Journal of Theoretical Biology 427 (2017) 77–89

Contents lists available at ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/jtbi

Aggregation of biological particles under radial directional guidance

Ion Bica[a,*], Thomas Hillen[b], Kevin J. Painter[c,d]

[a] MacEwan University, Edmonton, Canada
[b] Centre for Mathematical Biology, Department of Mathematical and Statistical Sciences, University of Alberta, Canada
[c] Department of Mathematics and Maxwell Institute for Mathematical Sciences, Heriot-Watt University, Edinburgh, UK
[d] Department of Mathematical Sciences, Politecnico di Torino, Torino, Italy

ARTICLE INFO

Article history:
Received 23 December 2016
Revised 21 April 2017
Accepted 31 May 2017
Available online 14 June 2017

MSC:
35Q92
92B05
34B30

Keywords:
Anisotropic diffusion
Degenerate diffusion
Large time behaviour
Singularity formation
pattern formation

ABSTRACT

Many biological environments display an almost radially-symmetric structure, allowing proteins, cells or animals to move in an oriented fashion. Motivated by specific examples of cell movement in tissues, pigment protein movement in pigment cells and animal movement near watering holes, we consider a class of radially-symmetric anisotropic diffusion problems, which we call the *star problem*. The corresponding diffusion tensor $D(x)$ is radially symmetric with isotropic diffusion at the origin. We show that the anisotropic geometry of the environment can lead to strong aggregations and blow-up at the origin. We classify the nature of aggregation and blow-up solutions and provide corresponding numerical simulations. A surprising element of this strong aggregation mechanism is that it is entirely based on geometry and does not derive from chemotaxis, adhesion or other well known aggregating mechanisms. We use these aggregate solutions to discuss the process of pigmentation changes in animals, cancer invasion in an oriented fibrous habitat (such as collagen fibres), and sheep distributions around watering holes.

1. Introduction

Movement of biological particles, whether molecules, cells or organisms, is heavily dictated by their environment. We explore the impact of oriented environments, where a particle's motion is influenced by the anisotropic nature of its surroundings. Examples cover a broad range of biological scales: within single cells, the structured cytoskeleton offers a transport system for efficient shuttling of molecules and organelles (Alberts et al., 2014); in tissues, cell migration and consequently tumour invasion can be facilitated by movement along collagen fibres, neuronal axons and capillaries (Gritsenko et al., 2012); at a landscape level, animals often follow (or avoid) paths, roads and other linear structures (Brown et al., 2006; James and Stuart-Smith., 2000; McKenzie et al., 2012). Oriented environments may also have less manifestly physical forms: chemicals, the geomagnetic field, sound, visual cues and many other factors can present orientating information.

In Hillen et al. (2013) we termed the *fully anisotropic diffusion equation* as the linear parabolic equation

$$u_t = \nabla\nabla : (D(t,\mathbf{x})u) = \sum_{i,j=1}^{n} \frac{\partial}{\partial \mathbf{x}_i}\frac{\partial}{\partial \mathbf{x}_j}(D^{ij}(t,\mathbf{x})u) \tag{1.1}$$

on a bounded or unbounded domain in $\mathbb{R}^n$, equipped with appropriate boundary conditions. The tensor $D(t,\mathbf{x}) = (D^{ij}(t,\mathbf{x}))_{i,j}$ describes anisotropic diffusion, in which diffusive spread is distinct along different axial directions. This model arises as a description for particle movement in terms of their macroscopic density $u(t, \mathbf{x})$: models similar to (1.1) have been used to explain cell migration along collagen fibres (see Hillen, 2006) and the invasion of glioma (brain tumour) cells along neural fibre tracts (see Engwer et al., 2015; Painter and Hillen, 2013); for animal populations, they have been used to describe wolf movement along linear features in boreal habitats (Hillen and Painter, 2013; McKenzie et al., 2009; 2012), sea turtle navigation (Painter and Hillen, 2015) and butterfly movement (Painter, 2014). The wolf movement problem led to the specific exploration into the dynamics of (1.1) under a mathematically convenient straight-line structure, such as a road: the population is shown to accumulate onto the line and, under certain limiting scenarios, solutions blow up in infinite time (Hillen et al., 2013).

