

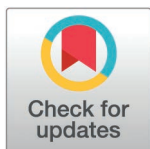
RESEARCH ARTICLE

Communication through autoattractants can enhance and limit collective migration of immune cells

David M. Versluis^{1*}, Robert H. Insall¹

Department of Cell & Developmental Biology, University College London, London, United Kingdom

* d.versluis@ucl.ac.uk



OPEN ACCESS

Citation: Versluis DM, Insall RH (2026) Communication through autoattractants can enhance and limit collective migration of immune cells. PLoS Comput Biol 22(9): e1014809. <https://doi.org/10.1371/journal.pcbi.1014809>

Editor: Calina Copos, Northeastern University, UNITED STATES OF AMERICA

Received: May 29, 2026

Accepted: September 7, 2026

Published: September 22, 2026

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pcbi.1014809>

Copyright: © 2026 Versluis, Insall. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution,

Abstract

Many eukaryotic cells produce attractant molecules to which they themselves are also attracted. For example, neutrophils produce leukotriene B4 while swarming. These autoattractants create a secondary signalling layer that coordinates collective cell behaviour. The principles by which autoattractants shape migration, however, remain poorly understood. Here we use a hybrid agent-based computational model to dissect the effects of autoattractants on the collective chemotaxis of immune cells. We find that autoattractant signals strongly enhance cells' responses to primary attractant, but only if the autoattractant is sufficiently short-lived: at longer lifetimes, accumulation degrades the directional information cells can extract. The overall effect of autoattractants therefore depends crucially on the balance between production and efficient removal — whether through cellular uptake, enzymatic breakdown, or inherent chemical instability. Optimal lifetimes exist, determined by cell speed and autoattractant diffusion, yet remarkably independent of cell density and primary attractant concentration. Autoattractants whose removal is governed by inherent instability rather than direct cellular breakdown coordinate migration less efficiently, but work more robustly across different environments. In the absence of cell-mediated breakdown, the model further reveals a characteristic optimal cell–cell distance: too little communication leaves cells uncoordinated, while excessive signalling drives them into slow-moving aggregates. Strikingly, the conditions that produce the most efficient chemotaxis lie close to those that trigger aggregation, suggesting that many autoattractant systems operate near a critical boundary that can be tuned by evolution either to disperse cells or to bring them together.

Author summary

Immune cells must travel through the body to reach sites of injury, infection, and developing tissue. They are guided by chemical signals. Many immune cells, such as neutrophils gathering at wounds and microglia in the brain, also release

and reproduction in any medium, provided the original author and source are credited.

Data availability statement: All code used, as well as the parameter files for producing the data, and the code used for analysis, are on a GitHub repository at <https://github.com/DMvers/AutoTaxis>. We have also used Zenodo to assign a DOI to the repository at time of submission: <https://doi.org/10.5281/zenodo.20434528>.

Funding: This work was supported by the Wellcome Trust, Grant ID: 221786/Z/20/Z to RHI. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

their own signals that attract others of the same kind. We call these ‘autoattractants’. In effect, the cells tell each other where to go. This communication helps coordinate group movement, but little is known about how it works. We built a computer simulation of migrating immune cells to explore how autoattractants shape their collective behaviour. We find that autoattractants must be short-lived to be useful: when autoattractant accumulates, it obscures any sense of direction. Signals that cells actively break down, or that decay on their own, carry clear directional information. With signals that decay on their own, a delicate balance emerges: just enough cooperation leads to the most efficient coordinated migration, while a little too much causes cells to clump together instead of moving forward. Our work suggests that many more cell types may use this communication than we know, and that the same system can be tuned by evolution to spread cells out or to gather them together.

1. Introduction

Many eukaryotic cells produce attractant molecules that they themselves are also attracted to. We refer to these molecules as “autoattractants”. There are many examples of this behaviour, in particular in mammalian immune cells. For example, neutrophils that sense the attractant peptide fMLP produce leukotriene B₄ (LTB₄), which functions as a signal-relay molecule during chemotaxis, amplifying a recruitment of additional neutrophils to sites of inflammation often characterised as ‘swarming’ [1–3]. LTB₄ is also quickly bound and sequestered from the medium by neutrophils [4]. In response to LPS neutrophils also produce IL-8, which functions as a chemoattractant for neutrophils [5,6]. Autoattraction can also exist without swarming, however. For example, microglia are attracted to ATP, and also release it by exocytosis in response to LPS [7,8], but they do not move in swarms as neutrophils do. This may be because ATP is degraded both near microglia and in the broader extracellular space [9,10], which would limit swarm formation. Autoattractants can also be produced in response to attractant chemokines, such as in eosinophils, which produce the short-lived autoattractant prostaglandin D₂ in response to the activation of its chemokine receptor CCR3 [11–15].

Despite the prevalence of autoattractant signalling across these systems, the mechanics of transmitting information through autoattractants remain understudied. In particular, we focus on a specific class of interactions: the exchange of signals among identical cells during chemotaxis along self-generated gradients. Self-generated gradients are widespread among many cell types and attractants, and often play a large role in cell migrations [16–18]. We focus on self-generated gradients specifically because they are inherently temporary and dynamic. If a stable, externally imposed gradient were already present and sufficient for directed migration, the additional information carried by autoattractant signalling would be less useful.

As self-generated gradients are inherently temporary, they are hard to study *in vivo* and *in vitro*. We used computational modelling to create an overview of how cells,

with a particular focus on immune cells, may use autoattractant signals to enhance collective chemotaxis in self-generated gradients. We based our modelling on earlier successful work using agent-based modelling of this system [17,19], and we have previously used this technique to create predictions for migrating macrophages [20]. Crucially, we have expanded the conceptual framework to include autoattractants as separate species that can be produced, broken down, or decay in various ways. Here, we used modelling to explore: (i) how autoattractants can enhance the ability of cells to gather information during chemotaxis to weak or noisy signals; (ii) the trade-offs of various strategies for creating useful autoattractant signals; (iii) the interaction between cell speed and effective communication; and (iv) the conditions under which autoattractant signalling leads to aggregation rather than enhanced migration.

2. Results

2.1 Approach

We used a hybrid agent-based modelling approach in which cells are represented as individual off-lattice agents operating on a regular lattice of attractant concentrations. The model simulates a chemotaxis chamber: cells start at one end of a rectangular domain filled with an attractant that is initially present, which we call the primary attractant. The model is then run in discrete timesteps to generate predictions for cell behaviour and attractant concentrations across the environment over time. This approach can represent many different types of migrating immune cells and situations. We will describe the working of the model here briefly, and refer to the methods for a full description.

Each cell is approximated by a circle (Fig 1A), representing the area over which a cell can sense, add, and remove attractants within each simulation timestep (6 s). Each timestep, the cell uses saturable receptors to sense and break down primary attractant in the area it covers. It then moves in the direction of the gradient it senses (Fig 1B). Random noise is added to cell perception to prevent excessively shallow gradients from being followed, and the attractant diffuses between timesteps so that smooth gradients can be formed. The combination of attractant removal and movement towards attractant leads to a self-generated gradient and limited migration away from high densities of cells (Fig 1C). We have previously shown that this approach leads to a good reproduction of migration to self-generated gradients [16,19].

Cells also produce autoattractant, which is modelled similarly to the primary attractant, except that it is not initially present but instead produced by the cells in proportion to the amount of primary attractant they break down (Fig 1D). For example, if a cell breaks down 1 unit of attractant in a timestep and the ratio is set to 10, the cell will produce 10 units of autoattractant. The ratio of production is determined by the parameter settings of specific simulations. Cells also sense and break down autoattractant using receptors separate from those used for primary attractant (Fig 1E). Each cell uses information from both kinds of receptor to arrive at a single target direction, towards which it will move with a fixed speed. Though speed per model timestep is fixed, cells will vary in how consistently they head towards the migration goal, so the speed measured over timescales longer than one timestep (6 seconds) will also vary. Taken together, this leads to complex migrations, where cells can indirectly follow the gradient of primary attractant through following the autoattractant that was produced based on it (Fig 1F). We used several sets of parameters for the model, based as far as possible on plausible values for immune cells (Tables 1 and 2).

2.2 Autoattractants can improve migration

We first initialised the model with a parameter set based on fast-moving immune cells (Table 1 and 2), such as neutrophils. We initialise all cells on one side of the rectangular area, and consider a cell to have migrated successfully if it is in the bottom quarter of the area by the end of the simulation. As a control, we first initialise the model with no autoattractant production. The primary attractant on its own can only recruit a limited number of cells (Fig 2A and S1 Video). When we add autoattractant production by cells we find that more cells migrate successfully (Fig 2B and S1 Video) and a clear gradient of autoattractant is formed (Fig 2B, right panel).

