On the shape of invading population in oriented environments

V. Blavatska

Received: date / Accepted: date

Abstract We analyze the properties of population spreading in oriented environments with spatial anisotropy within the frames of a lattice model of asymmetric (biased) random walkers. The expressions for the universal shape characteristics of population, such as asphericity, are found analytically and proven to be dependent only on the asymmetric transition probabilities in different directions. The model under consideration is shown to capture, in particular, the peculiarities of invasion in presence of an array of oriented tubes (fibers) in the environment.

1 Introduction

The problem of spreading of a population of agents in anisotropic environments with some preferred orientations of movement is encountered in a rich variety of biological phenomena and medicine. In general, the movement characteristics are influenced due to the environmental heterogeneity. Important examples include behavior of chemosensitive cells like bacteria or leukocytes in the gradient of a chemotactic factor [1,2,3,4], the motion of micro-organisms under the action of gravitational force (gravitaxis) or a light source (phototaxis) [5,6,7], the cell migration in fiber network of extracellular environment [8,9,10,11,12], and in particular the tumor invasion and metastasis in the tissue matrix [13,14,15]. The important problems of spatial ecology are connected with analysis of migrations of living organisms in oriented habitats with orientation given by magnetic cues, elevation profiles, spatial distributions of...
The variations of above characteristics has non-trivial influence on the population growth, persistence and dispersal \[16,17,18\]. In particular the presence of oriented factors in environment lead to occurrence of directed movement patterns, different from pure diffusion \[19,20,21\]. In this concern, it is worthwhile to mention also the modern technologies of controlled drug delivery, using an external oriented magnetic field \[24\], and the implants based on arrays of oriented TiO\(_2\) nanotubes, which control the directed release of drugs \[25,26\].

The model of a random walk (RW) on a regular lattice provides a good description of the stochastic movement processes \[27\]. In the simplest case, when there is no preferred direction, this process restores the Brownian motion and such a model may be shown to produce the standard diffusion equation. Making the probabilities of moving in different directions not equal causes the directional bias, which leads to the drift-diffusion equation. Such asymmetric biased random walks (BRW) are frequently used in biology to model the motion of living organisms and cells in oriented environments \[28,29\]. The bias may be caused both by the fixed external environmental factors (such as gravitational force or external magnetic field), and by varying factors (such as chemical gradient or food resources in oriented migration of organisms). Thus, the transition probabilities in BRW model can also be not only constants, but spatially dependent functions.

We address the question, how the presence of orientational factors and heterogeneity in environment impact the geometrical shape characteristics of a spreading population. To describe the shape properties of a group of invading agents quantitatively, it is convenient to introduce the quantities such as the asphericity \(A\) and prolateness \(S\) \[30,31\]. The parameter \(A\) takes on a minimal value of zero for a completely isotropic spherical configuration of population, corresponding e.g. to the case of simple diffusion of particles in isotropic environment, and equals one for completely stretched configuration, thus obeying the inequality: \(0 < A < 1\). The quantity \(S\) catches more subtle shape properties and allows to distinguish between the shapes of prolate ellipsoid (when it takes on a positive value) and oblate shapes (with \(S\) negative), being bounded to the interval \(-\frac{1}{4} < S < 2\). Recently, these quantities were used to describe the instantaneous shapes of particle puffs in turbulent flows \[32\].

The motivation of the present paper is to analyze the shape characteristics of a population of agents, spreading in anisotropic environment with preferred orientations, within the lattice model of BRW. As will be shown, this model allows us, in particular, to analyze the spreading process in presence of structural inhomogeneities in form of oriented lines. On the one hand, this can be related to the problem of movement of cells in extracellular matrix of connective tissues with collagen and elastin fibers, on the other hand such a model resembles the arrays of oriented nanotubes in controlled drug delivery implants, mentioned above.

The layout of the paper is as follows. In the next section, we introduce the model and define the observables we are interested in. The analytical expressions of shape parameters are given in Section 3, followed by examples
of some model cases presented in Section 4. We end up by giving conclusions and outlook.

