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Does Reaction-diffusion Dynamics on a Fractal Space Imply Power Law Behaviour?

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Abstract

In biological systems, chemical reactions often take place in complex spatial environments. For example, the translation of m-RNA to produce protein within eukaryotic cells takes place within the extremely crowded cytoplasmic environment and appears to require the spatial coordination of many translation factors. It is important, therefore, to understand the transport processes within such an environment. While there is growing interest in both experimental and computational studies of such environments, it is also important to develop suitable mathematical models. Here, as an example of such a model, we study a reaction-diffusion equation defined on the Sierpinski gasket. Both experimental and computational studies of analogous systems have shown power law behaviour and associated deviations from mass action kinetics. The analysis presented here allows us to distinguish the roles of the fractal domain and of the discreteness of molecular interactions in producing this effect. Indeed, we show that the fractal domain alone is insufficient.

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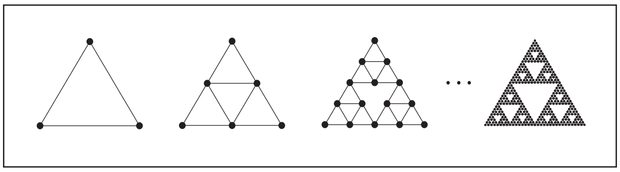

FIG. 1: The sequence of graphical approximations to the Sierpinski gasket. From left to right, each approximation is obtained by contracting its predecessor by a factor of a half and then combining three copies as shown. Note that the original vertices—the boundary points of the gasket—have degree two, and all other vertices have degree four.

I. INTRODUCTION

In systems biology there is a great need for mathematical models of chemical reactions in complex spatial environments. Here we consider an approach motivated by recent work[1, 2] which enables the rigorous definition of various differential operators—in particular, the Laplacian—on the class of post-critically finite (PCF) fractal sets. A well-known example of a PCF fractal is the Sierpinski gasket and this will be the focus here.

The analysis we shall use is based on the construction of a sequence of graphs which are successive approximations to the fractal (see Fig. 1). For each graph one can calculate the graph Laplacian[2]. In addition, the theory gives a rescaling which enables the definition of the Laplacian on the fractal as a limit of the graph Laplacians. In particular, we will be able to define (and make rigorous mathematical statements about) reaction-diffusion equations on PCF fractals.

We have used this machinery to investigate a simple, well-understood chemical system with the result that we are able to tease apart two issues which have tended to be conflated in the literature (see the review by Schnell and Turner[3] and references cited there): the effect of working in a fractal domain; and the role of the discreteness of molecular interactions at extreme dilutions.

A. The history of the problem

In his 1986 paper Kopelman[4] describes a very elegant experiment which probes the effect of a fractal domain on the observed dynamics of a chemical reaction. The experiment studied the rate of annihilation of triplet excitons in mixed crystals of isotopically substituted naphthalene. These crystals consisted of dilute mixtures of naphthalene in fully deuterated naphthalene. The arrangement of deuterated and undeuterated components within the crystal is random and within the range of fractions used there is a phase transition at which the undeuterated component forms a percolating cluster within the whole.

Kopelman exploited the fact that, at sufficiently low temperatures, triplet excitons can be generated which are mobile, but confined to the regions occupied by the undeuterated component. Collisions between triplet excitons result in a reaction which produces singlet excitons. By simultaneously studying the phosphorescence of decaying triplets and the delayed fluorescence of the singlets produced by the triplet-triplet reaction, it was possible to monitor continuously the kinetics of the reaction

$$A + A \rightarrow \mathsf{product}$$

on the fractal domain provided by the percolating cluster.

If the law of mass action holds for this reaction, the following ODE should model the observed kinetics:

$$\frac{d\overline{A}}{dt} = -k\overline{A}^2 \tag{1}$$

where $\overline{A}$ is the concentration of triplet averaged over the whole sample and k is the mass action rate constant. Kopelman gives a log-log plot of experimentally derived values of

$$\kappa \overset{\text{def}}{=} \frac{d\overline{A}}{dt} \Big/ \overline{A}^2 \tag{2}$$

as a function of time for a range of concentrations of the undeuterated component close to the percolation phase transition. Mass action kinetics would require that all of these plots be independent of time. Indeed, when the concentration of undeuterated naphthalene is sufficiently larger than the critical value, this was seen to be the case. However, at lower concentrations κ appeared to be time dependent, and—particularly near the critical concentration—seemed to be well approximated as a power law decay. A particular consequence of this observation is that κ tends to zero at large times.