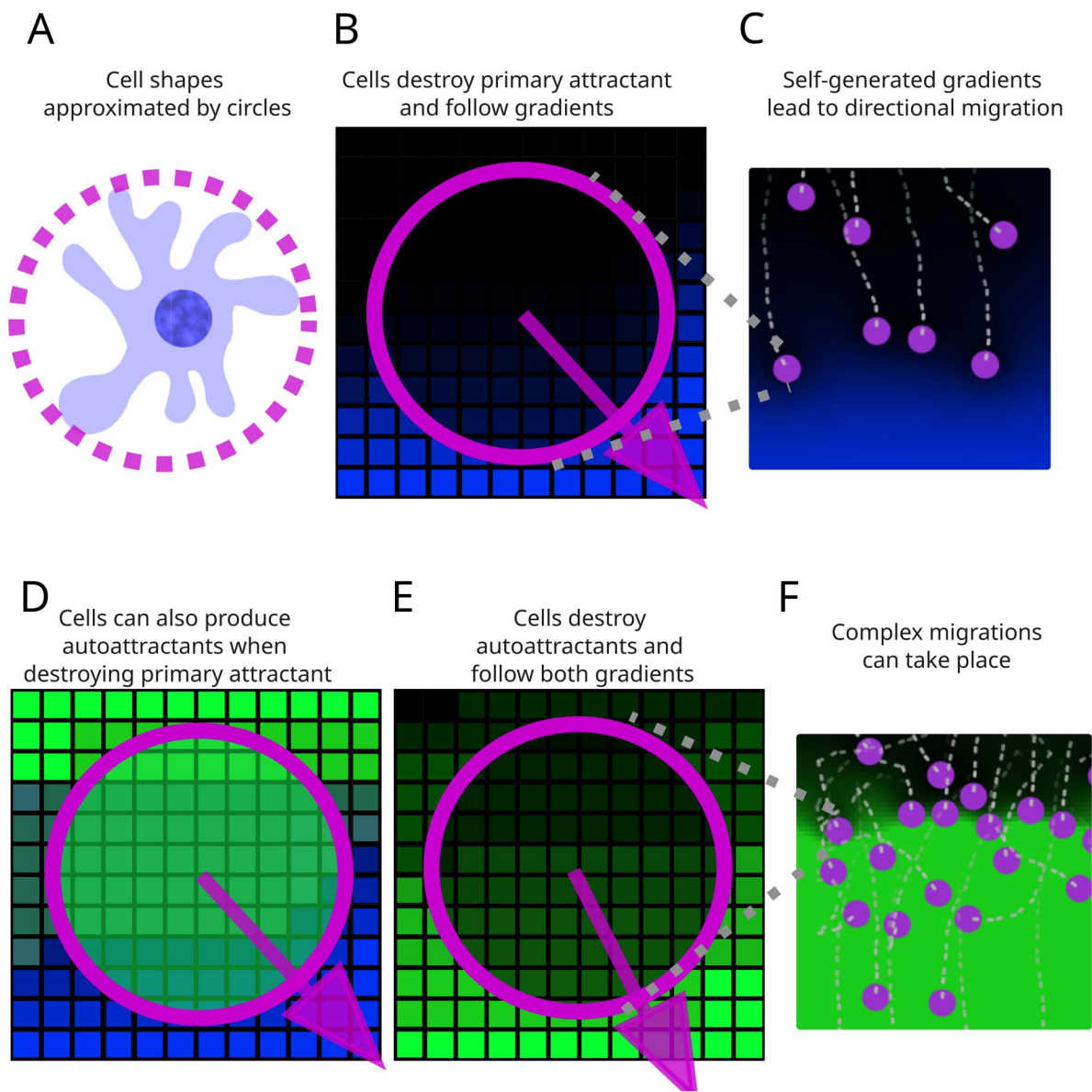


Fig 1. Schematic model setup. **A.** The area within which a cell can sense attractants is approximated by a circle. **B.** Schematic of a single modelled cell breaking down primary attractant while also following its gradient. **C.** Visualisation of cells chemotaxing to a self-generated gradient of primary attractant in a sample simulation. **D.** Schematic of cell producing autoattractant while creating and following a gradient mostly composed of primary attractant. **E.** Schematic of a cell breaking down autoattractant and following a gradient mostly composed of autoattractant. **F.** Visualisation of cells chemotaxing to a self-generated gradient of autoattractant in a sample simulation.

<https://doi.org/10.1371/journal.pcbi.1014809.g001>

The number of cells that migrate depends on the amount of autoattractant produced (Fig 2C), but with a clear optimal level above which migration returns to a baseline level similar to that without autoattractant production. Interestingly, no amount of autoattractant causes less migration than that of the baseline without autoattractant. Smaller amounts than the optimum lead to a smaller migration (Fig 2D and S1 Video), as the wave of autoattractant formed by the frontrunners is broken down before it reaches all cells. Larger amounts also lead to less migration, as the part of the autoattractant

Table 1. Environmental and simulation parameters.

Parameter	Default value	Source/Notes
Simulation area width	1000 μm	Model assumption
Simulation area length	2000 μm	Model assumption
Simulation area height	20 μm	Height of Insall chamber bridge [21]
Diffusion of attractants	50 $\mu\text{m}^2/\text{s}$	[22,23], varied around this value
Initial concentration of primary attractant	20 nM	[20], varied around this value
Environmental noise	0-10 nM	Plausible fit
Initial density of cells	40 cells on bridge	[20], results with lower value also shown
Lattice side length	10 μm	Model approximation
Timestep duration	6 s	Model approximation

<https://doi.org/10.1371/journal.pcbi.1014809.t001>

Table 2. Cell-specific parameters.

Parameter	Fast-moving cells	Slow-moving cells	Source/Notes
	(e.g., neutrophils)	(e.g., macrophages)	
Simulation duration	1000 steps (100min)	20000 steps (2000min)	Plausible fit
Movement speed	20 $\mu\text{m}/\text{min}$	1 $\mu\text{m}/\text{min}$	[20,24]
Minimum time to reverse direction	2.8 min	2.8 min	[25]
Sensing distance from cell centre	30 μm	30 μm	Plausible fit
Receptor K_d	10 nM	10 nM	[26]
K_m of primary attractant breakdown	10 nM	10 nM	Matched with K_d
V_{max} of primary attractant breakdown	200 nM/min	10 nM/min	Plausible fit
K_m of autoattractant breakdown	10 nM	10 nM	Matched with K_d
V_{max} of autoattractant breakdown	variable	variable	Varied throughout
Autoattractant production ratio α	variable	variable	Varied throughout

<https://doi.org/10.1371/journal.pcbi.1014809.t002>

gradient that can be sensed is further away from the first wave (Fig 2E and S1 Video). The front wave still functions normally: as the concentration is very high, the autoattractant receptors are saturated in all directions.

2.3 Optimal autoattractant production and breakdown depend on environment, but optimal lifetimes are similar

To be effective, autoattractant must reach other cells that do not sense the primary attractant gradient, and do so in the right concentration. We have shown that there is a range of different autoattractant production rates that function, but we also expect the rate of breakdown to influence the effectiveness. By altering the maximum rate of autoattractant breakdown (Eq. 10) we can effectively vary the dynamics. We systematically analyse pairs of production and breakdown values across a wide range (Fig 3A). This shows that there is a linear relationship between optimal production and optimal breakdown, leading to an optimal balance in parameter space (schematically shown in Fig 3B). Where there is relatively too much production, autoattractant accumulates as in Fig 2E. Where there is relatively too much breakdown there is insufficient autoattractant to form a large wave, as in Fig 2D.

We next investigated how robust this migration is by looking into how different initial conditions may influence this relationship. In an *in vivo* context cells cannot expect to always encounter the same concentration of attractant, or to be at a high density optimal for collective migration. We test a lower cell density, a lower initial concentration of primary attractant, and a higher initial concentration of primary attractant (Fig 3C–3E). These show different optimal production and breakdown balances. This means that the same cells may chemotax much more or less depending on these environmental

