



UNIVERSITY OF AMSTERDAM

UvA-DARE (Digital Academic Repository)

Stochasticity in signal transduction pathways

Vidal Rodriguez, J.

Publication date
2009

[Link to publication](#)

Citation for published version (APA):

Vidal Rodriguez, J. (2009). *Stochasticity in signal transduction pathways*.

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

Contents

1	Introduction	1
1.1	The Computer in Systems Biology	2
1.1.1	The Research Cycle	3
1.2	Models: Purpose and Focus	5
1.2.1	Macro, Meso and Microscopic Scales	6
1.2.2	Regimes	6
1.3	Stochastic Phenomena in Bacteria	8
1.4	Computer Methods for Stochastic Chemical Reactions	10
1.5	Signalling Systems in Bacteria	13
1.5.1	Two-Components Signalling Systems	15
1.6	Objectives of this Thesis	17
1.7	Overview of this Thesis	18
2	Gillespie Multiparticle Method	21
2.1	Background	21
2.2	Description of GMP	22
2.2.1	The Operator-Split Reaction-Diffusion	22
2.2.2	The Diffusion Process	24
2.2.3	The Reaction Process	25
2.2.4	Choosing a Lattice Discretisation Size	26
2.3	Enhancements for Low Numbers of Particles	26
2.3.1	Qualitative Computational Cost Comparison	28
2.4	Detailed Analysis of the GMP Reaction Mechanism	30
2.4.1	The Reversible Diffusion-Limited Reaction of a Pair of Molecules	30
2.4.2	Effects of the Operator-split on the Distribution	32
2.5	Discussion	34
2.6	Conclusions	35
3	Noise and Spatial Comparisons	37
3.1	Noise in Gene Expression	38
3.1.1	The Model	39
3.1.2	Comparison of Noise	40
3.1.3	Reversible Pair	42

3.1.4	Discussion	45
3.2	PTS in <i>Escherichia coli</i>	46
3.2.1	The Model	46
3.2.2	Results	48
3.2.3	Discussion	50
3.3	Chemotaxis: Activation of Flagellar Motors	51
3.3.1	The Model	52
3.3.2	Results	54
3.3.3	Conclusions	56
3.4	Conclusions	57
4	Response Time of TCSP	59
4.1	The Two-Component Signalling System Model	61
4.2	Analysis of the Individual Processes	63
4.2.1	Scattered Sensors Reduce Response Time	63
4.2.2	Few Transcriptions Suffice to Reduce Time Significantly	65
4.2.3	Time to Deliver the Signal to a Promoter	65
4.3	Analysis of the Response Time	66
4.3.1	Modelling the Signalling Response Time	66
4.3.2	Similar Numbers of Histidine-Kinases and Transcription Factors for an Optimal Response Time	68
4.3.3	Correlated Numbers of HK and TF	70
4.3.4	Assuming non-Diffusion-Limited Rates	71
4.4	Discussion	72
4.5	Conclusions	75
5	Processivity Effects in Gene Expression	77
5.1	Statistical Properties of <i>Escherichia Coli</i> Gene Length	78
5.1.1	Is <i>E. coli</i> Representative of Microbes?	79
5.2	Modelling Expression of HK and RR	83
5.2.1	Transcription	84
5.2.2	Translation	86
5.3	Expression Ratios and Optimality	88
5.4	Dynamics of Translation	88
5.5	Discussion	92
5.6	Conclusions	94
6	Summarising discussion	95
6.1	Future work	99
	Summary	101
	Samenvatting	103
	Acknowledgements	105
	Publications	109

References	111
Index	119