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Reaction front propagation of actin polymerization in a comb-reaction system

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ABSTRACT

We develop a theoretical model of anomalous transport with polymerization-reaction dynamics. We are motivated by the experimental problem of actin polymerization occurring in a microfluidic device with a comb-like geometry. Depending on the concentration of reagents, two limiting regimes for the propagation of reaction are recovered: the failure of the reaction front propagation and a finite speed of the reaction front corresponding to the Fisher-Kolmogorov-Petrovskii-Piscounov (FKPP) at the long time asymptotic regime. To predict the relevance of these regimes we obtain an explicit expression for the transient time as a function of geometry and parameters of the experimental setup. Explicit analytical expressions of the reaction front velocity are obtained as functions of the experimental setup.

1. Introduction

Microfluidics is an indispensable tool of modern bio-physical research. It allows to perform complex single-cell experiments with an immense throughput and high level of control. A flexible design allows for custom geometries and control of flows and chemical reactions. Recently, to probe the dynamics of actin polymerization, as well as to use the geometry of microfluidic device having the main supply channel with numerous identical side channels or chambers of different shapes, the following experimental setup, shown in Fig. 1, has been suggested [1,2]. The main channel serves to deliver and fill the side chambers with reagents where the corresponding reactions can be observed. The flow in the main channel and diffusion in the side-channels are dominating means of transport in such devices. Remarkably, the process of diffusion in this particular geometry was extensively studied in the context of anomalous diffusion. It is known as a comb model [3–5] and it was demonstrated that the transport of particles along the main channel (called backbone in the model) can become subdiffusive when the particles get trapped by diffusing into the side channels. Until recently it was mostly an abstract model, which was, however, extremely useful in understanding the principles of anomalous subdiffusive transport. In particular, the comb model was introduced for understanding the anomalous transport in percolating clusters [3,4] and it was considered as a toy model for a porous medium used for exploration of low dimensional percolation clusters [3,6]. It is a particular example of a non-Markovian phenomenon, which was explained within the framework of continuous time random walks [4,7,8]. Nowadays, comb-like models are widely used to describe different experimental applications like the transport in low-dimensional composites [9], the transport of calcium in spiny dendrites [10–12]. They also play an important role in developing the effective comb-shaped configuration of antennas [13] and modeling and simulating flows in the cardiovascular and ventilatory systems, related to techniques of virtual physiology [14].

The experimental setup on actin polymerization [1,15] is the direct implementation of the comb model, where the effects of complex diffusion should have a substantial effect on the observed phenomena. Interestingly, the comb structure not only leads to an anomaly in transport but also to a very remarkable effects on the propagation of chemical reactions [12].

The goal of this paper is to combine the consideration of anomalous transport and reaction dynamics to provide the theoretical grounds for the corresponding experimental efforts. Our analytical results on reaction propagation can help to guide the design of microfluidic devices but also can lead to real experimental tests of anomalous diffusion and reaction dynamics. For the reaction of polymerization, depending on the concentration of reagents we can recover such remarkable phenomena as the failure of the reaction front propagation [16,17] or a finite speed, which eventually leads to a Fisher-Kolmogorov-Petrovskii-Piscounov (FKPP) long

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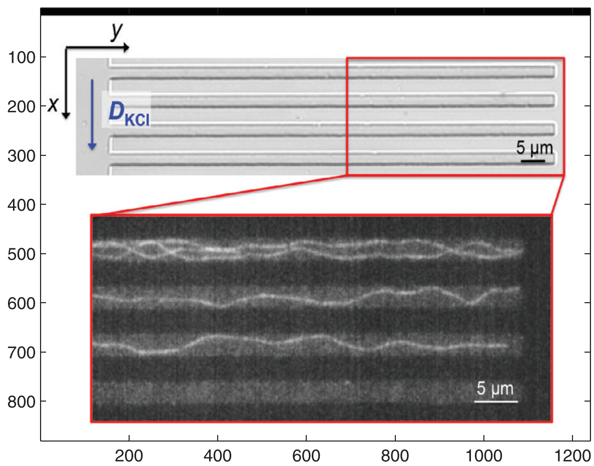

Fig. 1. (Color online) Optical micrograph of a segment of the microfluidics comb-like structures (on top). On bottom: microfluidic micrographs of fluorescently-labeled, polymerized actin filaments in a comb-like structure.

time asymptotic regime [18,19]. In the finite comb geometry of the experimental setup, these two processes correspond to different time scales. While the FKPP is a long time asymptotic regime, the reaction front propagation at subdiffusion is a transient process and takes place on the intermediate asymptotic times. A rigorous derivation of the governing equations allowed us to calculate the characteristic time scale separating these regimes explicitly. This time scale is determined by the geometry of the microfluidic device and be used to tune the regimes of diffusion and reactions in experiments.