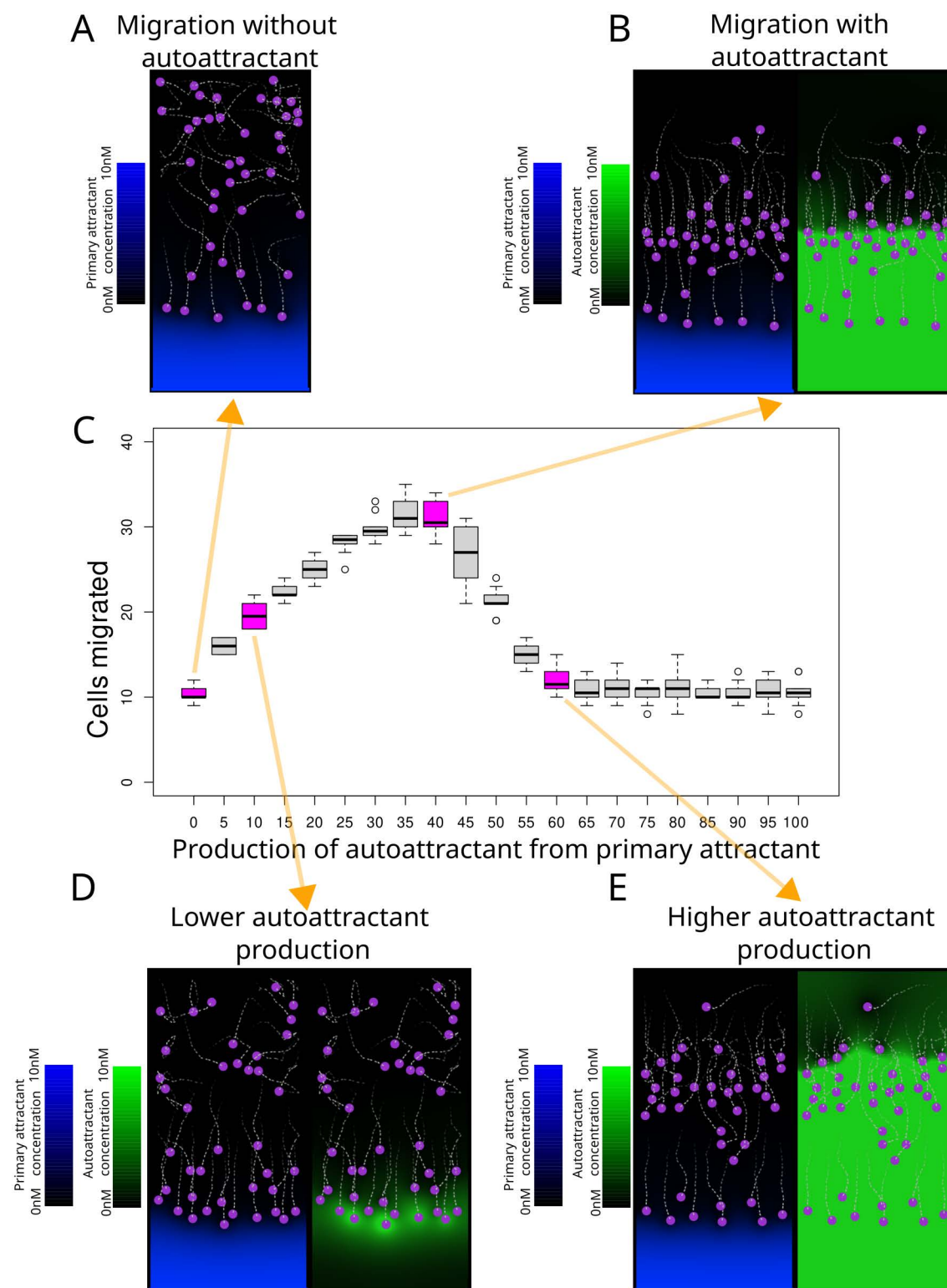


Fig 2. Autoattractant leads to more migration at correct production ratios. **A.** Cell locations and primary attractant distribution during a representative model simulation with only a primary attractant. **B.** Cell locations and primary attractant (left) and autoattractant (right) concentration during a model

simulation with an added autoattractant. **C.** Cell migration over a wide range of autoattractant production ratios. $n = 10$ per condition. **D, E.** Visualisations as in A of the effects of lower and higher production, which both lead to less migration compared to B, as either a very small autoattractant gradient forms (D), or it forms very far away (E).

<https://doi.org/10.1371/journal.pcbi.1014809.g002>

factors. However, we can show that the dynamics at play are still the same by calculating the average time that an autoattractant molecule can be expected to exist, given how much autoattractant is produced and how much is broken down. We call this the lifetime of the autoattractant. In Fig 3F we examine the relationship between this lifetime and migration. This shows that all simulations in which cells migrate efficiently are within the same range of autoattractant lifetimes, between roughly 250 and 1000 seconds, despite differences in the environmental factors.

2.4 Decaying autoattractants allow for migration less dependent on environment

We showed how similar autoattractant lifetimes are optimal across environments, despite requiring very different amounts of autoattractant production and breakdown. This suggests that an autoattractant with a fixed lifetime could cause a very consistent migration in different environments. This could occur if the autoattractant decays at a consistent rate, due to enzymes being present across the tissue or due to the autoattractant oxidising rapidly on its own. Examples are ATP [10] and prostaglandin D2 [13–15]. We implement this as an autoattractant that is continuously broken down over time everywhere, instead of only near cells, so that its decay depends only on time. Effectively, the autoattractant always has a fixed lifetime. Similar to the broken down autoattractant, this decaying autoattractant leads to much more effective migration than without an autoattractant (Fig 4A and S2 Video). As before, we systematically examine the relation between production and decay in this system, and a very different relationship emerges: above a certain production, the same decay is optimal (Fig 4B and S2 Video). There is now accumulation of autoattractant when decay is slow, leading to accumulation of autoattractant without a discernible gradient. An autoattractant that decays very quickly similarly does not lead to a discernible gradient, leading to poor performance at either extreme. The optimal values remain similar when we vary cell density and attractant concentration (Fig 4C–4E). We can compare how well the outcomes of different parameters correlate with the baseline by examining the relation between the number of cells migrated for the same combination of autoattractant production and breakdown or decay. This shows that for cells with a broken down autoattractant the same parameters cause very different levels of migration depending on the initial attractant concentration and cell density (Fig 4F), but with a decaying autoattractant the same parameter values produce migrations that are well-correlated between conditions (Fig 4G).

2.5 Slow-moving cells can migrate better or aggregate

We have previously examined only fast-moving migrating cells, with parameters based on measurements of neutrophils, but many immune cells, such as macrophages or microglia, move much more slowly. We now examined how a parameter set with cells that move 1/20th of the speed of the cells we studied previously (Table 2) affects the migration. We assumed these cells also break down the primary attractant slower, so that they still create discernible self-generated gradients, and we give them an appropriate amount of time to reach the other side of the environment.

We found that with a broken down autoattractant the general dynamics of the slow-moving cells were similar to those of the fast-moving cells, as autoattractants enhanced migration (Fig 5A and 5B and S3 Video), and there was a similar linear relationship with breakdown (Figs 5C and S1) and an optimal lifetime that was roughly 20 times as long, in proportion to the change in cell speed, and which was again similar for all conditions, though with greater variability than before (Figs 5D and S1A–S1C). Furthermore, we found that a decaying autoattractant again led to similar optimal lifetimes regardless of conditions (Figs 5E and S1D–S1F), but there was also an unusual new behaviour: with a large production of a rapidly decaying autoattractant, cells formed transient clumps (Fig 5E, inset lower left, S4 Video). These clumps consist

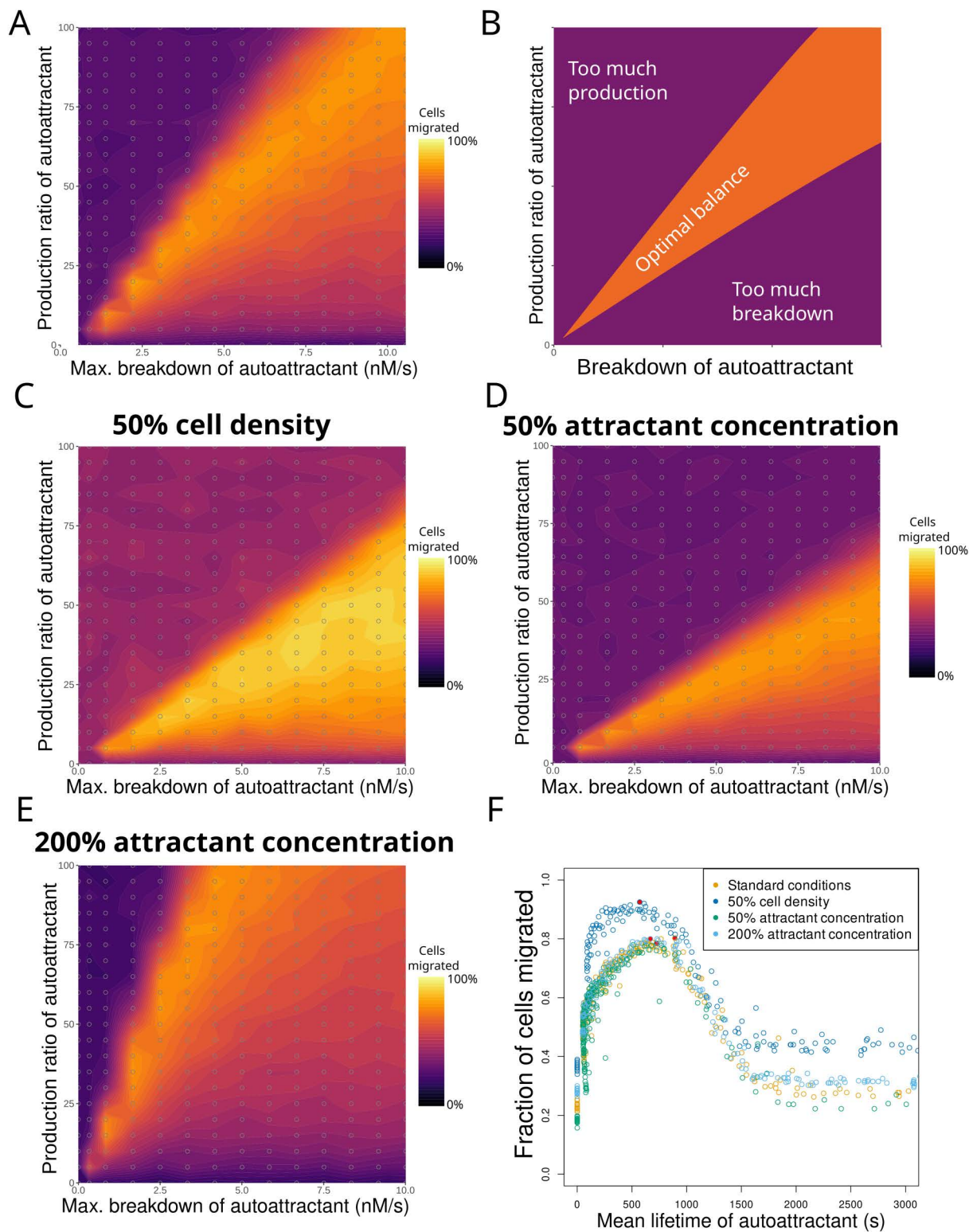


Fig 3. Optimal production and breakdown values vary, but optimal autoattractant lifetimes are similar. **A.** The effect of autoattractant production (as a ratio of breakdown of primary attractant) and autoattractant breakdown on migration. $n = 10$ per point. **B.** Schematic of the relation from A, highlighting that an optimal balance exists between the production and the breakdown of autoattractant. **C–E.** The combined effect of production and breakdown

of autoattractant for different cell densities and attractant concentrations. $n=10$ per point. **F.** Overview of the relation between migration and the mean lifetime of autoattractant for each parameter combination in A,C,D&E. Capped at a mean lifetime of 3000 s for readability. $n=10$ per point. Filled circles represent the best migration for that condition.