* Corresponding author.
E-mail addresses: bicai@macewan.ca (I. Bica), thillen@ualberta.ca (T. Hillen), K.Painter@hw.ac.uk (K.J. Painter).

http://dx.doi.org/10.1016/j.jtbi.2017.05.039
0022-5193/

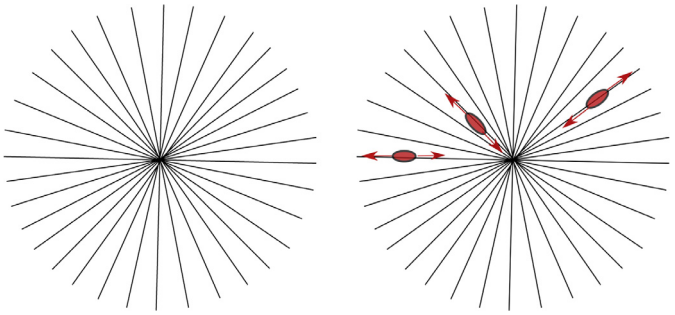

Fig. 1. Left: schematic of the anisotropy of the star problem. Right: sketch of moving particles in the star domain.

A second logical abstraction is to assume radially-aligned orienteering information. With respect to earlier examples, cytoskeletal microtubules are arranged into spokes radiating from the cell nucleus (or other organising centres) (Alberts et al., 2014); radially-aligned collagen fibres can be found in both healthy and pathological scenarios, such as emanating from the nipple of mammary tissue or oriented orthogonally to the tumour boundary in malignant breast tumours (Provenzano et al., 2006); at a landscape scale, animal trails radiate from waterholes in arid environments (Lange, 1969). The *star problem* investigated here emerges as an idealised description of movement along (or perpendicular to) radial lines that converge on some origin, under assumed radial symmetry. Given a planar polar coordinate system (r, ϕ), where for each point the direction away from the origin will be given by radial unit vector $(\cos\phi, \sin\phi)$, and assuming that movement is aligned radially, the fully anisotropic diffusion problem (1.1) is shown to have diffusion tensor

$$D(r,\phi) = \begin{cases} \dfrac{1-\alpha(r)}{2}\mathbb{I}_2 + \alpha(r)\begin{pmatrix} \cos^2\phi & \sin\phi\cos\phi \\ \sin\phi\cos\phi & \sin^2\phi \end{pmatrix} & \text{if } r \neq 0 \\ \dfrac{1}{2}\mathbb{I}_2 & \text{if } r = 0 \end{cases} \tag{1.2}$$

For now we simply state $|\alpha(r)| \leq 1$ to be a given function that describes the precision to which movement along the radial direction (positive α) or perpendicular to it (negative α) is maintained. Radially symmetric solutions to (1.1) under (1.2) are then found to be determined by the star problem,

$$\frac{\partial u(r,t)}{\partial t} = \frac{1}{2}\Big((1+\alpha(r))u\Big)_{rr} + \frac{1}{2r}\Big((1+3\alpha(r))u\Big)_r, \tag{1.3}$$

on the interval $(0, R]$ (where R is potentially infinity), under suitable boundary and initial conditions (Fig. 1). We explore whether the Eq. (1.3) is capable of creating aggregative behaviour, whether blow-up is possible and whether this blow-up occurs in finite or infinite time. For $0 \leq \alpha \leq 1$ we show that solutions to Eq. (1.3) contain a leading order term of the form

$$\frac{c}{r^{2\alpha/(\alpha+1)}}. \tag{1.4}$$

In particular, when $\alpha = 0$ we obtain constant solutions and for $\alpha = 1$ we observe a $1/r$ singularity at 0. The latter implies that solutions to the star problem have the potential to instantly blow up, representing a "strong aggregation" at the origin. This arises purely from the underlying structure of the environment and hence is distinct from the typical aggregations associated with a process such as chemotaxis. For orientation along radial circles (perpendicular to radial directions, $-1 \leq \alpha < 0$) aggregation does not occur and solutions to (1.3) remain bounded for all time.

