Mesoscopic methods for noisy biochemical processes (I)

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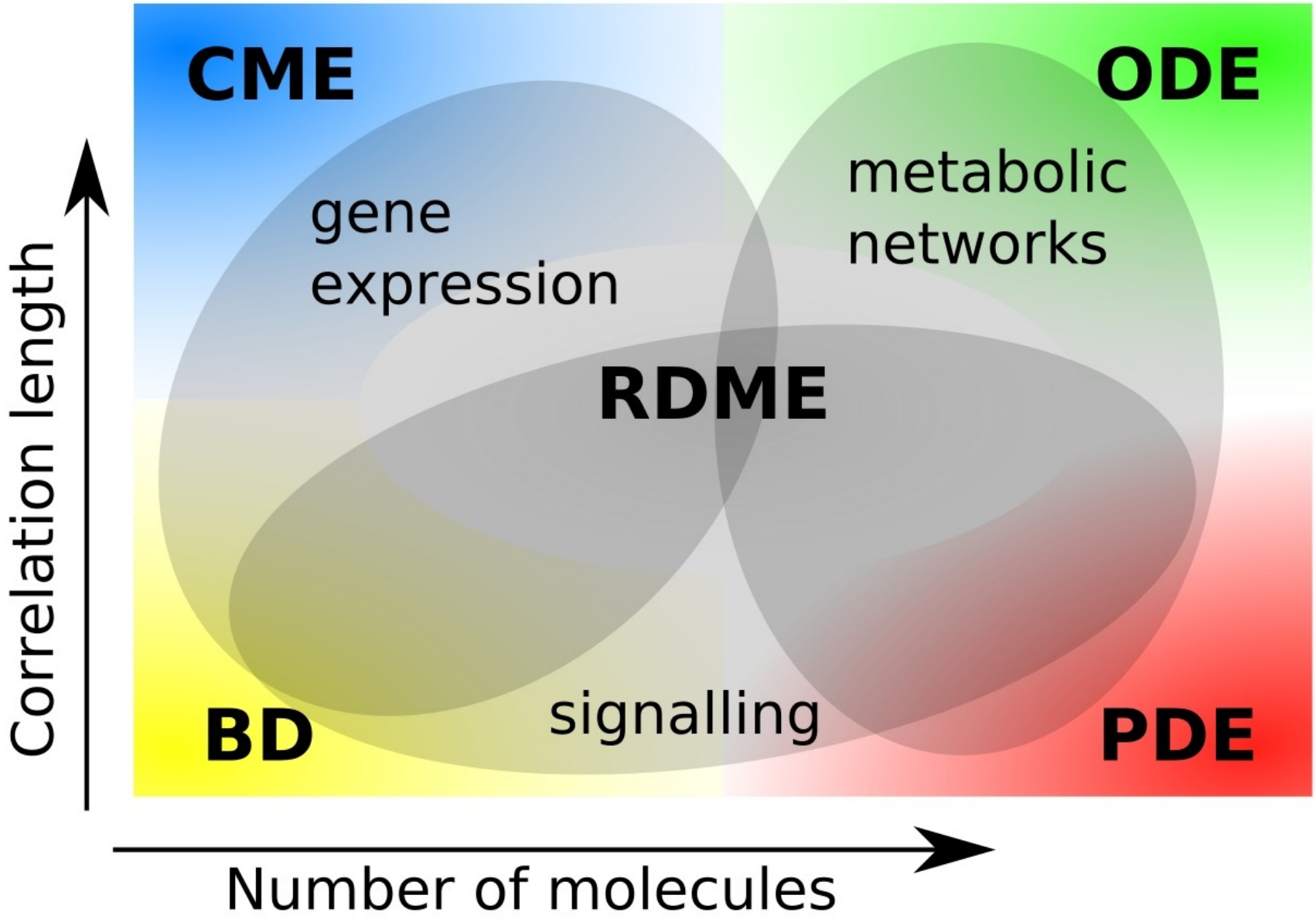
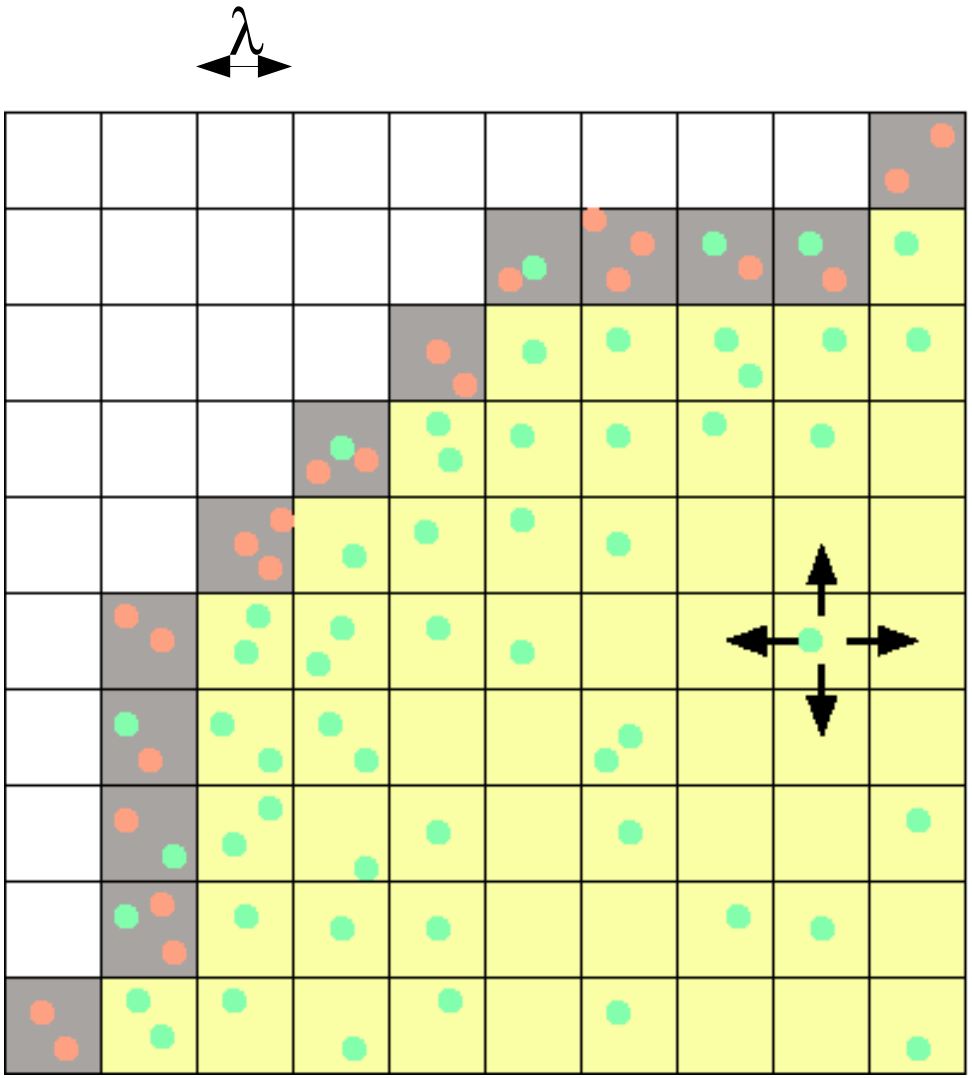
Noise in Life, Barcelona, June 2006