<https://doi.org/10.1371/journal.pcbi.1014809.g003>

of cells whose steering is more biased towards neighbouring cells than up the primary attractant gradient. Together they moved slower than individual cells, leading to an inhibited migration that is worse than that without autoattractants, which never occurred with the fast-moving cells. Other conditions within this set showed varying degrees of efficiency and direct cell-cell contact ([Fig 5E](#) insets, [S4 Video](#)).

2.6 Increased diffusion of autoattractant leads to shorter optimal lifetimes and decreased clumping

We noted that the conditions where autoattractants inhibited effective migration were very close to those that promoted effective migration. To gain additional insights into the role of the attractant and autoattractant in this process we examined both slower and faster diffusion speeds for both attractants and autoattractants. Diffusion speeds of attractants vary across several orders of magnitude for different signalling molecules and conditions [[22,23](#)], such as $6.2 \mu\text{m}^2/\text{s}$ for the chemokine CXCL13 [[27](#)] and up to $710 \mu\text{m}^2/\text{s}$ for ATP under ideal conditions [[28](#)]. We examined the effect of diffusion speeds 5x slower and 5x faster than our baseline ($10 \mu\text{m}^2/\text{s}$ and $250 \mu\text{m}^2/\text{s}$) with a broken down autoattractant for both fast ([Figs 6A](#) and [S2](#)) and slow ([Figs 6B](#) and [S3](#)) cells. We found that the optimal mean lifetime was shorter with faster autoattractant diffusion in both conditions, regardless of attractant diffusion speed. Slower autoattractant diffusion speeds consistently led to poorer migration with slow cells, but not fast cells. However, the shape of the relationship between production and breakdown was maintained throughout.

We next examined how different diffusion speeds affect migration with decaying autoattractants. Fast-moving cells maintained similar dynamics regardless of diffusion speed, though migration was impaired in the more extreme cases ([S4 Fig](#)). For slow-moving cells, however, the effects depended on which substance diffused faster. Increasing attractant diffusion alone or decreasing autoattractant diffusion alone caused slow-moving clumps to form under many more parameter combinations ([Fig 6C](#), left middle and lower middle), as the short-range influence of the autoattractant increased relative to the attractant. Conversely, increasing autoattractant diffusion alone or decreasing attractant diffusion alone reduced the number of parameter combinations that led to slow-moving clumps ([Fig 6C](#), right middle, upper middle). When diffusion of both attractant and autoattractant was increased together, the amount of migration resembled that of the baseline, but the parameter space of optimal migration was shifted toward shorter autoattractant lifetimes — similar to the effect seen with broken down autoattractant. Conversely, when both were decreased the area of optimal migration shifted towards longer lifetimes.

Under the conditions with high diffusion, we noted that the parameters that led to optimal migration were located very close to those that caused slow-moving clumps. To further examine this relation, we calculated the mean distance to the nearest cell for each cell in our simulations, and its relation to migration ([Fig 6D](#)). We found that very close cells were associated with inefficient migration, but also that slightly less close cells were associated with optimal migration. Distant cells were associated with suboptimal migration. We also find that the cell-cell distance is determined by the strengths of cell-perceivable gradients across the narrow axis of the model area ([S5A Fig](#), calculation details in Methods section 4.5). Interestingly, the association between cell-cell distance and migration efficiency does not hold for faster-moving cells, or for slow-moving cells that break down autoattractant ([S5B Fig](#)), but there is a clear association between the strengths of perceived gradients and migration efficiency that does hold for fast-moving cells with decaying autoattractants ([S5C Fig](#)). Here perceptible gradients of intermediate strength are optimal, with gradients that are too weak or too strong leading to less migration. In contrast, in cells that do break down autoattractant directly there is a simple positive linear relationship between cell-cell gradient strength and migration efficiency ([S5D Fig](#)). Taken together, this suggests that there is an

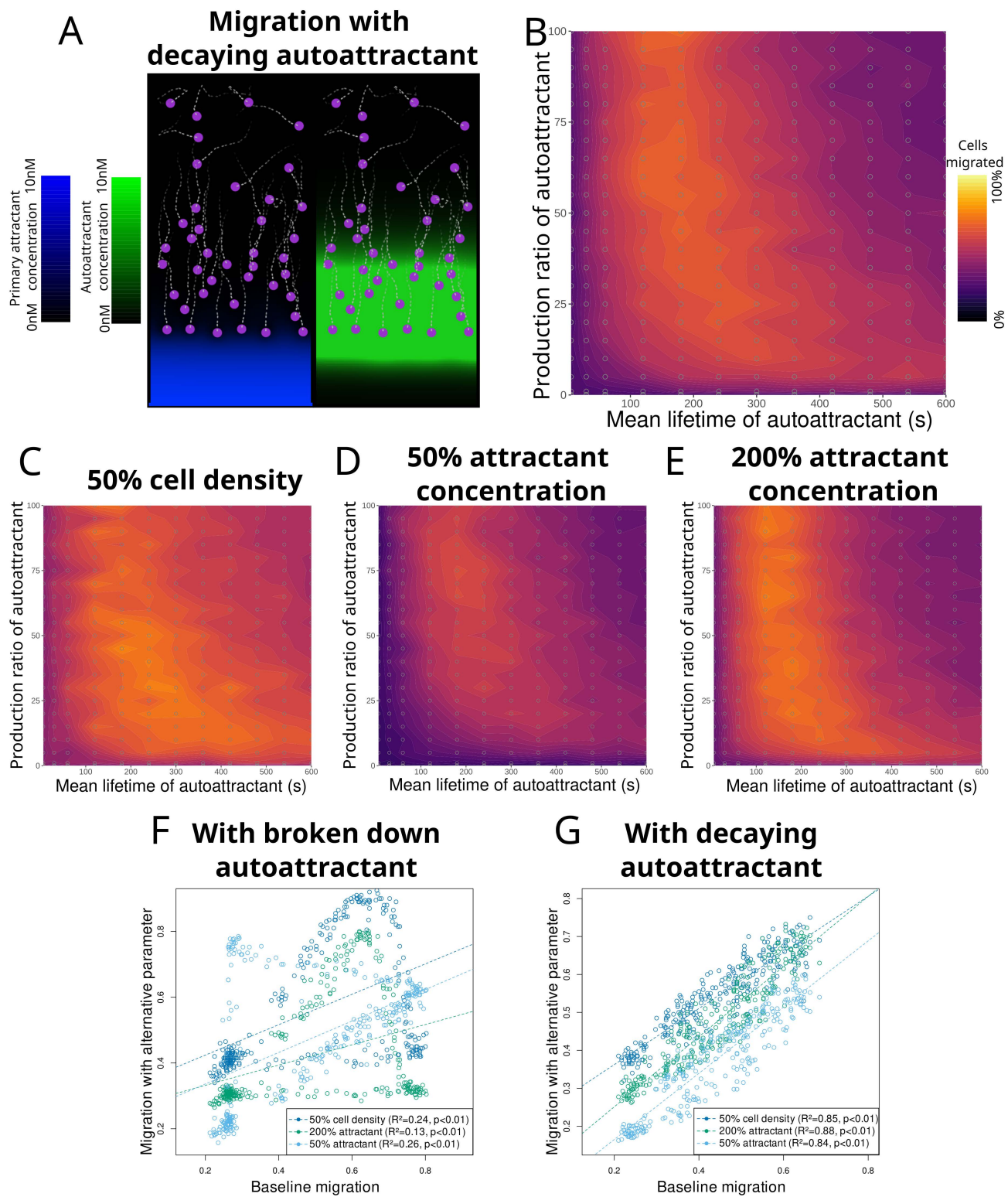


Fig 4. Decaying autoattractants lead to migration that is more stable across environments. **A.** Cell locations and primary attractant (left) and autoattractant (right) concentration in a sample model simulation with an autoattractant that decays constantly instead of being broken down by cells. **B.**

The relationship between autoattractant decay and production and migration outcomes. $n = 10$ per point. **C–E.** As in B, but for low cell density, low initial primary attractant concentration, and high initial primary attractant concentration, respectively. **F.** The relationship between migration efficiency with the baseline conditions of Fig 3A (on the X axis) compared to those of Fig 3C–3E (on the Y axis), each dot represents one combination of autoattractant production and autoattractant breakdown. **G.** The relationship between migration efficiency with the baseline conditions of Fig 4B compared to those of Fig 4C–4E. Each dot represents one combination of autoattractant production and autoattractant breakdown, as in the previous panel.

