Reaction and Diffusion on Fractal Sets

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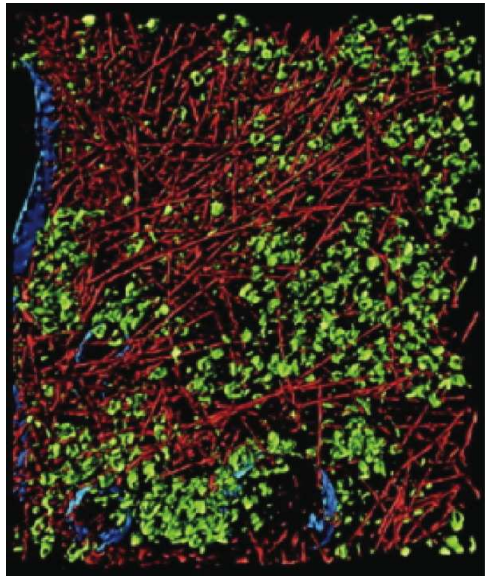
Chemical Processes in Cells

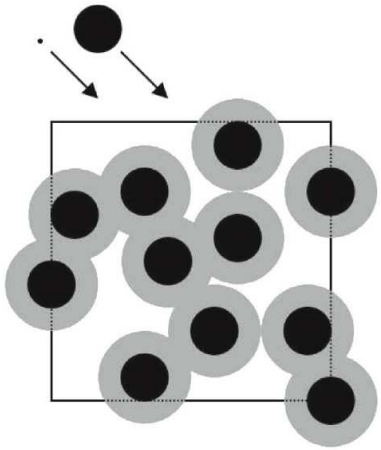
- When modelling chemical processes in cells, it is usual to build models which:
  - are based on mass action kinetics
  - have no spatial structure beyond simple compartmentalisation
- Is the mass action assumption appropriate?
  - the cytoplasm is a very crowded place (5 – 40% of volume is occupied by macromolecules)
  - reactive species can often be *extremely* dilute
- Experimental techniques are beginning to resolve spatial detail—perhaps dynamically in the not too distant future
- What can we do about modelling spatio-temporal dynamics within cells?

Molecular Crowding

- Molecular crowding has a number of well-established thermodynamic consequences
- Here we will be interested in dynamical consequeces:
- The available volume through which a given molecule can move depends on its size and shape
- Molecules can be effectively confined to low-dimensional spaces
  - For example: 1D pores
  - Highly ramified (fractal) spaces
- Can we model this mathematically? What issues need to be addressed?



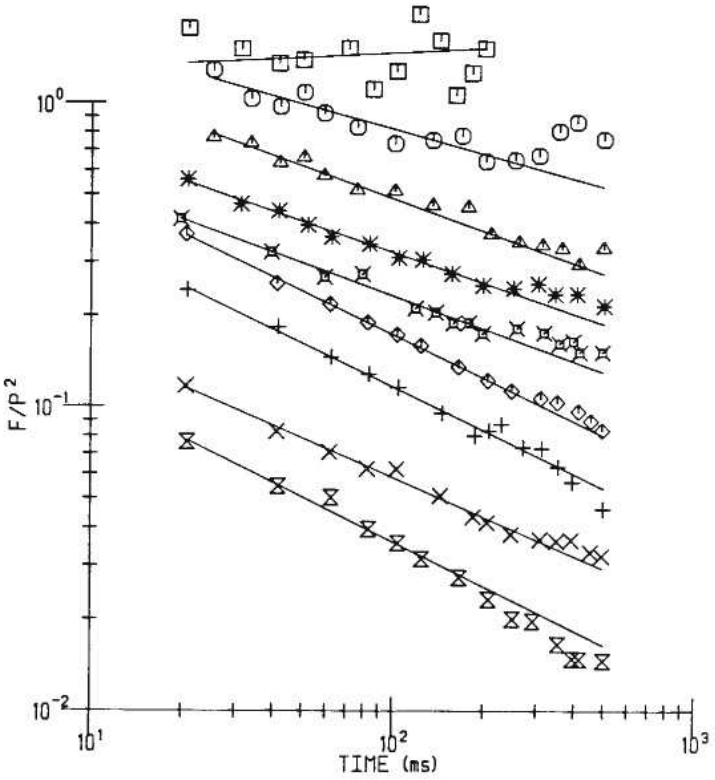
Medalia et al Science **298** (2002) 1209