1.1. Experimental setup

To study the dynamics of actin polymerization in diffusion controlled comb-like structures, we refer to a multi-height microfluidic device [1]. The microfluidic system consists of a main channel with a width $h_1 = 5$ µm, connected with comb-like structures that are smaller in width $h_2 = 0.5$ µm. Since the height of the main channel is ten-fold larger than that of the comb-like structures, a diffusion interface between the main, advective channel and the comb-like structure is generated due to the large hydraulic resistance of the connecting structures. Therefore, it is possible to add a solution of polymerization-inducing KCl to a solution of monomeric fluorescently labeled actin, including ATP necessary for in vitro polymerization, through the main channel, whereby KCl will diffuse into the comb-like structure and induce the polymerization of actin monomers into filaments. Similarly, magnesium (Mg^{2+}) can be used to induce the assembly of actin filaments into fibers. In what follows we will consider a very general reaction scheme referring to magnesium or KCl as an inducer, and the reaction itself as a reaction of polymerization. In experiments, the design of the side chambers can be varied and they can, for example, have circular or rectangular shapes. These shapes can also be incorporated into the analytical approach we develop below.

2. Mapping of the Laplace operator on a comb equation

Mapping the Laplace operators, acting in a three dimensional continuous-discrete geometry, as in Fig. 1, on a continuous two dimensional comb model equation, is related to averaging in the xyz-space [20–22] over some characteristic volume.

Anomalous diffusion of the inducer on the comb is described by the two dimensional probability distribution function (PDF) $P(x, y, t)$, and a special condition is that the displacement in the x direction is only possible along the structure axis (x-axis at $y = 0$). Therefore, this two dimensional diffusion is determined by the diagonal components of a diffusion tensor, where $D_x(y) = D_x\delta(y)$ and D_y are the diffusion coefficients in the x and y directions, correspondingly. In this case, the process of mapping of the Laplace operator on the comb model corresponds to establishing relations between the geometry parameters of geometrical constraint for the Laplace operator and the transport constants D_x and D_y.

In reality, we have the Laplace operator, which acts on the distribution function in a bulk of the main channel $P(x, y, z) = P_b(x, y, z)$ and in fingers (side channels, where reactions take place) $P(x, y, z) = P_f(x, y, z)$. Therefore, the following algorithm of mapping can be suggested. In the bulk of an infinite length along the x coordinate and yz surface with a cross-section $a \times a$, one has for the Laplace operator

$$D\Delta P_b(x, y, z) = D(\partial_x^2 + \partial_y^2 + \partial_z^2)P(x, y, z)$$

with the diffusivity of the inducer D and boundary conditions for $P(x, y, z) = P_b(x, y, z)$

$$\partial_z P|_{z=-a/2} = \partial_z P|_{z=a/2} = \partial_y P|_{y=-a/2} = \partial_y P|_{y=a/2} = 0.$$

Integration over z leads to the disappearance of the z component of the Laplace operator due to the boundary condition. For the PDF, one obtains

$$\int_{-a/2}^{a/2} P_b(x, y, z)dz \approx aP_b(x, y, 0),$$

where we used the middle point theorem. Integration over y in the bulk yields zero except those y regions where the bulk is connected with the fingers. Plunging the fingers inside the bulk, one arrives at the dynamics along the backbone which is at $y = 0$. Note, that the process of "plunging" mathematically corresponds to use of the middle point theorem. Therefore, we have for the bulk diffusion at arbitrary x

$$\frac{1}{a^3}\int_{-a/2}^{a/2} dxdydz\Delta P_b(x, y, z) \approx D\partial_x^2 P(x, y = 0, z = 0) = D\delta(y/a)\partial_x^2 P(x, y). \quad (2.1)$$

Here we disregarded the z coordinate in the distribution function $P(x, y, z = 0) \equiv P(x, y)$.

Now we consider fingers, which have length h and their xz cross-section is $b \times b$. It is worth noting that to work with the symmetrical PDF, we are mapping the Laplace operator on a two-sided symmetrical comb model that is practically, reflected in a choice of the symmetric boundary conditions at $y = \pm h$. The Laplace operator with diffusivity d inside the fingers reads

$$d\Delta P_f(x, y, z) = d(\partial_x^2 + \partial_y^2 + \partial_z^2)P(x, y, z).$$

Taking into account the boundary conditions, integration/averaging over x and z leads to zero, except ∂_y^2 in periodic (in x) regions of the fingers at arbitrary x and $y \in [-h, h]$. We have for a single finger

$$\frac{1}{b^3}\int_{-b/2}^{b/2} dxdydz\partial_y^2 P(x, y, z) \approx \partial_y^2 P(x, y, z = 0).$$

Therefore, we obtain the average Laplace operator for the fingers with the finger density ρ

$$\frac{d}{b^3}\int_{-b/2}^{b/2} dxdydzd\Delta P_f(x, y, z) \approx \rho d\partial_y^2 P(x, y, z = 0). \quad (2.2)$$

The finger density ρ is a number of fingers on the interval of length a along the x direction. Without restriction of the generality we take $\rho \sim a/b$. Since z component disappears from the averaged Laplace operator, we disregard z again in the distribution function $P(x, y, z = 0) \equiv P(x, y)$.