<https://doi.org/10.1371/journal.pcbi.1014809.g004>

optimal amount of cooperation for cells that do not break down autoattractant directly, schematically shown in Fig 6E. An intermediate level of cell-cell attraction through autoattractants leads to optimal migration, with lower levels causing insufficient coordination between the cells near to the attractant gradient and those further away, and so leading to cells being left behind. Higher cooperation levels caused slow-moving clumps as cells coordinated too strongly with each other and too little to the primary attractant. In contrast, cells that break down autoattractant around them migrate best when they generate a very strong gradient.

3. Discussion

Our model makes several key predictions about the role of autoattractants in collective cell migration. Firstly, autoattractants enhance collective migration by providing a secondary signalling layer that allows trailing cells to follow the path of frontrunner cells, even when those trailing cells cannot directly sense the primary attractant gradient. This is consistent with the signalling observed in neutrophil swarming [3,29] and *Dictyostelium* aggregation [30].

Secondly, autoattractants must be short-lived to be functional, as a long-lived autoattractant cannot give useful information on the location of the front of a moving wave. Optimal autoattractant lifetimes depend on cell and attractant characteristics more than on the environment. While the specific production and breakdown rates that yield optimal migration vary with cell density and primary attractant concentration, the optimal lifetime for autoattractants is remarkably consistent. This suggests that many autoattractants may have tightly controlled short lifetimes.

Thirdly, decaying autoattractants - those removed by spontaneous degradation or ubiquitous enzymes rather than by cellular breakdown - are more robust across environments, although they achieve a somewhat lower migration optimum. This robustness arises because the autoattractant lifetime is determined by a fixed decay rate rather than by the variable number of consuming cells, so that the lifetime varies much less across conditions.

Fourthly, slow cells are generally more efficient at migration relative to their speed, but can also clump more easily. This clumping occurs when the front cells are attracted more towards each other than towards the primary attractant, and so stop moving directionally. We find that efficient migration relies on close cell-cell interactions that are not far removed from conditions that lead to clumping instead of migration.

3.1 Implications for *in vivo* systems

The dynamics we describe are likely prevalent in many more systems. Autoattractant-like behaviours have been most extensively studied in *Dictyostelium*, where cAMP relay drives collective aggregation [30], and in neutrophils [1,3], but are also key in microglia [7,10]. We have shown that close associations of cells that communicate through short-lived autoattractants are the most efficient at collective migration. Because they would be short-lived, it is inherently difficult to find additional autoattractants *in vitro* or *in vivo*: samples collected would be depleted of autoattractant before measurements could be made. New techniques may find autoattractants in many more cell types.

In this text we have assumed that the attractant and autoattractant receptors have the same K_d , but this is not a requirement of the model. For example, an autoattractant that was produced with a tenfold higher production ratio and a tenfold higher K_d , K_m and V_{max} would show identical behaviour (eqs. 5, 10 and 11).

We have described good migration here as “optimal,” but it is important to keep in mind that recruiting of a large number of cells is one of several outcomes that may be selected for *in vivo*. In many biological systems, evolution will have

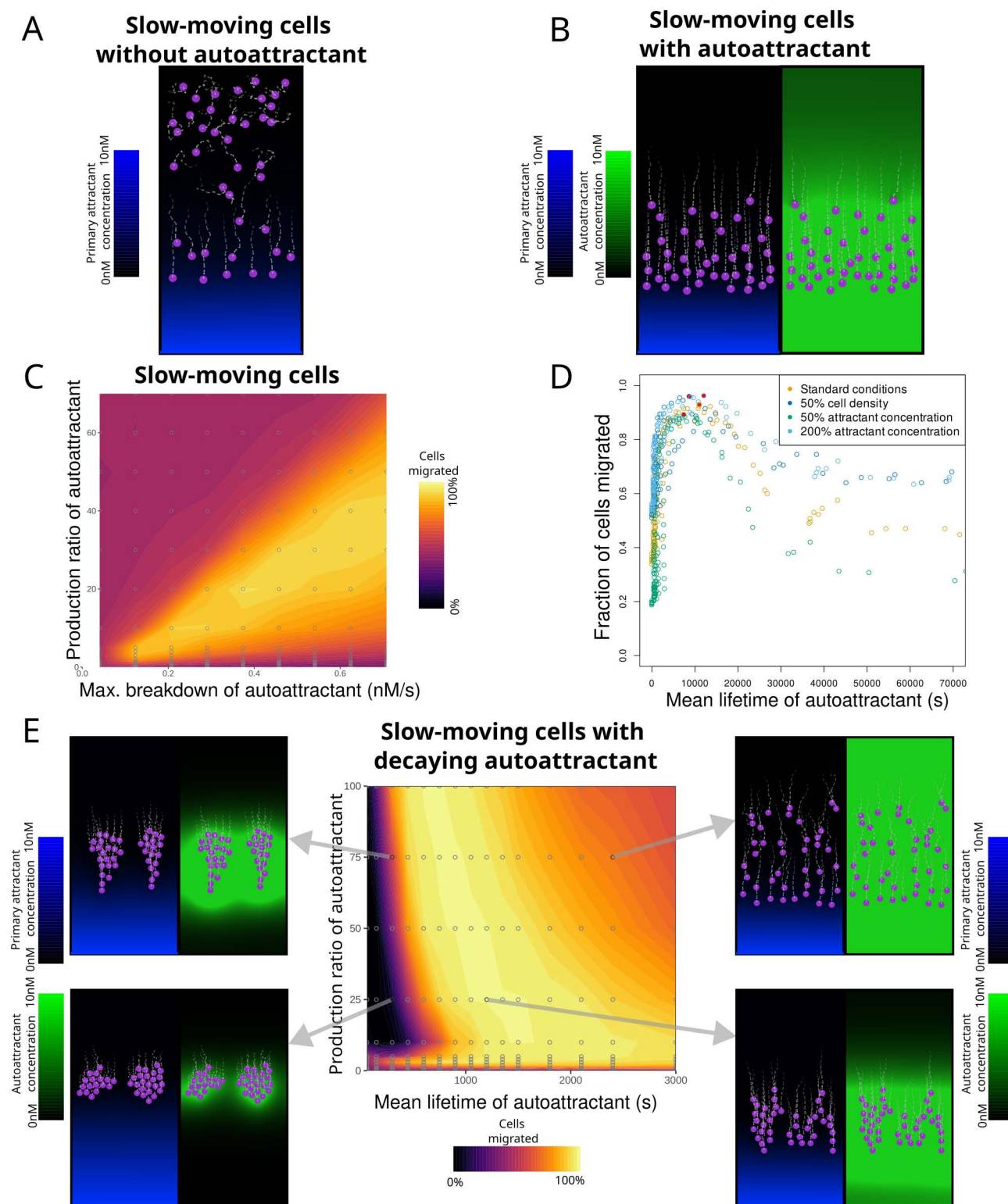


Fig 5. Slow-moving cells have longer optimal autoattractant lifetimes and can more easily aggregate during migration. **A.** Cell locations and primary attractant distribution in a representative model simulation with slower cells (Table 2) and only a primary attractant. **B.** As A, but with an added autoattractant that is broken down by the cells, displayed on the right. **C.** The relationship between autoattractant breakdown and production and

migration outcomes. $n = 10$ per point. **D.** Overview of the relation between migration and the mean lifetime of autoattractant for the parameters in C, as well as with lower cell density and lower and higher initial primary attractant concentration. Capped at a mean lifetime of 70000 s for readability. $n = 10$ per point. Filled circles represent the best migration for that condition. **E.** The relationship between autoattractant decay and production and migration outcomes. $n = 10$ per point. Insets show examples of different behaviour across this spectrum.

<https://doi.org/10.1371/journal.pcbi.1014809.g005>

shaped cells to exhibit a particular level of migration, which will often be only limited migration rather than maximal migration. This is reflected in the diversity of existing systems that may use autoattractants - each likely tuned to its specific functional requirements. Similarly, the clumping behaviour we observe could be an advantageous effect of autoattractant signalling in contexts where it is desirable for cells to find each other while migrating. For example, in lymph nodes, the aggregation of dendritic cells and T cells is functionally important for initiating adaptive immune responses, and autoattractant-driven clustering could facilitate this process [31,32].

Autoattractants released in response to primary attractants, as modelled here, should be distinguished from migration with co-attraction, where cells constitutively attract each other regardless of external gradients [33,34]. In our model, autoattractant production depends directly on sensing the primary attractant, creating a signal that transmits information about the direction of migration, rather than a simple aggregation signal. However, as we have shown, the signal can also become primarily an aggregation signal when it is so short-lived that it forms very strong local gradients.

3.2 Future extensions

Several extensions of this model merit future investigation. First, further enhancement of migration may exist through the production of an inhibitor derived from the autoattractant. Such an inhibitor could bind the same receptors as another attractant, but not provide as strong of a chemotactic signal, and so could create a smaller but more directional secondary wave [19]. Variation in chemotactic response between different receptors in general would also allow the model to potentially cover more situations. Second, pulsatile release of autoattractant, as observed in neutrophil swarming [3], could modulate the temporal dynamics of the signal. Finally, relay of the autoattractant signal, where cells amplify the signal by producing additional autoattractant in response to sensing it, could extend the effective communication range, as observed in microglial ATP signalling [7].