1.1. Outline

In the following Section 2 we systematically motivate Eq. (1.3) as an idealised description for movement of biological particles in radially symmetric oriented environments. Starting with a transport equation for the aligned movement of particles, we state the macroscopic continuous drift-anisotropic diffusion equation obtained under scaling. Eq. (1.3) subsequently emerges following the transformation to polar coordinates and assuming radial symmetry. Specific examples are provided within the context of organelle transport along microtubules, cell movement along collagen fibres and animal movement along the trails that surround water holes. For the special case of constant α, the resulting singular Sturm–Liouville problem is solved in Section 3.3. The leading order term in this solution is derived and we use Section 4 to compare numerical solutions of (1.2) to the asymptotic formula, as well as demonstrate the utility of the model in applications. We conclude with a discussion of the results in the context of our motivating examples.

2. Derivation and motivations

Velocity-jump random walk models (Othmer et al., 1988) describe movement as a piecewise-continuous path of smooth runs punctuated by turns into new velocities. As such they provide a plausible approximation of actual movement paths and can be parameterised against standard datasets. The transport equation is the corresponding continuous description for this process and, in a series of papers (Hillen, 2006; Hillen and Othmer, 2000; Hillen and Painter, 2013; Othmer and Hillen, 2002), it is shown how first choosing a distribution where turns are biased into specific axial directions and then taking a course-grain limit leads to the anisotropic diffusion formulation (1.1), with appropriate diffusion tensor D.

2.1. Transport equations to anisotropic diffusion

The transport equation postulates the time evolution of the particle population distribution, $p(t, \mathbf{x}, \mathbf{v})$, parameterised by time $t \in [0, \infty)$, position $\mathbf{x} \in \Omega \subset \mathbb{R}^n$ and velocity $\mathbf{v} \in V \subset \mathbb{R}^n$. Here, turning is chosen to be (effectively) instantaneous and the new velocity is assumed to not depend on the previous velocity, yielding

$$p_t(t,\mathbf{x},\mathbf{v}) + \mathbf{v}\cdot\nabla p(t,\mathbf{x},\mathbf{v}) = -\mu p(t,\mathbf{x},\mathbf{v}) + \mu q(t,\mathbf{x},\mathbf{v})u(t,\mathbf{x}), \tag{2.5}$$

where $u(t,\mathbf{x}) = \int_V p(t,\mathbf{x},\mathbf{v})d\mathbf{v}$ is the macroscopic (or observable) particle density. $q(t, \mathbf{x}, \mathbf{v})$ describes the turning distribution, i.e. the probability that a particle turns into velocity $\mathbf{v}$ at time t and position $\mathbf{x}$. The parameter μ measures the turning rate and is taken here to be constant. We also simplify by assuming that the particles move with a fixed mean speed s and, consequently, trivial rescaling allows us to set $s = \mu = 1$ (and subsequently drop these notations). Hence $V \equiv \mathbb{S}^{n-1}$ (the unit sphere) and $q(t, \mathbf{x}, \mathbf{v})$ becomes a directional distribution on the unit sphere,

$$\int_{\mathbb{S}^{n-1}} q(t,\mathbf{x},\mathbf{v})d\mathbf{v} = 1\,.$$

In fact, an equation similar in form to (2.5) was used in Painter (2009) to model cell migration along collagen fibres. There, radial fibre arrays were shown to generate focussed aggregations at the origin, suggesting that oriented environments could act to spatially organise populations. Those simulations partially motivate the current work, where a more detailed investigation is conducted through exploring the macroscopic version. This macroscopic model can be obtained through moment closure techniques