Schnell, Turner Prog.Biophys & Mol.Biol. **85** (2004)

Exciton Annihilation Experiment

- Experiment used random naphthalene crystals where $\sim 8\%$ mole fraction was undeuterated.
- Triplet excitons mobile in the undeuterated component which forms a percolating cluster within the crystal
- Triplets can annihilate when two collide—naïve mass action kinetics implies the rate of loss of triplet is proportional to the square of the triplet concentration.
- Experimentally, however, this 'constant' decays in time as a power law $\kappa(t) \sim t^{-h}$
- The experimental h fits the theoretical value $1 - d_s/2$, where d_s is the spectral dimension of the fractal



Kopelman J.Stat.Phys. **42** (1986) 185

Rate Constants

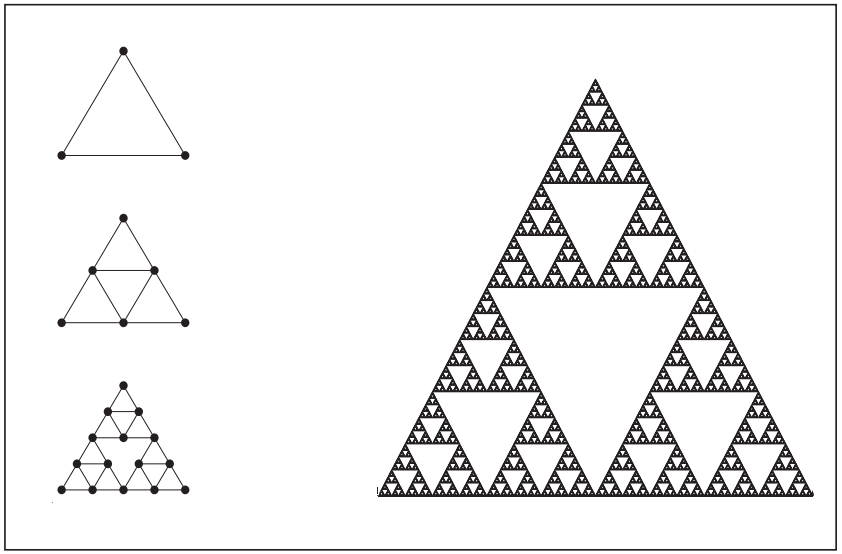
- Smoluchowski's theory (1917) is based on computing a diffusive flux of reactants onto one another
- The observed rate depends on both the intrinsic rate (k) and the relative diffusion (D) (here R is the distance of closest approach of the molecules)

$$\kappa = \frac{4\pi DRk}{4\pi DR + k}$$

- It is assumed that chemical concentrations are continuous functions of space
- The derivation fails in less than 3 dimensions
- We shall assume a reaction-diffusion model of the dynamics.
  - The rates will be assumed to be intrinsic
  - We will work on a fractal domain—the Sierpinski Gasket
  - We are interested in models which give insight into the role of the complex spatial structures that arise in cells

The Sierpinski Gasket

- An uncountable, compact, self-similar subset of $\mathbb{R}^2$
- Hausdorff dimension $d_H = \log 3/\log 2$ and spectral dimension $d_s = \log 9/\log 5$
- Approximate with a sequence of graphs (V_n, E_n) whose vertices become dense in the set
- $V_{n+1} = f_0(V_n) \cup f_1(V_n) \cup f_2(V_n)$ where $f_i = (x - p_i)/2 + p_i$ and the p_i are three fixed non-colinear points in the plane