4. Methods

4.1 Model overview

We developed a multi-scale agent-based model of immune cell chemotaxis in which individual cells are represented as off-lattice circular agents operating on a two-dimensional regular lattice of chemical concentrations. The simulation represents a chemotaxis chamber with cells initially placed at one end and a primary attractant uniformly distributed throughout the domain. The model integrates chemical diffusion dynamics with discrete cell decision-making at each timestep.

4.2 Environment and chemical dynamics

4.2.1 Lattice and geometry. The simulation domain is a two-dimensional grid of size $N_x \times N_y$ lattice sites, where each site represents a $\Delta x = 10 \mu\text{m}$ square. The domain is bounded by no-flux boundary conditions. Two chemical species are tracked on the lattice: a primary attractant and an autoattractant, each stored as a concentration value at every lattice site. In what follows, C_{ij} denotes the concentration at site (i,j) of a generic species (each species obeys the dynamics below independently); where species must be distinguished (Eq. 5) we write $C_{\ell,ij}$ for ligand ℓ .

4.2.2 Diffusion. Chemical diffusion is computed each timestep using the DuFort–Frankel finite difference scheme. For an interior lattice site (i,j) that is not a wall, the concentration C_{ij} is updated as:

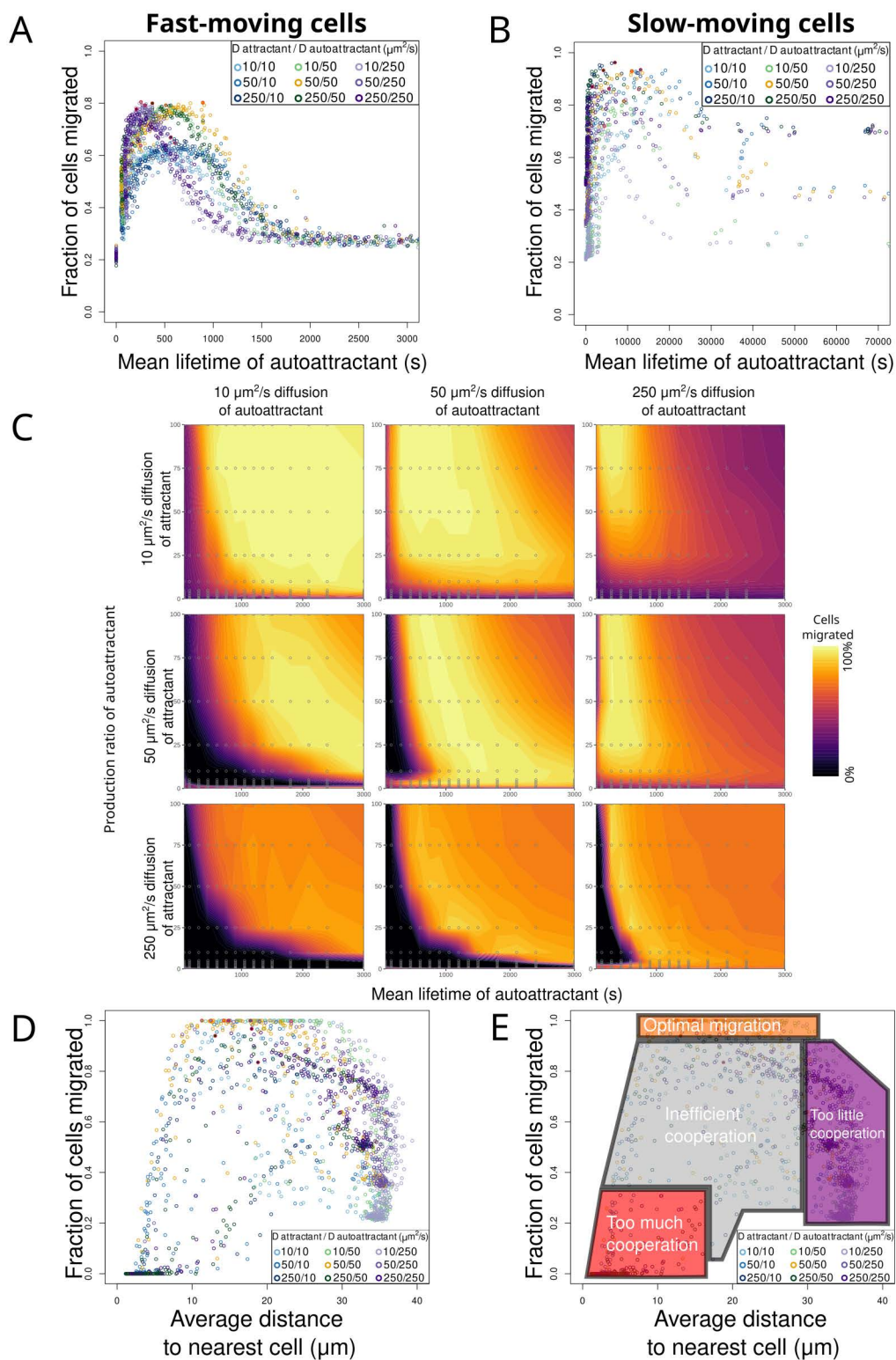


Fig 6. Higher diffusion promotes shorter lifetimes and efficient chemotaxis, but very short lifetimes can promote clumping. A, B. Lifetime for fast-moving (A) and slow-moving (B) cells with different diffusion speeds. Filled circles represent the best migration for that condition. $n = 10$ per point. C.

The relationship between production and mean lifetime of a decaying autoattractant, for different diffusion speeds of attractant and autoattractant. **D.** The relation between how many cells have migrated by the end of the simulation, and their average distance to the nearest cell in the first half of the simulation, for all simulations of C. **E.** Schematic of the relation between cell migration and cooperation, based on D.

<https://doi.org/10.1371/journal.pcbi.1014809.g006>

$$C_{ij}^{n+1} = \frac{1-4\hat{D}}{1+4\hat{D}} C_{ij}^{n-1} + \frac{2\hat{D}}{1+4\hat{D}} (C_{i+1,j}^n + C_{i-1,j}^n + C_{i,j+1}^n + C_{i,j-1}^n), \quad (1)$$

where $\hat{D} = D \Delta t / \Delta x^2$ is the dimensionless diffusion number, D is the diffusion coefficient ($\mu\text{m}^2/\text{s}$), $\Delta t = 6$ s is the timestep duration, and $\Delta x = 10 \mu\text{m}$ is the lattice spacing. If a neighbouring site is a wall, the concentration at the current site from the previous timestep is used in place of that neighbour. The first diffusion step of each timestep uses a forward Euler step to provide the two-level initial condition required by the DuFort–Frankel scheme:

$$C_{ij}^1 = C_{ij}^0 + \hat{D} (C_{i+1,j}^0 + C_{i-1,j}^0 + C_{i,j+1}^0 + C_{i,j-1}^0 - 4 C_{ij}^0). \quad (2)$$

To reduce errors, multiple sub-steps of diffusion are performed per timestep, with proportionally reduced $\hat{D}$, so that $\hat{D}$ is never larger than 0.1. The lattice sites at the bottom three rows are set to a concentration of attractant equal to that of the initial condition (Table 1) at the start of every timestep to represent inflow from the environment.

4.2.3 Decay of autoattractant. For the simulations with a decaying autoattractant, concentration decays at every lattice site each timestep:

$$C_{ij}^{n+1} = C_{ij}^n \cdot \exp\left(-\frac{1}{\tau}\right), \quad (3)$$

where τ is the decay time constant parameter (in timesteps).

4.3 Cell behaviour

4.3.1 Cell geometry. Each cell is represented as a circle of radius r defining the set of lattice sites it occupies. The occupied sites S_{cell} are all lattice sites (defined by their midpoint (i,j)) satisfying:

$$\sqrt{(x_{\text{cell}} - i)^2 + (y_{\text{cell}} - j)^2} < r, \quad (4)$$

where $(x_{\text{cell}}, y_{\text{cell}})$ is the continuous-valued cell centre position.

4.3.2 Gradient sensing and movement. Every timestep each cell senses the local chemical gradient across its occupied sites using a receptor-binding model with saturable kinetics. For each occupied lattice site (i,j) and each ligand ℓ , the perceived signal is computed as:

$$B_{\ell}(i,j) = \frac{C_{\ell,i,j}}{C_{\ell,i,j} + K_{d,\ell}}, \quad (5)$$

where $C_{\ell,i,j}$ is the concentration of ligand ℓ at site (i,j) and $K_{d,\ell}$ is the corresponding receptor dissociation constant. The net attraction $A(i,j)$ at each site is the sum over all ligand contributions:

$$A(i,j) = \sum_{\ell} B_{\ell}(i,j), \quad (6)$$

Additionally, environmental noise is added to the attractant grids before sensing by adding a uniform random value $U(0, \sigma_e)$ to every lattice site, where σ_e is the environmental noise amplitude. This random value is determined separately for each lattice site and each timestep, and is not carried forward.

The target direction is then computed as the angle from the unweighted centroid of its occupied sites to the attraction-weighted centroid of its occupied sites:

$$\theta_{\text{target}} = \text{atan2} \left(\frac{\sum_{(i,j) \in S_{\text{cell}}} A(i,j) \cdot j}{\sum_{(i,j) \in S_{\text{cell}}} A(i,j)} - \bar{y}, \frac{\sum_{(i,j) \in S_{\text{cell}}} A(i,j) \cdot i}{\sum_{(i,j) \in S_{\text{cell}}} A(i,j)} - \bar{x} \right), \quad (7)$$

where $\bar{x}$ and $\bar{y}$ are the arithmetic mean coordinates of the occupied sites.