We can see that this observation represents transitional behaviour. At concentrations which are significantly smaller than the critical value, the rate coefficient, κ, might be expected to go to zero in finite time. In such cases, the excitons are localised to small finite clusters and therefore, after a finite time, all possible configurations, including those which result in the annihilation of triplet pairs will have been explored. Beyond this time, the sample will contain a distribution of isolated excitons which are unable to interact. In the case of the percolating cluster, although many of the triplets are now found on a single, macroscopic, connected set, transport in this set is highly constrained by the low-dimensional geometry of the fractal. Kopelman described a theory which explains diffusion-limited rates in terms of the rate at which random walks are able to explore new regions of the domain. This theory suggests that $\kappa \sim t^{-h}$ where $h = \dim_s(\text{cluster})/2 - 1$ and $\dim_s(\text{cluster})$ is the spectral dimension of the domain. He found that $\dim_s(\text{cluster}) = \frac{4}{3}$ (the theoretical value for a percolating cluster) gives an excellent fit of the data for crystals near to the percolation transition.

II. THE MATHEMATICAL MODEL

In our mathematical setting we solve the following reaction-diffusion equation on the Sierpinski gasket:

$$\frac{\partial A}{\partial t} = D\nabla^2 A - kA^2 \tag{3}$$

Here A, a function of both time and location in the gasket, now represents the local concentration of species A, D is the corresponding diffusion constant and k is the mass action rate constant. Note that A is a smooth function of position and hence it makes sense to define a local mass action rate $-kA^2$. We use Neumann (zero flux) boundary conditions, (this approach to defining differential operators on fractals allows the definition of the normal derivative on the boundary[2]). This equation is solved numerically by using one of the higher-order graphical approximations of the gasket. The Laplacian on this graph is calculated by what is, in effect, a finite-difference formula. We use several graphs of different order to ensure that the level of approximation does not affect the numerical outcome.

In order to make contact with Kopelman's work we calculate the mean concentration (averaged over the gasket, K) of the triplet by computing the following integral:

$$\overline{A} = \int_K A d\mu \tag{4}$$

where μ is the uniform measure on the Sierpinski gasket. Using this definition, we also find that κ is time dependent, and therefore, that the system deviates from simple mass action kinetics. However, $\kappa(t)$ does not decay as a power law in time. Indeed, although it decays monotonically, the value of $\kappa(t)$ appears to be bounded from below by the rate k. In this system, the numerical results suggest that as time increases, the law of mass action provides an increasingly accurate description of the kinetics.

A. analysis of numerical results

These numerical results are rather disturbing because they do not reproduce the experimental results of Kopelman, nor the results of lattice gas simulations of this system[3]. They do, however, tell us something fundamental about this class of reaction-diffusion models because there is a simple proof that $\kappa(t) \geq k$.

Integrating Eq. (3) over the whole gasket with respect to the uniform measure μ gives the following expression for the time evolution of the mean concentration:

$$\begin{aligned} \int_K \frac{\partial A}{\partial t} d\mu &= D \int_K \nabla^2 A d\mu - k \int_K A^2 d\mu \\ \Rightarrow \frac{d\overline{A}}{dt} &= -k\overline{A^2} \end{aligned} \tag{5}$$

In this derivation the Gauss-Green formula and the Neumann boundary conditions have been employed to show that the integral $\int_K \nabla^2 A d\mu = 0$. In addition, we have introduced the obvious notation for the mean of the squared concentration.

Now we compare Eq. (5) with Eq. (2) to relate the rate coefficient $\kappa(t)$ with the rate constant k:

$$\kappa(t) = \frac{\overline{A^2}}{\overline{A}^2}\, k \tag{6}$$

The inequality $\overline{A^2} \geq \overline{A}^2$ shows that the rate constant is a lower bound of the observed rate coefficient

$$\kappa(t) \geq k \tag{7}$$

with equality if and only if A is uniform. This analysis excludes the possibility that $\kappa(t) \sim t^{-h}$ and provides a rigorous justification of the numerical results.

B. remarks

There is a simple interpretation of these results. The rate coefficient κ represents an average over a nonlinear rate. Where there are local peaks in the concentration of A, the reaction goes disproportionately faster in those regions and this makes the overall rate greater. If, on the contrary, the initial concentration of A is uniform on the gasket, then the system appears to satisfy mass action kinetics because κ begins at its lower bound.