Models and Scales



Solving RDME – GMP



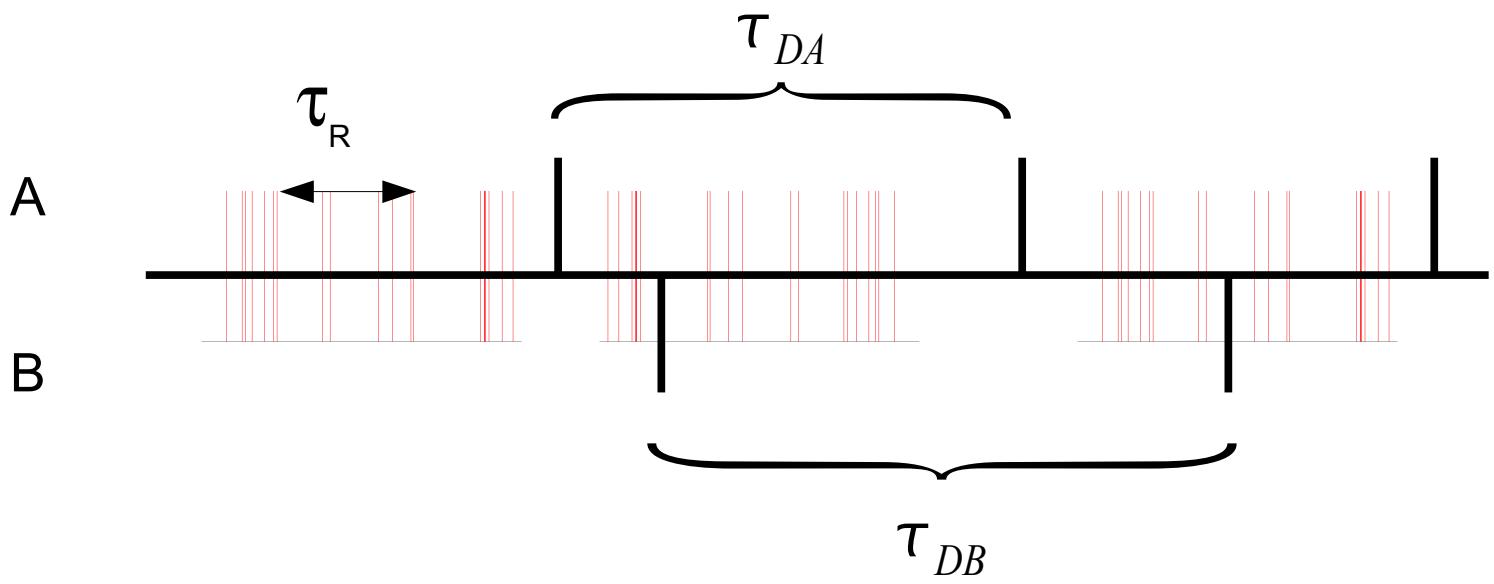
- Lattice with L^d cells
- No exact position of particles is used.
- Compartments
- Two processes:
  - Diffusion
  - Reaction

GMP – Reaction and Diffusion

In the lattice cell we have a *reaction-limited* system:

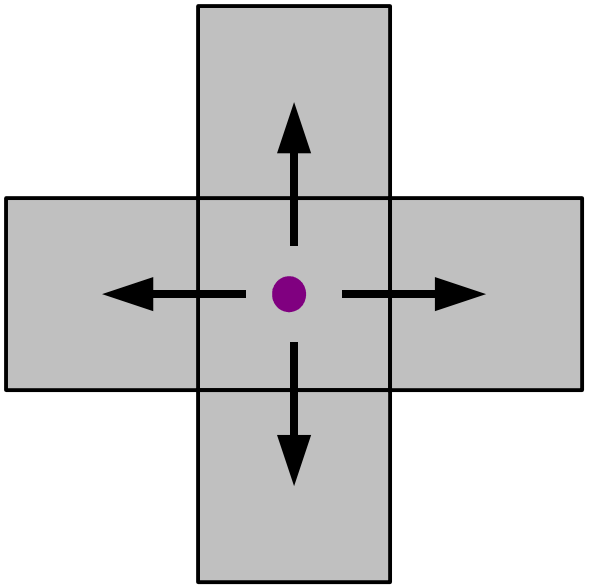
- Particles are close enough that reaction times do not depend on diffusion.
- Reaction events are independent: reaction intervals are *exponentially* distributed

Splitting Reaction and Diffusion

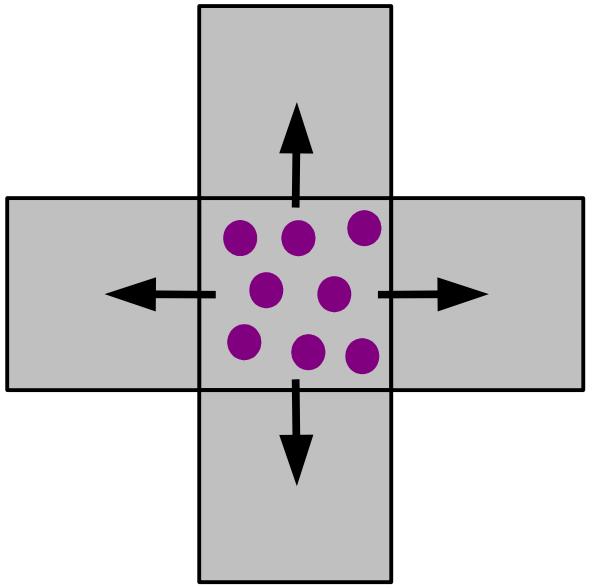


Gillespie, *J. Phys. Chem.* 81(25) 1977
Vidal *et. al.*, *Bioinformatics* 2006

GMP – Diffusion



Particle by particle



Normally distributed

- Link between jumps and diffusion coefficient

From the mean square displacement equation, a step takes on average:

$$\tau = \frac{1}{2\mathrm{d}} \frac{\lambda^2}{D}$$

Chopard, *et. al.*, *Int. J. Mod. Phys.* 5(1) 1994

Limitations of GMP

- For systems that have spatial inhomogeneity (i.e. gradients, patterns,...) we have to choose a proper cell size.

