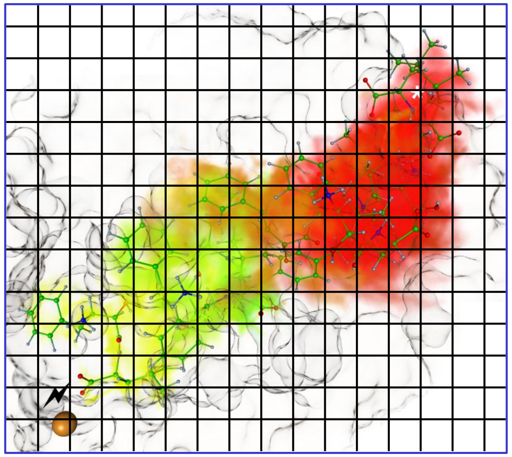
$$L = \mu(D^{-1}AD + E)$$

diag(negative row sums)

unknown flux

probabilities dependening on energy

adjacency matrix („dimension“?)



project B05 in CRC 1114

Algebraic Structure

$$
P = \begin{array}{|cccc|}
\hline
P11 & P12 & P13 & P14 \\
P21 & P22 & P23 & P24 \\
P31 & P32 & P33 & P34 \\
P41 & P42 & P43 & P44 \\
\hline
\end{array}
$$

$$P_{ij} = \exp\left(\tau L_{ij}\right)$$

Linear Algebraic Problem

$$P = X\Lambda$$

real Schur matrix

$$\begin{matrix} 1 & * & * & * & * \\ 0 & \lambda_1 & * & * & * \\ 0 & 0 & \lambda_2 & * & * \\ 0 & 0 & * & \lambda_2 & * \\ 0 & 0 & 0 & 0 & \lambda_3 \end{matrix}$$

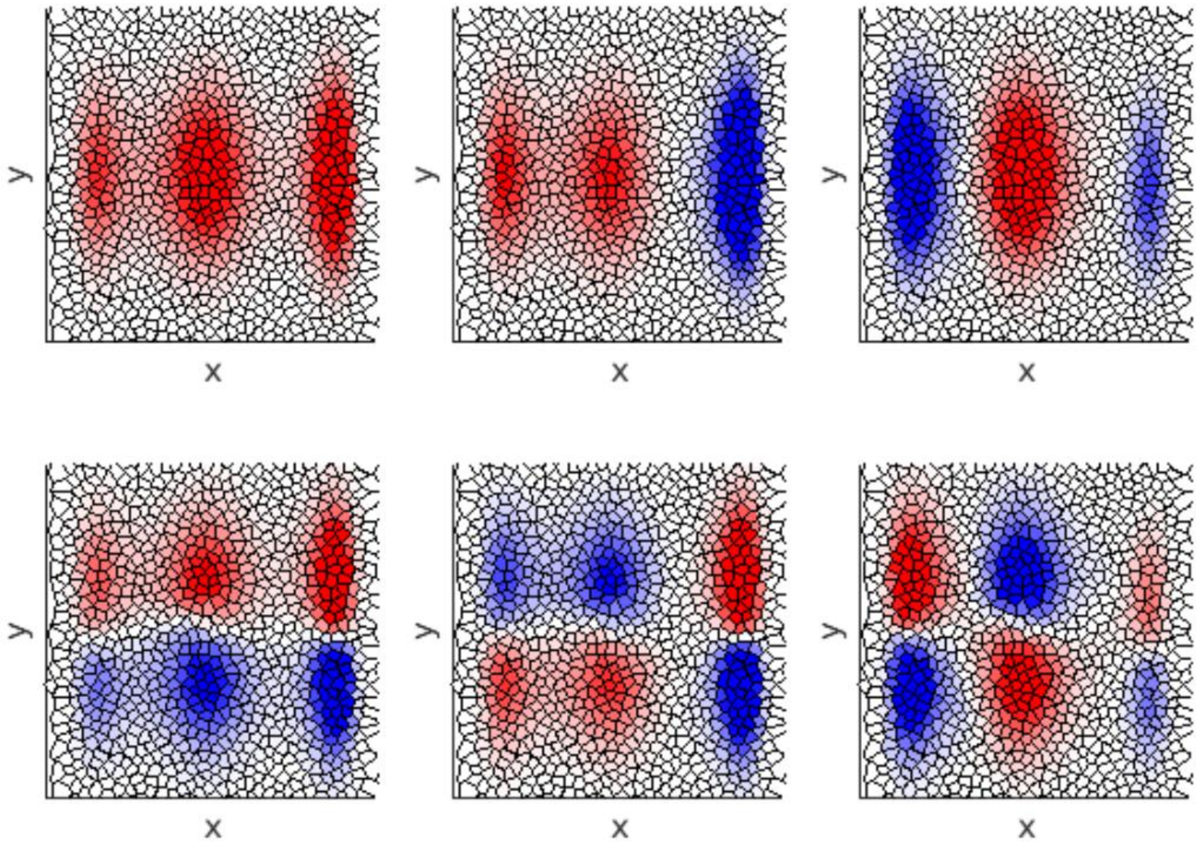
Schur vectors

$$X^T D^2 X = I$$

-slowest timescales
-rate-determining steps
-reaction coordinates
-reversibility (entropy production)