2 The model

We start with considering a population of \( N \) random walkers, spreading on an infinite 3-dimensional lattice. At each time step, each the walker jumps towards one of 6 nearest neighbor sites with corresponding probability \( p_i, i = 1, \ldots , 6 \) such that \( \sum_{i=1}^{6} p_i = 1 \) (as schematically shown on Fig. 1). In the simplest case of isotropic uncorrelated random walk, all the transition probabilities are equal: \( p_i = \frac{1}{6} \). We assume, that all the walkers start to move from the same starting point (let it be the center of coordinate system), so that we start with highly dense configuration ("drop"), localized in space. The walkers move independently, without any interactions or correlations between them.

Let \( \mathbf{R}_a(t) = \{x^a(t), y^a(t), z^a(t)\} \equiv \{x^a_1(t), x^a_2(t), x^a_3(t)\} \) be the position vector of the \( a \)th walker at time \( t \) \( (a = 1, \ldots , N) \). The shape properties of an instantaneous configuration of the population can be characterized \(^{30,31}\) in terms of the gyration tensor \( \mathbf{Q} \) with components:

\[
Q_{ij}(t) = \frac{1}{N(N-1)} \sum_{a,b=1}^{N} (x^a_i(t) - x^b_i(t))(x^a_j(t) - x^b_j(t)), \quad i, j = 1, 2, 3. \tag{1}
\]

The spread in eigenvalues \( \lambda_i(t) \) \( (i = 1, 2, 3) \) of the gyration tensor describes the distribution of particles in an instantaneous configuration and thus measures the asymmetry of a shape. In particular, in completely isotropic symmetric case all the eigenvalues \( \lambda_i(t) \) are equal.
Let us introduce the rotationally invariant universal combinations of components of the gyration tensor \([30,31]\). Let 
\[
\lambda(t) \equiv \text{Tr} Q / 3 \]
be the average eigenvalue of the gyration tensor. Then the extent of asphericity of an instantaneous configuration of population is characterized by quantity \(A\) defined as:
\[
A = \frac{1}{6} \sum_{i=1}^{3} \frac{(\lambda_i(t) - \lambda(t))^2}{\lambda(t)} = \left( \sum_{i=1}^{3} (Q_{ii}(t))^2 + 3 \sum_{i<j}^{3} (Q_{ij}(t))^2 - \sum_{i<j}^{3} (Q_{ij}(t))(Q_{ji}(t)) \right) / \left( \sum_{i=1}^{3} (Q_{ii}(t)) \right)^2. \tag{2}
\]
Here and below \(\langle \ldots \rangle\) denotes averaging over an ensemble of possible configurations of a group of particles at given time. This universal quantity equals zero for a completely isotropic spherical configuration, where all the eigenvalues are equal \(\lambda_i = \lambda\), and takes a maximum value of one in the case of a stretched highly anisotropic configuration, where all the eigenvalues equal zero except of one. Thus, the inequality holds: \(0 \leq A \leq 1\). Another rotationally invariant quantity, defined in three dimensions, is the so-called prolateness \(S\):
\[
S = \frac{\prod_{i=1}^{3} (\lambda_i(t) - \lambda(t))}{\lambda(t)} = \left( 2 \sum_{i=1}^{3} (Q_{ii}(t))^3 - 3 \sum_{i=1}^{3} (Q_{ii}(t))^2 \sum_{j \neq i}^{3} (Q_{ij}(t)) 
- 9 \sum_{i=1}^{3} (Q_{ii}(t))(2 \sum_{k \neq j \neq i}^{3} (Q_{kj}(t))^2 - \sum_{j \neq i}^{3} (Q_{ij}(t))^2) 
+ 12 \prod_{i=1}^{3} (Q_{ii}(t)) + 54 \prod_{i \neq j} (Q_{ij}(t)) \right) / \left( \sum_{i=1}^{3} (Q_{ii}(t)) \right)^3. \tag{3}
\]
For absolutely prolate, stretched rod-like configuration \((\lambda_1 \neq 0, \lambda_2 = \lambda_3 = 0)\), the parameter \(S\) equals two, whereas for absolutely oblate, disk-like shape \((\lambda_1 = \lambda_2, \lambda_3 = 0)\) it takes on a value of \(-1/4\). In general, \(S\) is positive for prolate ellipsoid-like shape \((\lambda_1 \gg \lambda_2 \approx \lambda_3)\) and negative for oblate ones \((\lambda_1 \approx \lambda_2 \gg \lambda_3)\), whereas its magnitude measures how oblate or prolate the configuration is.

Next, we will find the exact values of quantities \((2)\) and \((3)\) for a system of non-interacting \(N\) asymmetric random walkers on a lattice.