- A minimum and safe value is 2σ, σ diameter of particle (What if different σ?).
- A reasonable value is the reaction mean free path:

$$\lambda_{rmfp} = \sqrt{\langle \tau_R \rangle (D_A + D_B)}$$

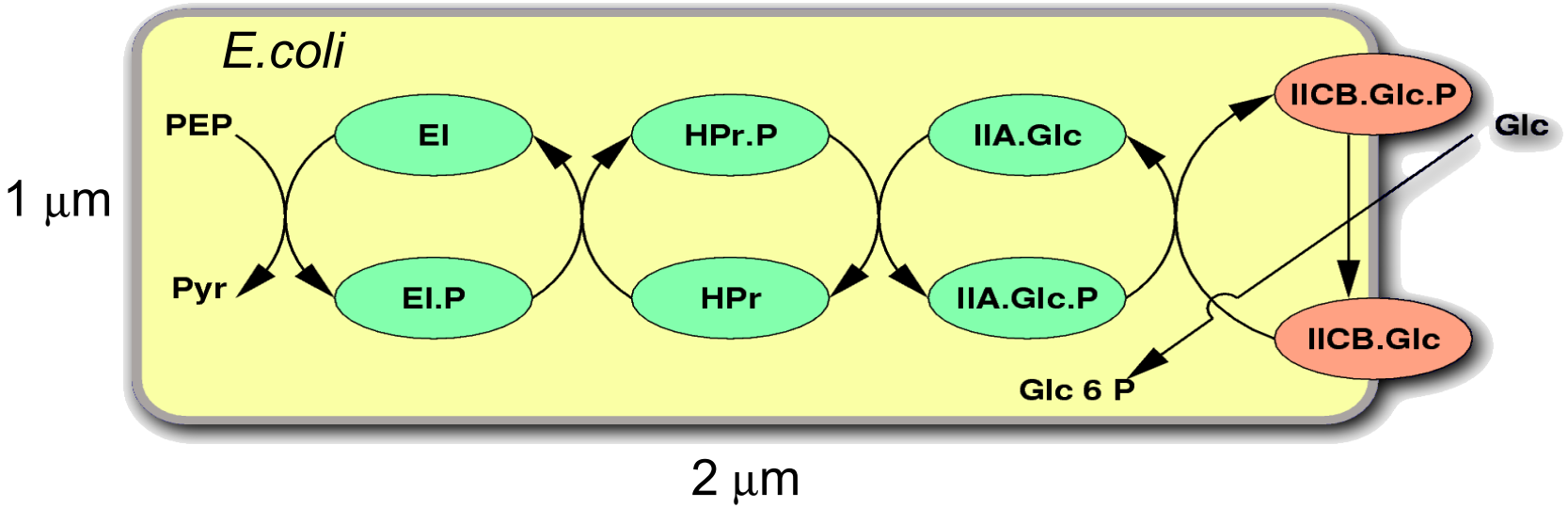
$$\langle \tau_R \rangle = \frac{V N_A}{k A B}$$

- These limitations are applicable to RDME methods.