Intepretation of Solution

For one point in time:



Computational Alternatives (Theory)

$$P = \begin{bmatrix} P11 & P12 & P13 & P14 \\ P21 & P22 & P23 & P24 \\ P31 & P32 & P33 & P34 \\ P41 & P42 & P43 & P44 \end{bmatrix}$$

$$P_{ij} = \exp\left(\tau L_{ij}\right)$$

K. Fackeldey, P. Koltai, P. Nevir, H. Rust, A.Schild, M. Weber: From Metastable to Coherent Sets -- time-discretization schemes. *Chaos,* 29:012101, 2019.

Computational Alternatives (Missing Data)

$$P = \begin{pmatrix} \mathbf{x} & \dots & \dots & \mathbf{x} \\ \mathbf{u} & \dots & \dots & \mathbf{u} \\ \vdots & & & \vdots \\ \mathbf{x} & \dots & \dots & \mathbf{x} \\ \mathbf{u} & \dots & \dots & \mathbf{u} \\ \mathbf{x} & \dots & \dots & \mathbf{x} \\ \mathbf{x} & \dots & \dots & \mathbf{x} \\ \mathbf{u} & \dots & \dots & \mathbf{u} \\ \vdots & & & \vdots \\ \vdots & \dots & \dots & \vdots \end{pmatrix} \rightsquigarrow P_R = \begin{pmatrix} \mathbf{x} & \dots & \dots & \mathbf{x} \\ \mathbf{x} & \dots & \dots & \mathbf{x} \\ \mathbf{x} & \dots & \dots & \mathbf{x} \\ \vdots & & & \vdots \\ \mathbf{x} & \dots & \dots & \mathbf{x} \end{pmatrix}$$

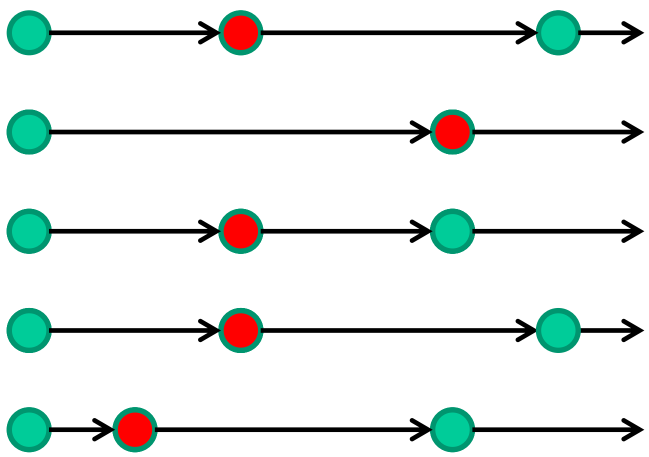
Figure 2: Given the matrix P we delete the unknown rows and obtain P_R which is rectangular. The matrix P_R has k rows and n columns.

$$\widetilde{P} = \begin{pmatrix} * & \dots & \dots & \mathbf{x} \\ \mathbf{x} & \ddots & \dots & \mathbf{x} \\ \mathbf{x} & \dots & \ddots & \mathbf{x} \\ \mathbf{x} & \dots & \dots & * \end{pmatrix}$$

Figure 3: The matrix $\widetilde{P}$ is constructed by skipping the corresponding columns $\ell \in [n-k]$ and summing the skipped values row-wise onto the diagonal , * - summed diagonal elements according to (5).

K. Fackeldey, A. Niknejad, M. Weber: Finding Metastabilities in Reversible Markov Chains based on Incomplete Sampling: Case of Molecular Simulation. *Spec. Matrices,* 5:73–81, 2017

Computational Alternatives (Concept)



L11	L12	L13	L14
L21	L22	L23	L24
L31	L32	L33	L34
L41	L42	L43	L44

Research Question

Algorithms to compute (partial, real) Schur decompositions of matrices which are not sparse, but which are constructed block-wise from exponentials of sparse matrices.

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