The cell's actual heading for movement is a weighted combination of its previous heading θ_{prev} and the newly sensed target θ_{target} , governed by a persistence parameter $p \in [0, 1]$ which imposes an implicit limit on how sharply a cell can turn in a single timestep:

$$\theta_{\text{new}} = \text{atan2} \left(p \sin \theta_{\text{prev}} + (1-p) \sin \theta_{\text{target}}, p \cos \theta_{\text{prev}} + (1-p) \cos \theta_{\text{target}} \right). \quad (8)$$

We used a persistence of $p=0.9$ throughout, corresponding to the minimum time to reverse direction (i.e., turn 180 degrees) of 2.8 minutes listed in [Table 2](#).

The cell then attempts to move a fixed distance d in the direction θ_{new} :

$$x_{\text{new}} = x_{\text{cell}} + d \cos \theta_{\text{new}}, \quad y_{\text{new}} = y_{\text{cell}} + d \sin \theta_{\text{new}}. \quad (9)$$

Movement is rejected if it would place any part of the cell outside the domain boundaries, cause overlap with a wall, or cause overlap with another cell. If the move is rejected the cell selects a new random heading, but will not try to move until the next timestep, which effectively slows it down. If movement is successful the cell's lattice sites ([Eq. 4](#)) are recalculated.

4.3.3 Attractant breakdown. Each cell breaks down the primary attractant, and where relevant also the autoattractant, from the lattice sites it covers using Michaelis–Menten kinetics. The amount broken down at each occupied site $(i,j) \in S_{\text{cell}}$ is

$$C_{i,j}^{n+1} = C_{i,j}^n - q_{i,j}, \quad q_{i,j} = \frac{V_{\text{max}} \cdot C_{i,j}^n}{K_m + C_{i,j}^n}, \quad (10)$$

where V_{max} is the maximum breakdown rate and K_m is the Michaelis constant. The concentration is set to zero if it would become negative.

4.3.4 Autoattractant production. Each cell produces autoattractant in proportion to the total primary attractant it broke down this timestep ([Eq. 10](#)), distributed uniformly across its occupied sites. The autoattractant concentration at each occupied site $(i,j) \in S_{\text{cell}}$ is incremented by

$$C_{\text{auto}, i,j}^{n+1} = C_{\text{auto}, i,j}^n + \frac{\alpha}{|S_{\text{cell}}|} \sum_{(k,l) \in S_{\text{cell}}} q_{k,l}, \quad (11)$$

where α is the production ratio, $q_{k,l}$ is the primary attractant broken down at site (k,l) ([Eq. 10](#)), and $|S_{\text{cell}}|$ is the number of occupied sites.

4.4 Simulation parameters

Simulations were parameterised to represent two broad classes of immune cells: fast-moving cells (e.g., neutrophils) and slow-moving cells (e.g., macrophages). Environmental and cell-specific parameters are summarised in [Tables 1](#) and [2](#), respectively.

For each parameter combination, $n = 10$ replicate simulations were performed with different random seeds.

4.5 Analysis

4.5.1 Migration outcome. Migration was quantified as the fraction of cells that had crossed into the lower quarter of the simulation domain (i.e., $y < N_y/4$) by the final timestep. For each parameter combination, $n = 10$ replicate simulations were performed with different random seeds, and the mean fraction of migrated cells was computed across replicates.

4.5.2 Autoattractant lifetime. In some figures we calculate the mean effective lifetimes of autoattractant. At each recorded timestep, the total autoattractant concentration across all lattice sites was divided by the total amount of autoattractant removed by breakdown in that interval. This ratio gives the average time that a unit of autoattractant persists in the system at each point in the simulation. The mean over all recorded timesteps was then taken as the effective lifetime for that simulation.

4.5.3 Gradient strength. To quantify the perceived cell-cell gradient strength, the concentration C_{ij} at each lattice site is first transformed using the same receptor-binding equation used for gradient sensing ([Eq. 5](#)), giving a receptor-occupancy field $B(i, j, t)$. The gradient strength is then the summed absolute difference in receptor occupancy between neighbouring lattice sites along the short axis of the domain, normalised by the lattice size:

$$G(t) = \frac{1}{N_x N_y} \sum_{j=1}^{N_y} \sum_{i=3}^{N_x-3} |B(i, j, t) - B(i+1, j, t)|, \quad (12)$$

where lattice columns with $i < 3$ or $i > N_x - 2$ are excluded to avoid boundary artefacts. This yields $G(t)$ at each recorded timestep.

4.6 Implementation and data availability

All code used, as well as the parameter files for producing the data, and the code used for analysis, are on a GitHub repository at <https://github.com/DMvers/AutoTaxis>. We have also used Zenodo to assign a DOI to the repository at time of submission: <https://doi.org/10.5281/zenodo.20434528>

4.7 AI usage

The authors used Claude Opus to create a draft from an outline the authors wrote. The same tool was used to draft documentation and bash scripts for the software, as well as to aid in proofreading of both code and text. After using this tool, the authors reviewed and edited the output as needed and take full responsibility for the contents.

Supporting information

S1 Fig. The relationship, for slow-moving cells, between autoattractant decay and production and migration outcomes for (A–C) a broken down autoattractant at low cell density, low initial primary attractant concentration, and high initial primary attractant concentration, and (D–F) the same for a decaying autoattractant.
(TIF)

S2 Fig. The relationship between production and breakdown for fast-moving cells and a broken down autoattractant, for different diffusion speeds of attractant and autoattractant.

(TIF)

S3 Fig. The relationship between production and breakdown for slow-moving cells and a broken down autoattractant, for different diffusion speeds of attractant and autoattractant.

(TIF)

S4 Fig. The relationship between production and mean lifetime for fast-moving cells and a decaying autoattractant, for different diffusion speeds of attractant and autoattractant.

(TIF)

S5 Fig. For A,C,D: Gradient strength is represented by the average difference in autoattractant receptor binding over every 10 μm (one grid site) distance across the narrow side of the environment. Higher gradient strength indicates stronger cell-cell attraction. Details of calculation in methods section 4.5. **A.** The relation between gradient strength and the average distance between cells in the first half of the simulation as in [Fig 6D](#). **B.** The relation between the fraction of cells migrated by the end of the simulation, and the average distance between cells in the first half of the simulation, for the simulations of [Figs 3A, 4B, 5C, and 5E](#). **C.** The relation between gradient strength and the fraction of cells migrated, for cells with decaying autoattractant, as in [Figs 4B and 5E](#). **D.** The relation between gradient strength and the fraction of cells migrated, for fast and slow-moving cells with broken down autoattractant, as in [Figs 3A and 5C](#).

(TIF)

S1 Video. Visualisation of the simulations corresponding to [Fig 2A, 2B, 2D and 2E](#), showing the effect of different production ratios on the migration of fast-moving cells that break down autoattractant.

(MP4)

S2 Video. Visualisation of the simulation corresponding to [Fig 4A](#) and two additional conditions from [Fig 4B](#), showing the effect of a decaying autoattractant on the migration of fast-moving cells that do not break down autoattractant.

(MP4)

S3 Video. Visualisation of the simulations corresponding to [Fig 5A and 5B](#), showing the effect of an autoattractant on the migration of slow-moving cells that break down autoattractant.

(MP4)

S4 Video. Visualisation of the simulations corresponding to the four insets of [Fig 5E](#), showing the effect of different production ratios and autoattractant lifetimes on slow-moving cells that do not break down autoattractant.

(MP4)

Acknowledgments

The authors acknowledge the use of the UCL Myriad High Performance Computing Facility (Myriad@UCL), and associated support services, in the completion of this work. The authors also acknowledge the use of the UCL Condenser private cloud platform, and the support of the UCL Centre for Advanced Research Computing, in the completion of this work.

Author contributions

Conceptualization: David M. Versluis, Robert H. Insall.

Formal analysis: David M. Versluis.

Funding acquisition: Robert H. Insall.

Investigation: David M. Versluis.

Methodology: David M. Versluis.

Software: David M. Versluis.

Supervision: Robert H. Insall.

Visualization: David M. Versluis.

Writing – original draft: David M. Versluis.

Writing – review & editing: David M. Versluis, Robert H. Insall.