3 Results

The probability \(P(t, n_i^n)\) that the walker \(a\) had performed \(n_i^n\) steps in direction \(i\) \((i = 1, \ldots, 6)\) after the total amount of \(t\) steps (so that \(t = \sum_{i=1}^{6} n_i^n\)) is given by:
\[
P(t, n_i^n) = \frac{t!}{n_i^n!(t - n_i^n)!} p_i^n (1 - p_i)^{t-n_i^n}. \tag{4}
\]
Thus, we can evaluate the mean values $\langle n_i^a \rangle$ and $\langle (n_i^a)^2 \rangle$ ($a = 1, \ldots, M$):

$$\langle n_i^a \rangle = \sum_{n_i^a = 0}^{t} n_i^a P(t, n_i^a) = t p_i,$$

$$\langle (n_i^a)^2 \rangle = \sum_{n_i^a = 0}^{t} (n_i^a)^2 P(t, n_i^a) = t p_i + t(t - 1) p_i^2.$$  

Correspondingly, introducing the combined probability $P(t, n_i^a, n_j^a)$ that the walker at time $t$ had performed $n_i^a$ and $n_j^a$ steps in directions $i$ and $j$:

$$P(t, n_i^a, n_j^a) = \frac{t!}{n_i^a!(t - n_i^a)!} \frac{(t - n_j^a)!}{n_j^a!(t - n_j^a)!} p_i^{n_i^a} p_j^{n_j^a} (1 - p_i - p_j)^{t-n_i^a-n_j^a}$$

we evaluate the correlation

$$\langle n_i^a n_j^a \rangle = \sum_{n_i^a = 0}^{t} \sum_{n_j^a = 0}^{t-n_i^a} n_i^a n_j^a P(t, n_i^a, n_j^a) = t(t-1)p_i p_j, \ i \neq j.$$  

And finally, let us introduce the combined probability $P(t, n_i^a, n_i^b)$ that the walker $a$ had performed $n_i^a$ steps in directions $i$ whereas the walker $b$ had performed $n_i^b$ steps in direction $j$. Since we assume, that the walkers $a$ and $b$ move independently, we simply have: $P(t, n_i^a, n_i^b) = P(t, n_i^a) \cdot P(t, n_i^b)$ and thus:

$$\langle n_i^a n_j^b \rangle = \sum_{n_i^a = 0}^{t} n_i^a P(t, n_i^a) \sum_{n_j^b = 0}^{t} n_j^b P(t, n_j^b) = t^2 p_i p_j.$$  

We can thus easily find the averaged values of coordinates of random walkers at given time $t$. Really, since e.g. the averaged coordinate $\langle x_1(t) \rangle$ of a walker is given by a difference of number of steps to the right and to the left along the $x_1$-axis, we have:

$$\langle x_1^a(t) \rangle = \langle n_i^a - n_i^a \rangle = t(p_1 - p_2),$$

$$\langle x_1^b(t) \rangle = \langle n_3^b - n_3^b \rangle = t(p_3 - p_4),$$

$$\langle x_1^c(t) \rangle = \langle n_5^c - n_5^c \rangle = t(p_5 - p_6).$$

so that: $\langle x_1^a(t) \rangle = t(p_{2i-1} - p_{2i})$. Correspondingly:

$$\langle (x_1^a(t))^2 \rangle = t(p_{2i-1} + p_{2i}) + t(t-1)(p_{2i-1} - p_{2i})^2,$$

$$\langle x_1^a(t)x_1^b(t) \rangle = t(t-1)(p_{2i-1} - p_{2i})(p_{2i-1} - p_{2i}),$$

$$\langle x_1^a(t)x_1^b(t) \rangle = t^2(p_{2i-1} - p_{2i})^2,$$

$$\langle x_1^a(t)x_1^b(t) \rangle = t^2(p_{2i-1} - p_{2i})(p_{2i-1} - p_{2i}).$$
Expressions (11)-(14) allow us to find the averaged components of gyration tensor. For example:

\[
\langle Q_{11}(t) \rangle = \frac{1}{N(N-1)} \left( \sum_{a,b=1}^{N} (x_a^2(t) - x_b^2(t))^2 \right) = \langle (x_a^2(t))^2 \rangle - \langle x_a^2(t) \rangle^2 = t \left( (p_1 + p_2) - (p_1 - p_2)^2 \right). \tag{15}
\]