Baras,F. and Malek Mansour,M., *Phys. Rev. E* 54(6) 1996

Test Case – Spatial Localisation

Phosphoenolpyruvate-dependent phosphotransferase pathway



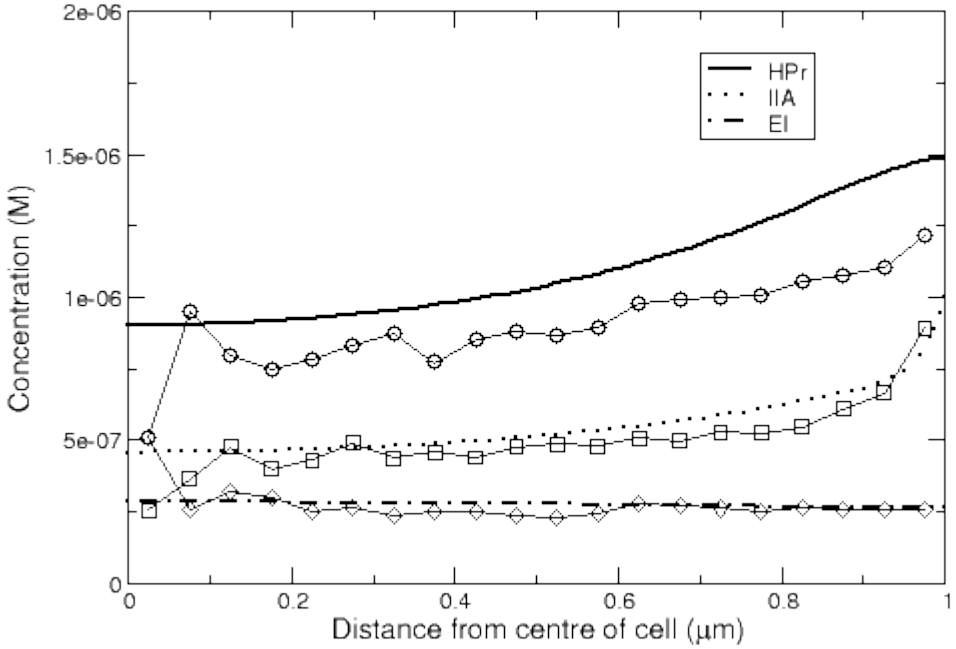
	Numb. Molec.
EI	1500
Hpr	15000
IIA	12000
PEP	880000

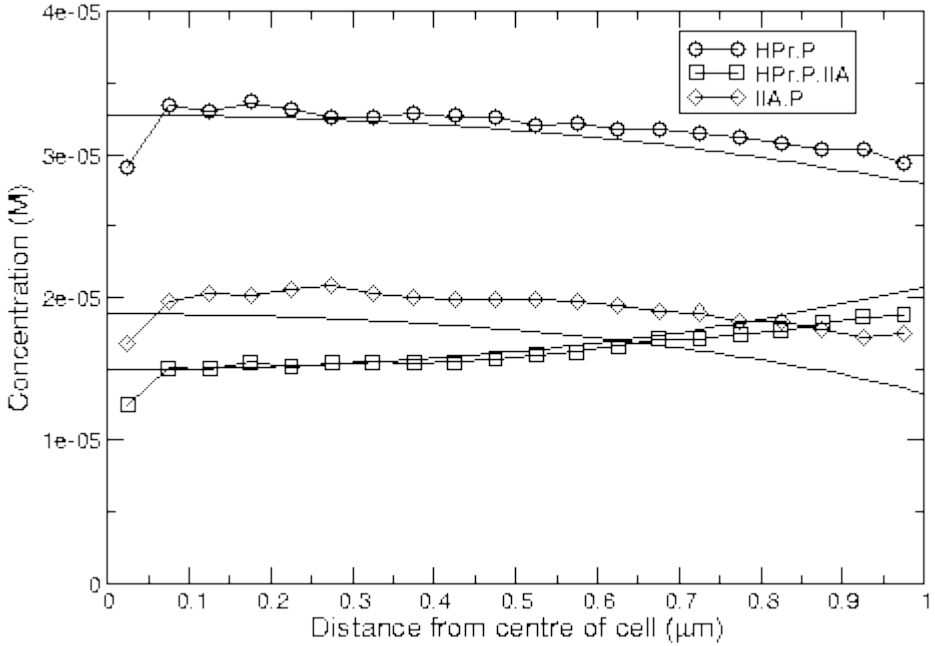
Diffusion approx. 200-300 $\mu m^2\, min^{-1}$

Reaction rates:
- Bimolecular 300 – 21000 $\mu M^{-1}\, min^{-1}$
- Monomolecular 4000 – 108000 min^{-1}

Rohwer *et. al.*, *J. Biol. Chem.* 2000

Test Case – Results





Lattice size λ=1/20 μm, after compromise between different λs.

Vidal *et. al.*, *Bioinformatics* 2006

Conclusions

- In *complex* biochemical cell processes we need to cope with broad ranges of problem scales: From the discrete and stochastic to the continuous and deterministic.

- Localization, spatial and stochastic effects occur in large biochemical systems.

- We can deal with them, at least approximately.

- GMP (and the class of RDME solvers) is a flexible tool to tackle these broad-scales complex systems.

- Still more work is needed to determine lattice size *a priori* to obtain proper noise.

Thanks

- Jaap Kaandorp (UvA)
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- Joke Blom (CWI)

Netherlands Organization for Scientific Research

Computational Life Sciences http://www.siliconcell.net/sica/

NWO-CLS-635.100.007

To you all for your attention.

More information on:

Vidal *et. al.*, *Bioinformatics* 2006
http://www.science.uva.nl/research/scs/CellMath/GMP