In effect, a uniform initial concentration means that the system begins in a well-stirred state and since neither the chemistry nor the diffusion provide a mechanism which can break this symmetry, this is how it remains. If the initial concentration of A is not uniform, both the chemistry and the diffusion have the effect of flattening out the peaks in the concentration of A. As a consequence, we expect that as $t \to \infty$, $\overline{A^2} \to \overline{A}^2$.

At the heart of the mathematical argument leading to Eq. (7) is the Gauss-Green formula for the Sierpinski gasket. However, this is a property that the fractal has in common with classical domains such as the unit interval or the unit disc. In particular, we note that the result is completely independent of the dimension of the domain; we are not speaking about the effect of excluding fluctuations, the formula given in Eq. (6) would appear to be exactly the same if we were working in a region of $\mathbb{R}^3$ with μ representing Lebesgue measure.

The difference between our formulation and the experimental system or lattice gas simulations of the system is that ultimately the experiment and the lattice gas have discrete reacting entities. In our formulation, as $A(x,t)$ tends to zero at large t it is always a smooth function of x, the position in the gasket. It is impossible for $A(x,t)$ to represent the situation where either one or zero excitons are present in a region (indeed, as it tends zero it will imply the existence of fractions of excitons). Thus, the power law behaviour of $\kappa(t)$ owes its existence to both the fractal character of the domain *and* the discreteness of the reacting entities.

III. THE ROLE OF THE FRACTAL DOMAIN

It is possible to see an effect due to the fractal domain as $\kappa(t)$ approaches its limiting value. However, this effect is subtle. To investigate this consider the evolution of small perturbations from the uniform state

$$A(x,t) = \overline{A}(t) + \varepsilon\alpha(x,t) + O(\varepsilon^2) \tag{8}$$

where ε is a small parameter. We note that according to the definition of $\overline{A}$ (Eq. (4)), the average of each higher order term must vanish.

Substituting Eq. (8) into Eq. (3) and equating coefficients of the powers of ε gives the law of mass action form, Eq. (1) to lowest order (ε^0). This equation can be integrated directly to give

$$\overline{A}(t) = \frac{\overline{A}(0)}{1+\overline{A}(0)kt} \tag{9}$$

To order ε^1 we obtain the following PDE

$$\frac{\partial\alpha}{\partial t} = D\nabla^2\alpha - 2k\overline{A}(t)\alpha \tag{10}$$

which can be solved by introducing the set of orthonormal, Neumann eigenfunctions of the Laplacian[2]

$$\alpha(x,t) = \sum_{n=1}^{\infty} a_n(t)u_n(x) \tag{11}$$

(since the mean of α is zero there is no need to include the constant eigenfunction u_0 in this sum). Using the orthogonality of the u_n we obtain linear ODEs for the amplitudes

$$\dot{a}_n(t) = -(D\lambda_n + 2k\overline{A}(t))a_n(t) \tag{12}$$

where λ_n it the magnitude of the eigenvalue corresponding to u_n. The solution to these equations can be written down explicitly

$$a_n(t) = \frac{e^{-\lambda_n Dt}a_n(0)}{(1+\overline{A}(0)kt)^2} \tag{13}$$

We wish to know how $\overline{A^2}$ behaves as the uniform state is approached. Given Eq. (8) it is easy to show that $\overline{A^2} = \overline{A}^2 + \varepsilon^2\overline{\alpha^2} + O(\varepsilon^3)$. Then by Parseval's Theorem we obtain $\overline{\alpha^2}(t) = \sum_{n=1}^{\infty} a_n^2(t)$ and hence the following expression for the rate coefficient

$$\kappa(t) = k + \frac{\varepsilon^2 k}{\overline{A}^2(0)(1+\overline{A}(0)kt)^2}\sum_{n=1}^{\infty} e^{-2\lambda_n Dt}a_n^2(0) + O(\varepsilon^3) \tag{14}$$

It will emerge that the geometry of the fractal enters this problem through the structure of the spectrum of the Laplacian. This is expressed in terms of the counting function, $\rho(x)$, which gives the number of eigenvalues of the Laplacian which have magnitude less than or equal to x. Fukushima and Shima[5] have given a decimation method which enables the spectrum to be calculated exactly and Kigami[1] has shown that asymptotically, $\rho(x) \asymp x^{d_s/2}$ where $d_s \overset{\text{def}}{=} \dim_s(K)$. This result can be extended to all $x \geq \lambda_1 > 0$ (for our purposes $\rho(x) = 0$ for $0 \leq x < \lambda_1$). There are positive constants $C_\pm$ such that $C_- x^{d_s/2} < \rho(x) < C_+ x^{d_s/2}$ (see Fig. 2).