So in general:

\[
\begin{align*}
\langle Q_{ij}(t) \rangle &= t \left( (p_{i-1} + p_{i+1}) - (p_{i-1} - p_{i+1}) \right), \quad (i \neq j) \quad \text{and} \\
\langle Q_{ii}(t) \rangle &= -t(p_{i-1} - p_{i+1}) (p_{j-1} - p_{j+1}). \quad (i = j)
\end{align*}
\tag{16, 17}
\]

Finally, substituting the values (16, 17) into Eqs. (2) and (3), we receive expressions for shape parameters \( A \) and \( S \) of the system:

\[
A(\{p_i\}) = \left( \sum_{i=1}^{3} (p_{2i-1} + p_{2i} - (p_{2i-1} - p_{2i})^2)^2 - \right.
- \sum_{i=1}^{3} (p_{2i-1} + p_{2i} - (p_{2i-1} - p_{2i})^2)^2 (p_{2j-1} + p_{2j} - (p_{2j-1} - p_{2j})^2) +
+3(p_{2i-1} - p_{2i})^2 (p_{2j-1} - p_{2j})^2 \right) \left( \sum_{i=1}^{6} p_i - \sum_{i=1}^{3} (p_{2i-1} - p_{2i})^2 \right)^2, \tag{18}
\]

\[
S(\{p_i\}) = \left( 12 \prod_{i=1}^{3} ((p_{2i-1} + p_{2i} - (p_{2i-1} - p_{2i})^2) +
+2 \sum_{i=1}^{3} (p_{2i-1} + p_{2i} - (p_{2i-1} - p_{2i})^2)^3 - 
-3 \sum_{i=1}^{3} (p_{2i-1} + p_{2i} - (p_{2i-1} - p_{2i})^2)^2 (p_{2j-1} + p_{2j} - (p_{2j-1} - p_{2j})^2) - 
-9 \sum_{i=1}^{3} (p_{2i-1} + p_{2i} - (p_{2i-1} - p_{2i})^2)^2 (p_{2j-1} - p_{2j})^2 - 
-18 \sum_{i=1}^{3} (p_{2i-1} + p_{2i} - (p_{2i-1} - p_{2i})^2)^2 (p_{2k-1} - p_{2k})^2 - 
-54 \prod_{i=1}^{3} (p_{2i-1} - p_{2i})^2 \right) \left( \sum_{i=1}^{6} p_i - \sum_{i=1}^{3} (p_{2i-1} - p_{2i})^2 \right)^3. \tag{19}
\]

The quantities (18), (19) are universal in the sense that they do not depend neither on time, no on number of particles, and appear to be the functions only of transition probabilities \( p_i \). Note, that in real experiments and in computer simulations, the quantities given by (18), (19) are the asymptotical values,
Fig. 2  Instantaneous configurations of population of $N = 100$ random walkers on a lattice after $t = 2000$ steps, results of computer simulations. (1) Isotropic case with $p_i = 1/6$. The values of shape parameters $A = 0$, $S = 0$. (2) Moving on the half-space of $xy$ plane with $p_1 = 0.4$, $p_3 = 0.6$, $p_2 = p_4 = p_5 = p_6 = 0$. Maximal anisotropic state with $A = 1$, $S = 2$. (3) The case, when moving in $x$ direction is more probable, than in others: $p_1 = p_2 = 0.4$, $p_3 = p_4 = p_5 = p_6 = 0.05$. The values of shape parameters: $A = 0.49$, $S = 0.68$.

obtained in the limits of large enough number of particles and long enough time of spreading process ($t \to \infty$, $N \to \infty$).

The above scheme can be generalized to the case, when $p_i$ are not just constants which are fixed in space, but random numbers taken from some distribution. Such situation may occur due to presence of some random fields or random structural disorder in the system. Let us assume, that at each site of the lattice the set of $p_{ik}$ is realized with corresponding probabilities $\rho(k)$. In this case, one can easily convince oneself, that all of observables of interest in relations above can be obtained by substituting $p_i$ by an averaged value $\overline{p}_i$, given by

$$\overline{p}_i = \sum_k \rho(k)p_{i,k}$$  \hspace{1cm} (20)

in corresponding equations.

In the next section, we illustrate the results obtained by considering several model cases of invasion in anisotropic environment.