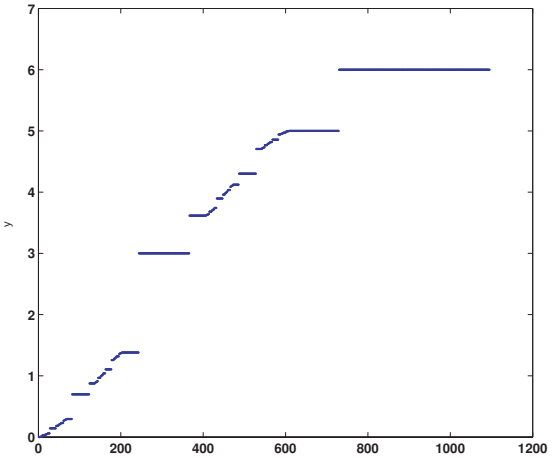


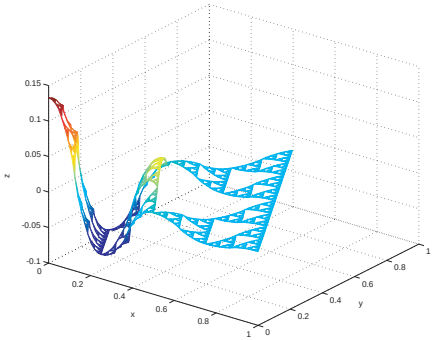
Calculus on the Sierpinski Gasket

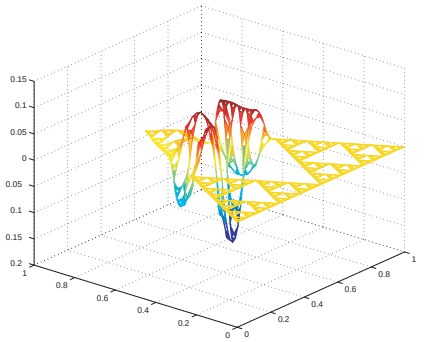
- The Laplacian can be constructed as a renormalised sequence of graph Laplacians
- A lot is known rigourously about this operator
- Its spectrum can be found by a decimation process
- A normal derivative (∂_n) can also be defined and then a Gauss-Green theorem can be proved. From which if follows that:

$$\int_{\mathrm{SG}} \nabla^2 A \, d\mu = \sum_{V_0} \partial_n A$$

- Green's functions can be constructed explicitly





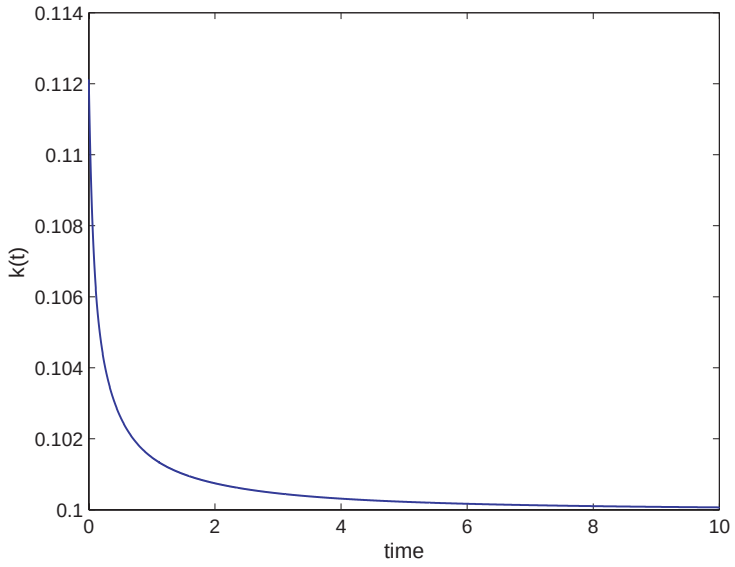


Numerics on the Gasket: symmetric case

- Can we model the exciton experiment using this?
- We solve the following reaction-diffusion equation (with $k = 0.1$ and $D = 0.01$) on the Sierpinski Gasket:

$$\frac{\partial A}{\partial t} = D\nabla^2 A - kA^2$$

- A plot of $\kappa(t) = \frac{d\overline{A}/dt}{\overline{A}^2}$ ($\overline{A}$ is the uniform average of A) does not show a power law—it decays to k



Relating the Rate Coefficients

Consider this case: $A + A \longrightarrow$ product, and write averages:

$$\overline{A} = \int_{\mathrm{SG}} A d\mu$$

We have two expressions:

$$\frac{d\overline{A}}{dt} = -\kappa(t)\overline{A}^2$$

and, using the reaction-diffusion form (with Neumann bcs)

$$\frac{\partial A}{\partial t} = D\nabla^2 A - kA^2 \longrightarrow \frac{d\overline{A}}{dt} = -k\overline{A^2}$$

