Reaction and Diffusion on Fractal Sets

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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 consequences:

- 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?

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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.

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 ($\partial_n$) can also be defined and then a Gauss-Green theorem can be proved. From which it follows that:

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

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

![Graph showing the decay of \(\kappa(t)\)]
Relating the Rate Coefficients

Consider this case: \( A + A \rightarrow \text{product} \), and write averages:

\[
\bar{A} = \int_{\text{SG}} A d\mu
\]

We have two expressions:

\[
\frac{d\bar{A}}{dt} = -\kappa(t)\bar{A}^2
\]

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

\[
\frac{\partial A}{\partial t} = D \nabla^2 A - kA^2 \quad \longrightarrow \quad \frac{d\bar{A}}{dt} = -k\bar{A}^2
\]

Equating the two gives:

\[
\kappa(t) = \frac{\bar{A}^2}{\bar{A}^2} k
\]
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)

\[ \overline{A^2} \geq \overline{A}^2 \Rightarrow \kappa(t) \geq k \]

- 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:

\[ A + B \rightarrow \text{product} \]

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:

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