4 Examples

1) In the most trivial isotropic case, when all $p_i$ are equal ($p_i = 1/6$), we have: $A = 0$, $S = 0$ (see Fig. 2(1)).

2) Let us consider the case, when $p_3 = 1 - p_1$, $p_2 = p_4 = p_5 = p_6 = 0$: the population is moving on the half-space of $xy$ plane with nonequal transition probabilities in $x$ and $y$ directions. It appears, that independently on the $p_1$ and $p_3$ values, we receive highly anisotropic, completely stretched configuration with $A = 1$, $S = 2$ (Fig. 2(2)).

3) Next, let us assume $p_1 = p_2$, $p_3 = p_4 = p_5 = p_6 = (1 - 2p_1)/4$: moving along the $x$-axis is more (or less) probable, then in two remaining directions...
Fig. 3 Shape parameters $A$ (as given by Eq. (21)) and $S$ (given by (22)) as functions of probability $p_1 = p_2$ (whereas $p_3 = p_4 = p_5 = p_6 = 0$).

(Fig. 2(3)). In this case, on the basis of (18), (19) we obtain:

$$A(p_1) = -3p_1 + 9p_1^2 + \frac{1}{4},$$

(21)

$$S(p_1) = \frac{1}{4}(6p_1 - 1)^3.$$  \hspace{1cm} (22)

Parameters $A$ and $S$ as functions of $p_1$ are shown on Fig. 3. Note, that $p_1$ can vary in this case from 0 to 1/2. At $p_1 = 0$, the population is spreading in 2 dimensions ($yz$ plane). At $p_1 = \frac{1}{2}$, we restore the isotropic case (1) with $A = S = 0$. Further increasing of $p_1$ leads to growing of anisotropy, until it reaches the final stage (configuration completely stretched along $x$ axis) at $p_1 = p_2 = \frac{1}{2}$, $p_3 = p_4 = p_5 = p_6 = 0$.

4) Finally, let us consider the most interesting case, when population of particles is spreading in environment with structural inhomogeneities (obstacles) in the form of parallel lines, randomly distributed in $xy$ plane and oriented along $z$ axis (see Fig. 4). Let $c$ be the concentration of lines ($0 \leq c \leq 1$). From point of view of each random walker, presence of lines does not prevent jumps in $z$ direction, but plays an essential role for movement in $xy$ plane. Really, for each lattice site, one of 4 nearest neighbors in $xy$ plane can be occupied with probability $c$ (belonging to the line) and is thus not allowed for random walker. The probability, that $k$ nearest neighbors ($0 \leq k \leq 4$) are occupied, is given by Bernoulli formula for binomial probability distribution:

$$\rho(k) = \frac{4!}{k!(4-k)!}c^k(1-c)^{4-k}.$$ \hspace{1cm} (23)

The given problem thus essentially differs from examples above, where transition probabilities were spatially-independent constants $p_i$. Here, due to
randomness of defects distribution in space, at each lattice site we observe one of possible $p_{ik} = 1/(6 - k)$ with corresponding probabilities $\rho(k)$ given by Eq. (23). Namely, for $i = 5, 6$ (transition probabilities in $z$ direction) taking into account Eq. (20) we have:

\[
\overline{p_i} = \sum_{k=0}^{4} p_{ik}\rho(k) = \sum_{k=0}^{4} \frac{1}{6-k}\rho(k) = \frac{1}{6}(1-c)^4 + \frac{4}{3}c(1-c)^3 + \\
+ \frac{3}{2}c^2(1-c)^2 + \frac{4}{3}c^3(1-c) + \frac{1}{2}c^4, \quad i = 5, 6. \quad (24)
\]
The corresponding transition probabilities $p_{ik}$ in $xy$ planes are smaller by the factor $(4-k)/4$ due to the fact, that $k$ jumps are forbidden by presence of defects, so that:

$$p_i = \frac{4}{4} \sum_{k=0}^{4} \frac{4-k}{4} \frac{1}{6-k} a(k) = \frac{1}{6}(1-c)^4 + \frac{3}{5}c(1-c)^3 +$$

$$+ \frac{3}{4}c^2(1-c)^2 + \frac{1}{3}c^3(1-c), \quad i = 1, \ldots, 4. \quad (25)$$

As expected, we have:

$$\sum_{i=1}^{6} p_i = 1. \quad (26)$$

The functions (24) and (25) are presented graphically on Fig. 5. At $c = 0$, we restore the pure isotropic case when all $p_i = 1/6$. Increasing of $c$ leads to separation of these quantities: transition probabilities of moving in $z$ direction are growing, whereas corresponding values in $xy$ plane are gradually tending to zero. Approaching the very large values of $c$ around 1, when there are practically no possibility of moving in $xy$ plane, $p_5$ and $p_6$ reach the limiting values of 1/2. Note also, that $c = 1$ (fully occupied lattice) has no physical meaning in our case, since there is no possibility for particles to move at all.