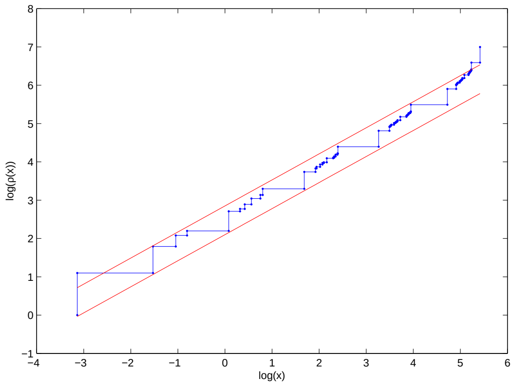

FIG. 2: A log-log plot of $\rho(x)$, the counting function of the Neumann spectrum of the Laplacian on the Sierpinski gasket. The straight lines have slope $d_s/2$ where $d_s \overset{\text{def}}{=} \dim_s(K)$.

To take the analysis further we have to assume something about the initial data. We proceed by assuming that there are fixed positive constants $a_\pm$ such that $a_- e^{-\gamma\lambda_n} \leq \varepsilon a_n(0) \leq a_+ e^{-\gamma\lambda_n}$ for some choice of $\gamma > 0$. The upper bound guarantees absolute convergence of Eq. (11) and looks like an assumption of analyticity of the initial data. The lower bound seems less natural, but has the effect of ensuring an initial distribution of power over all the modes. The effect we are looking for is a consequence of the power law form of $\rho(x)$. Although, individually, the energy of the modes decays exponentially, there is such a large number of the higher modes that, if they are all excited, then collectively, their energy can appear (for a limited time) to decay as a power law.

Now we need to estimate an infinite sum over the spectrum of the Laplacian, this can be written as a Riemann-Stieltjes integral[6]:

$$\sum_{n=1}^{\infty} e^{-2(\gamma+Dt)\lambda_n} = \int_0^\infty e^{-2(\gamma+Dt)x} d\rho(x) \tag{15}$$

which can be integrated by parts[7] to give

$$\int_0^\infty e^{-2(\gamma+Dt)x} d\rho(x) = 2(\gamma+Dt)\int_0^\infty \rho(x) e^{-2(\gamma+Dt)x} dx$$

(using Kigami's asymptotic result and the fact that $\rho(0) = 0$ to eliminate the boundary terms). We note that this has reduced the summation of interest to the Laplace transform of $\rho(x)$. If now we introduce the bounds on $\rho(x)$ and put everything back into Eq. (14) we find

$$K_- F(t) < \kappa(t) - k < K_+ F(t) \tag{16}$$

where $K_\pm = C_\pm k(\varepsilon a_\pm/\overline{A}(0))^2$, and

$$F(t) = \frac{\Gamma(1 + d_s/2, 2\lambda_1(Dt + \gamma))}{(1 + \overline{A}(0)kt)^2(2(\gamma + Dt))^{d_s/2}} \tag{17}$$

$\Gamma(\cdot, \cdot)$ is an incomplete gamma function (plica function).

Assume for the moment that $\lambda_1 D$ is very small so that the numerator of Eq. (17) is approximately a constant. Then $F(t)$ has the form of a product of two Zipf-Mandelbrot laws (see[3]), one coming from the kinetics and one from the diffusion on the fractal. As such it behaves in a regular way at small times if $\gamma > 0$, but at larger times ($t > (\overline{A}(0)k)^{-1}$ and $t > \gamma/D$) it can show what appears to be power law behaviour. However, since $\lambda_1 > 0$ the numerator is not a constant and indeed, since $\Gamma(a, z) \sim z^{a-1}e^{-z}$ as $z \to \infty$, ultimately $F(t) \sim t^{-2}e^{-2D\lambda_1 t}$. In this limit all dependence on d_s is lost, and the behaviour of the system is dominated by the most slowly decaying eigenfunction.

IV. FINAL REMARKS

Within the intracellular environment the spatio-temporal dynamics of species which are both crowded and dilute, seems a naturally candidate to be modelled using lattice gas simulations on a suitable fractal domain. However, there are also many species which play important roles in the system dynamics of the cell (small metabolites such as glucose for example) which are not dilute, and, as such, are not naturally modelled using the lattice gas technique. We propose that the chemistry of these species might best be dealt with using reaction-diffusion equations as we have described in this letter.

Acknowledgments

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