Equating the two gives:

$$\kappa(t) = \frac{\overline{A^2}}{\overline{A}^2}\, k$$

Relating the Rate Coefficients

Given the expression:

$$\kappa(t) = \frac{\overline{A^2}}{\overline{A}^2}\, k$$

We have the inequality (with equality iff A is uniform)

$$\overline{A^2} \geq \overline{A}^2 \quad \Rightarrow \quad \kappa(t) \geq k$$

- If, initially, the concentration of A is not uniform, the initial rate will exceed the intrinsic rate
- The intrinsic rate is a lower bound on the observed rate—this excludes the possibility that $\kappa(t) \sim t^{-h}$
- We have not used fractal geometry explicitly here: only that the Gauss-Green formula holds for a suitably defined Laplacian and normal derivative on the Sierpinski Gasket
- The fact that power law behaviour is observed in experiments and in lattice-gas simulations suggests that the discreteness of the reacting entities might be the issue

Rate Coefficients—non-symmetric case

Now we consider the non-symmetric case:

$$A + B \to \text{product}$$

As before, writing averages with an overline, and using an analogous argument, we get

$$\kappa(t) = \frac{\overline{AB}}{\overline{A}\,\overline{B}}\, k$$

- The quantity $\overline{AB}$ measures the correlation between the spatial distribution of A and B
- If A and B are uncorrelated, $\overline{AB} = \overline{A}\,\overline{B}$ and hence $\kappa = k$
- Initially, A and B could well be uncorrelated $\Rightarrow \kappa(0) = k$.
- If the kinetics dominate, A and B become anticorrelated:

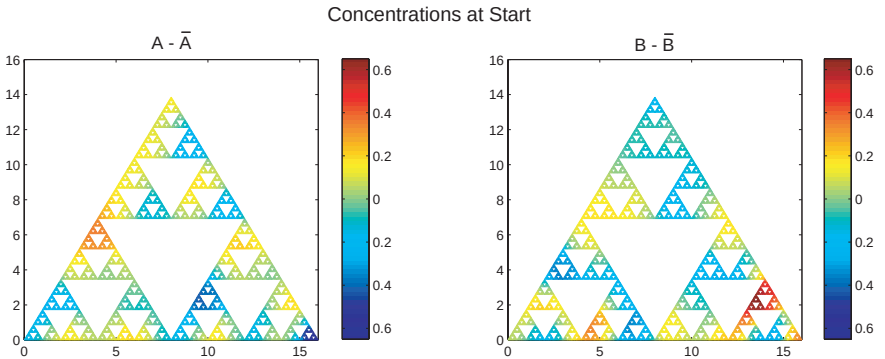
$$\overline{AB} < \overline{A}\,\overline{B} \quad \Rightarrow \quad \kappa(t) < k$$

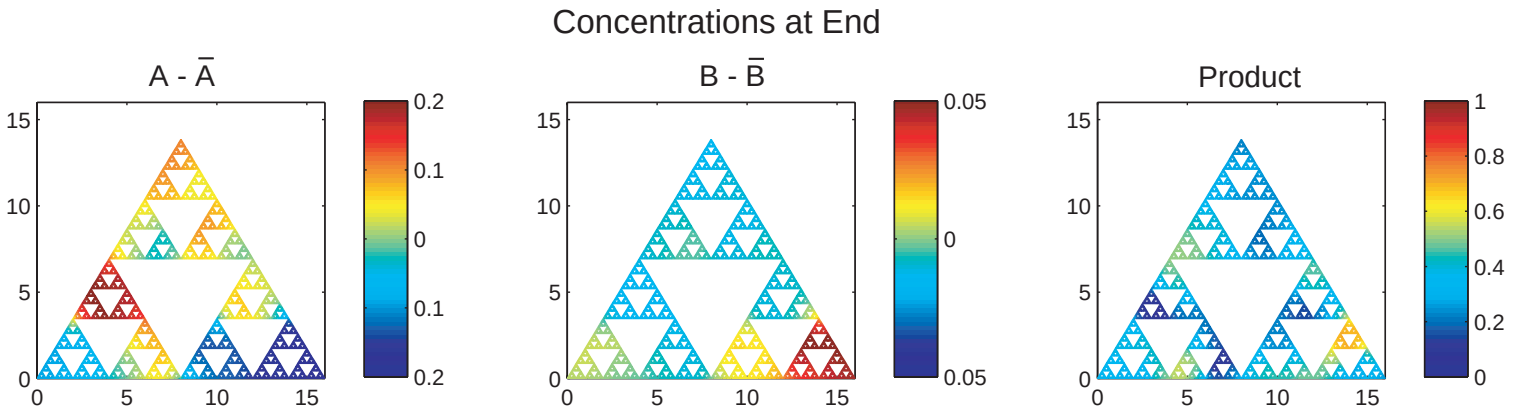
Numerics on the Gasket: non-symmetric case