Finally, substituting (24), (25) into expressions for the shape parameters (18), (19), we find corresponding expressions:

$$A = \frac{1}{100} c^2(c^6 + 4c^5 + 10c^4 + 20c^3 + 25c^2 + 24c + 16), \quad (27)$$

$$S = \frac{1}{500} c^3(c^5 + 6c^4 + 21c^3 + 56c^2 + 111c + 174c +$$

![Fig. 6](image-url) Shape parameters $A$ (given by Eq. (24)) and $S$ (Eq. (25)) as functions of concentration $c$ of oriented lines.
+219c^3 + 204c^2 + 144c + 64). \hspace{1cm} (28)

Expressions (27) and (28) as functions of \( c \) are plotted on Fig. 6. As expected, the asymmetry of shape is increasing with growing of the concentration of structural defects: the configuration of spreading population becomes more and more elongated in \( z \) direction. Thus, the presence of an array of oriented fibers (tubes) leads to considerable spatial organization of invading population in environment.

5 Conclusions

In the present work, we developed the simple mathematical model of population of agents, spreading in an oriented environment which is characterised by spatial anisotropy. It can be related to numerous processes, encountered in biology and medicine, such as chemotaxis or gravitaxis, the cell migration in extracellular environment or drug delivery.

The presence of orientational factors in environment may change the geometrical shape characteristics of a spreading population. The motivation of our study was to analyze the influence of anisotropy of environment on the universal shape parameters. For this purpose, we studied a system of non-interacting \( N \) random walkers, spreading on an infinite \( d = 3 \)-dimensional lattice, starting with initial very dense configuration (“drop”). The transition probabilities \( p_i \) \((i = 1, \ldots, 6)\) in different directions are assumed to be non-equal (asymmetric). We found the exact analytical values for the shape parameters, such as asphericity \( A \) (Eq. 18) and prolateness \( S \) (Eq. 19) as functions of transition probabilities \( p_i \). To illustrate the results obtained, we considered several model cases of oriented environment. Of particular interest is the case, when the array of lines (tubes) of parallel orientation is present in the system. This can serve as a model of extracellular matrix with collagen and elastin fibers or systems of oriented nanotube array in drug delivery implants. It is quantitatively shown, that presence of such objects leads to considerable spatial orientation and organization of invading population.