References

1. Afonso PV, Janka-Junttila M, Lee YJ, McCann CP, Oliver CM, Aamer KA, et al. LTB4 is a signal-relay molecule during neutrophil chemotaxis. *Dev Cell*. 2012;22(5):1079–91. <https://doi.org/10.1016/j.devcel.2012.02.003> PMID: [22542839](#)
2. McDonald PP, McColl SR, Braquet P, Borgeat P. Autocrine enhancement of leukotriene synthesis by endogenous leukotriene B₄ and platelet-activating factor in human neutrophils. *Br J Pharmacol*. 1994;111(3):852–60. <https://doi.org/10.1111/j.1476-5381.1994.tb14816.x> PMID: [8019762](#)
3. Strickland E, Pan D, Godfrey C, Kim JS, Hopke A, Ji W, et al. Self-extinguishing relay waves enable homeostatic control of human neutrophil swarming. *Dev Cell*. 2024;59(19):2659–2671.e4. <https://doi.org/10.1016/j.devcel.2024.06.003> PMID: [38971157](#)
4. Bray MA. The pharmacology and pathophysiology of leukotriene B₄. *Br Med Bull*. 1983;39(3):249–54. <https://doi.org/10.1093/oxfordjournals.bmb.a071828> PMID: [6313116](#)
5. Baggiolini M, Clark-Lewis I. Interleukin-8, a chemotactic and inflammatory cytokine. *FEBS Lett*. 1992;307(1):97–101. [https://doi.org/10.1016/0014-5793\(92\)80909-z](https://doi.org/10.1016/0014-5793(92)80909-z) PMID: [1639201](#)
6. Bazzoni F, Cassatella MA, Rossi F, Ceska M, Dewald B, Baggiolini M. Phagocytosing neutrophils produce and release high amounts of the neutrophil-activating peptide 1/interleukin 8. *J Exp Med*. 1991;173(3):771–4. <https://doi.org/10.1084/jem.173.3.771> PMID: [1997655](#)
7. Dou Y, Wu H-J, Li H-Q, Qin S, Wang Y-E, Li J, et al. Microglial migration mediated by ATP-induced ATP release from lysosomes. *Cell Res*. 2012;22(6):1022–33.
8. Imura Y, Morizawa Y, Komatsu R, Shibata K, Shinozaki Y, Kasai H, et al. Microglia release ATP by exocytosis. *Glia*. 2013;61(8):1320–30.
9. Tulapurkar ME, Schäfer R, Hanck T, Flores RV, Weisman GA, González FA, et al. Endocytosis mechanism of P2Y₂ nucleotide receptor tagged with green fluorescent protein: Clathrin and actin cytoskeleton dependence. *Cell Mol Life Sci*. 2005;62(12):1388–99. <https://doi.org/10.1007/s00018-005-5052-0> PMID: [15924261](#)
10. Calovi S, Mut-Arbona P, Sperlágh B. Microglia and the purinergic signaling system. *Neuroscience*. 2019;405:137–47. <https://doi.org/10.1016/j.neuroscience.2018.12.021> PMID: [30582977](#)
11. Humbles AA, Lu B, Friend DS, Okinaga S, Lora J, Al-Garawi A, et al. The murine CCR3 receptor regulates both the role of eosinophils and mast cells in allergen-induced airway inflammation and hyperresponsiveness. *Proc Natl Acad Sci U S A*. 2002;99(3):1479–84. <https://doi.org/10.1073/pnas.261462598> PMID: [11830666](#)
12. Amorim NRT, Luna-Gomes T, Gama-Almeida M, Souza-Almeida G, Canetti C, Diaz BL, et al. Leptin elicits LTC₄ synthesis by eosinophils mediated by sequential two-step autocrine activation of CCR3 and PGD₂ receptors. *Front Immunol*. 2018;9:2139. <https://doi.org/10.3389/fimmu.2018.02139> PMID: [30298073](#)
13. Liston TE, Roberts LJ 2nd. Metabolic fate of radiolabeled prostaglandin D₂ in a normal human male volunteer. *J Biol Chem*. 1985;260(24):13172–80. [https://doi.org/10.1016/s0021-9258\(17\)38853-1](https://doi.org/10.1016/s0021-9258(17)38853-1) PMID: [3863815](#)
14. Schuligoi R, Schmidt R, Geisslinger G, Kollrosier M, Peskar BA, Heinemann A. PGD₂ metabolism in plasma: Kinetics and relationship with bioactivity on DP₁ and CRTH₂ receptors. *Biochem Pharmacol*. 2007;74(1):107–17.
15. Hirai H, Tanaka K, Yoshie O, Ogawa K, Kenmotsu K, Takamori Y, et al. Prostaglandin D₂ selectively induces chemotaxis in T helper type 2 cells, eosinophils, and basophils via seven-transmembrane receptor CRTH₂. *J Exp Med*. 2001;193(2):255–61. <https://doi.org/10.1084/jem.193.2.255> PMID: [11208866](#)
16. Tweedy L, Knecht DA, Mackay GM, Insall RH. Self-generated chemoattractant gradients: Attractant depletion extends the range and robustness of chemotaxis. *PLoS Biol*. 2016;14(3):e1002404. <https://doi.org/10.1371/journal.pbio.1002404> PMID: [26981861](#)
17. Tweedy L, Insall RH. Self-generated gradients yield exceptionally robust steering cues. *Front Cell Dev Biol*. 2020;8:133.
18. Insall RH, Paschke P, Tweedy L. Steering yourself by the bootstraps: How cells create their own gradients for chemotaxis. *Trends Cell Biol*. 2022;32(7):585–96. <https://doi.org/10.1016/j.tcb.2022.02.007> PMID: [35351380](#)
19. Dowdell A, Paschke PI, Thomason PA, Tweedy L, Insall RH. Competition between chemoattractants causes unexpected complexity and can explain negative chemotaxis. *Curr Biol*. 2023;33(9):1704–1715.e3. <https://doi.org/10.1016/j.cub.2023.03.006> PMID: [37001521](#)

20. Kiran A, Thomason PA, Versluis DM, Paschke PI, Donnelly H, Tweedy L, et al. Macrophages self-generate and refine chemotactic gradients during migration towards complement C5a. *PLoS Biol.* 2026;24(4):e3003728. <https://doi.org/10.1371/journal.pbio.3003728> PMID: [41926388](#)
21. Muinonen-Martin AJ, Veltman DM, Kalna G, Insall RH. An improved chamber for direct visualisation of chemotaxis. *PLoS One.* 2010;5(12):e15309. <https://doi.org/10.1371/journal.pone.0015309> PMID: [21179457](#)
22. Young ME, Carrood PA, Bell RL. Estimation of diffusion coefficients of proteins. *Biotechnol Bioeng.* 1980;22(5):947–55. <https://doi.org/10.1002/bit.260220504>
23. Francis K, Pálsson BO. Effective intercellular communication distances are determined by the relative time constants for cyto/chemokine secretion and diffusion. *Proc Natl Acad Sci U S A.* 1997;94(23):12258–62. <https://doi.org/10.1073/pnas.94.23.12258> PMID: [9356436](#)
24. Hoang AN, Jones CN, Dimisko L, Hamza B, Martel J, Kojic N, et al. Measuring neutrophil speed and directionality during chemotaxis, directly from a droplet of whole blood. *Technology (Singap World Sci).* 2013;1(1):49. <https://doi.org/10.1142/S2339547813500040> PMID: [24809064](#)
25. Irimia D, Liu S-Y, Tharp WG, Samadani A, Toner M, Poznansky MC. Microfluidic system for measuring neutrophil migratory responses to fast switches of chemical gradients. *Lab Chip.* 2006;6(2):191–8. <https://doi.org/10.1039/b511877h> PMID: [16450027](#)
26. Snyderman R, Fudman EJ. Demonstration of a chemotactic factor receptor on macrophages. *J Immunol.* 1980;124(6):2754–7. <https://doi.org/10.4049/jimmunol.124.6.2754> PMID: [7373048](#)
27. Miller H, Cosgrove J, Wollman AJM, Taylor E, Zhou Z, O'Toole PJ, et al. High-speed single-molecule tracking of CXCL13 in the B-follicle. *Front Immunol.* 2018;9:1073. <https://doi.org/10.3389/fimmu.2018.01073> PMID: [29872430](#)
28. Bowen WJ, Martin HL. The diffusion of adenosine triphosphate through aqueous solutions. *Arch Biochem Biophys.* 1964;107:30–6. [https://doi.org/10.1016/0003-9861\(64\)90265-6](https://doi.org/10.1016/0003-9861(64)90265-6) PMID: [14211563](#)
29. Lämmermann T, Afonso PV, Angermann BR, Wang JM, Kastenmüller W, Parent CA, et al. Neutrophil swarms require LTB4 and integrins at sites of cell death in vivo. *Nature.* 2013;498(7454):371–5. <https://doi.org/10.1038/nature12175> PMID: [23708969](#)
30. Pálsson E, Lee KJ, Goldstein RE, Franke J, Kessin RH, Cox EC. Selection for spiral waves in the social amoebae *Dictyostelium*. *Proc Natl Acad Sci U S A.* 1997;94(25):13719–23. <https://doi.org/10.1073/pnas.94.25.13719> PMID: [9391092](#)
31. Eisenbarth SC. Dendritic cell subsets in T cell programming: Location dictates function. *Nat Rev Immunol.* 2019;19(2):89–103. <https://doi.org/10.1038/s41577-018-0088-1> PMID: [30464294](#)
32. Bousso P. T-cell activation by dendritic cells in the lymph node: Lessons from the movies. *Nat Rev Immunol.* 2008;8(9):675–84. <https://doi.org/10.1038/nri2379> PMID: [19172690](#)
33. Malet-Engra G, Yu W, Oldani A, Rey-Barroso J, Gov NS, Scita G, et al. Collective cell motility promotes chemotactic prowess and resistance to chemorepulsion. *Curr Biol.* 2015;25(2):242–50. <https://doi.org/10.1016/j.cub.2014.11.030> PMID: [25578904](#)
34. Carmona-Fontaine C, Theveneau E, Tzekou A, Tada M, Woods M, Page KM, et al. Complement fragment C3a controls mutual cell attraction during collective cell migration. *Dev Cell.* 2011;21(6):1026–37. <https://doi.org/10.1016/j.devcel.2011.10.012> PMID: [22118769](#)