We solve the system of PDEs (with $k = 0.1$ and $D = 0.01$):

$$\frac{\partial A}{\partial t} = D\nabla^2 A - kAB$$

$$\frac{\partial B}{\partial t} = D\nabla^2 B - kAB$$



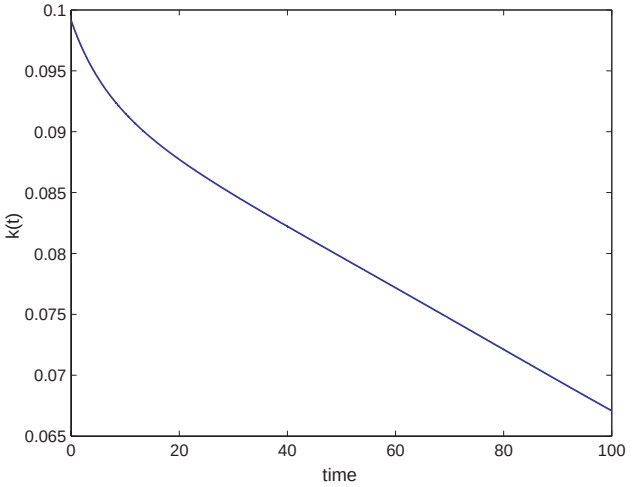


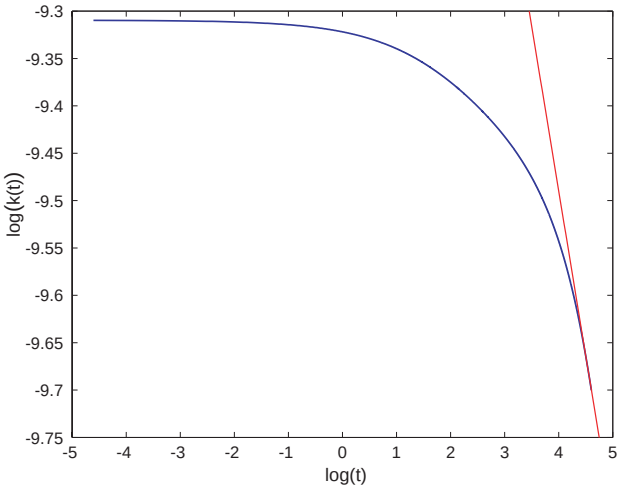
Remarks About the Numerics

- This anti-correlation effect (segregation) was predicted by Zeldovich et al in 1978
- It requires the chemistry to act faster than the diffusion and is strongly dependent on dimension—not observed in the steady state in $\mathbb{R}^2$ or $\mathbb{R}^3$ (Kopelman)
- Can be seen in lower dimensions—demonstrated using a lattice gas on the Sierpinski Gasket by Kopelman (1989)
- Behaviour entirely consistent with analysis given earlier
- Still not a power law, nor Zipf-Mandlebrot (Schnell and Turner: lattice gas model of Michaelis-Mentin)

$$\kappa(t) = k\tau/(\tau + t)^h$$

- Our numerics suggest $\kappa(t) \to\sim t$ at large t





Concluding Remarks

- Continuous dynamics on fractal sets appears to differ in a qualitative way from dynamics based on discrete entities.
- Lattice gas type modelling and reaction-diffusion seem complimentary
- We can define and analyse reaction-diffusion models in a class of fractal sets.
  - The Sierpinski Gasket
  - Analogous sets based on a tetrahedron. . . generally on an n-simplex.
  - Post-critically finite sets
- The behaviour is dependent on the topology of the set rather than a particular embedding and so continuous maps of these sets could be used to model spatial detail.
- Reaction-diffusion models are not dependent on the origin of time, unlike models with time-dependent rate coefficients