References

1. W. Alt. Biased random walk model for chemotaxis and related diffusion approximation. J. Math. Biol. 9, 147-177 (1980).
2. H.C. Berg. Motile Behavior of Bacteria. Physics Today 53, 24-29 (2000).
3. F.A.C.C. Chalub, P.A. Markowich, B. Perthame and C. Schmeiser. Kinetics models for chemotaxis and their drift-diffusion limits, Monatsh. Math. 142, 123-141 (2004).
4. Y. Dolak and C. Schmeiser. Kinetic models for chemotaxis: Hydrodynamic limits and spatiotemporal mechanics. J. Math. Biol. 51, 595-615 (2005).
5. T.J. Pedley and J.O. Kessler. A new continuum model for suspensions of gyrotactic micro-organisms. J. Fluid Mech. 212, 155-182 (1990).
6. R.V.V. Vincent and N.A. Hill. Bioconvection in a suspension of phototactic algae. J. Fluid Mech. 327, 343-371 (1996).
7. N. A. Hill and D.P. Hader, A biased random walk model for the trajectories of swimming micro-organisms. J. Theor. Biol. 186, 563-526 (1997).
8. R.B. Dickinson, S. Guido and R.T. Tranquillo. Biased cell migration of fibroblasts exhibiting contact guidance in oriented collagen gels, Ann. Biomed. Eng. **22**, 342-356 (1994).
9. R.B. Dickinson. A generalized transport model for biased cell migration in an anisotropic environment, J. Math. Biol. **40**, 97-135 (2000).
10. T. Hillen. Meso-macroscopic and macroscopic models for mesenchymal motion. J. Math. Biol. **53**, 585-616 (2006).
11. A. Chauviere, T. Hillen, and L. Preziosi. Modeling cell movement in anisotropic and heterogeneous network tissues. Networks and Heterogeneous Media **2**, 333-357 (2007).
12. K.J. Painter. Modelling cell migration strategies in the extracellular matrix. J. Math. Biol. **58**, 511-543, (2009)
13. A.R.A. Anderson, M.A.J. Chaplain, E.L. Newman, R.J.C. Steele, and A.M. Thompson. Mathematical modelling of tumour invasion and metastasis. J. Theor. Med. **2**, 129-154 (2000).
14. T. Alarcon, H.M. Byrne, P.K. Main. A cellular automaton model for tumour growth in inhomogeneous environment, J. Theor. Biol. **225**, 257-274 (2003).
15. P. Friedl and K. Wolf. Tumour-cell invasion and migration: diversity and escape mechanisms, Nature Rev. **3**, 362-374 (2003).
16. P.R. Armsworth and J.E. Roughgarden. The impact of directed versus random movement on population dynamics and biodiversity patterns. Am. Nat. **165**, 449-465 (2005).
17. S. Dewhurst, F. Lutscher. Dispersal in heterogeneous habitats: thresholds, spatial scales, and approximate rates of spread, Ecology **90**, 1338-1345 (2009).
18. T. Hillen and K.J. Painter. in Dispersal, Individual Movement and Spatial Ecology. Lecture Notes in Mathematics, vol 2071 (Springer Berlin 2013), pp 177-222
19. R.S. Cantrell, C. Cosner, Y. Lou. Movement toward better environments and the evolution of rapid diffusion, Math Biosci **204**, 199-214 (2006)
20. B.P. Yurk. Homogenization analysis of invasion dynamics in heterogeneous landscapes with differential bias and motility, J. Math. Biol. **77**, 27-54 (2017).
21. T. Kirk, R. W. and Lewis, M. A. (1997). Integrodifference models for persistence in fragmented habitats. Bull. Math. Biol. 59, 107137.
22. PR Armsworth, L. Bode L. The consequences of non-passive advection and directed motion for population dynamics, Proc R Soc Lond A **455** :4045-4060 (1999)
23. F. Belgacem, C. Cosner, The effects of dispersal along environmental gradients on the dynamics of populations in heterogeneous environments, Can. Appl. Math. Quar. **3**, 379 (1995).
24. A. Zakarchenko, N. Guz, A.M. Laradji, E. Katz and S. Minko. Magnetic field remotely controlled selective biocatalysis, Nature Catalysis **1**, 7381 (2018).
25. D. Losic, M. S. Aw, A. S., K. Gulati, and M. Bariana. Titania nanotube arrays for local drug delivery: recent advances and perspectives, Expert Opin. Drug Deliv. **12**, 103-127 (2015).
26. Q. Wang, J.-Y. Huang, H.-Q. Li, A. Z.-J. Zhao, Y. Wang, K.-Q. Zhang, H.-T. Sun, and Y.-K. Lai. Recent advances on smart TiO$_2$ nanotube platforms for sustainable drug delivery applications, Int. J. Nanomedicine **12**, 151165 (2017)
27. M F Shlesinger and B West (ed ) Random Walks and their Applications in the Physical and Biological Sciences (AIP Conf Proc vol 109) (AIP New York 1984); F Spitzer Principles of Random Walk (Springer Berlin 1976)
28. Patlack, C. S. (1953). Random walk with persistence and external bias. Bull. Math. Biophys., 15, 31139.
29. E.A. Codling, M.J. Plank and S. Benhamou, Random walk models in biology, J. R. Soc. Interface **5**, 813-834 (2008).
30. J.A. Aronovitz and D.R. Nelson. Universal features of polymer shapes, J. Physique **47**, 1445-1456 (1986).
31. J. Rudnick and G. Gaspari. The asphericity of random walks, J. Phys. A **19**, L191-L194 (1986).
32. S. Bianchi, L. Biferale, A. Celani, M. Cencini. On the evolution of particle-puffs in turbulence, Eur. J. Mech. B Fluids **55**, 324-329 (2016).