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An Annotated Bibliography

Edwin Huras
UBC

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References

[1] J. P. Agnelli, B. Buffa, D. Knopoff, and G. Torres, "A Spatial Kinetic Model of Crowd Evacuation Dynamics with Infectious Disease Contagion," *Bulletin of Mathematical Biology*, vol. 85, no. 4, p. 23, February 2023.

Here is an annotation

[2] S. Jain, V. M. L. Cachoux, G. H. N. S. Narayana, S. de Beco, J. D'Alessandro, V. Cellerin, T. Chen, M. L. Heuzé, P. Marcq, R.-M. Mège, A. J. Kabla, C. T. Lim, and B. Ladoux, "The role of single-cell mechanical behaviour and polarity in driving collective cell migration," *Nature Physics*, vol. 16, no. 7, pp. 802–809, July 2020.

[3] F. Martinez-Gil, M. Lozano, and F. Fernández, "Emergent behaviors and scalability for multi-agent reinforcement learning-based pedestrian models," *Simulation Modelling Practice and Theory*, vol. 74, pp. 117–133, May 2017.

Somewhat recent and relatively well cited paper that cited Schweitzer's book. Not sure exactly how useful it will be.

[4] F. Schweitzer, *Self-Organization of Complex Structures: From Individual to Collective Dynamics*, 1st ed. Amsterdam, The Netherlands: CRC Press, July 1997.

Recommendation from Leah, older book but well respected author. I've had a lot of difficulty finding the text online (nothing shows up but a review on UBC library) and it appears to have been out of print for quite a while. Will try to find some recent sources that cited this book as a means to find relevant papers.

[5] L. Tweedy, P. A. Thomason, P. I. Paschke, K. Martin, L. M. Machesky, M. Zagnoni, and R. H. Insall, "Seeing around corners: Cells solve mazes and respond at a distance using attractant breakdown," *Science (New York, N.Y.)*, vol. 369, no. 6507, p. eaay9792, August 2020.

Self-generated chemotaxis: Self-generated chemotaxis cannot be directly measured and typically requires computational modeling to analyze. It is distinguished from classical chemotaxis by several key features:

- Gradients are sharp, local, and nonsaturating (unlike traditional source/sink gradients).
- Diffusion plays a central role (in contrast to constant or linear gradients).
- General chemotaxis is limited in effective range (500 μm) and attractant concentration.

Cells such as *Dictyostelium discoideum* and metastatic cancer cells use self-generated chemotaxis to navigate complex environments (e.g., tumor tissue or migration routes). These cells degrade attractants locally using surface enzymes, resulting in dynamic gradients that help them sense and respond to upcoming junctions. This enables cells to "see around corners" and map their environment.

Junction Navigation and Model Behavior:

- In classical chemotaxis, cells choose paths randomly at junctions.
- In self-generated chemotaxis:
  - Paths are evenly split unless one is a dead end.
  - If a branch is a dead end, only a few cells explore it. Their degradation of attractants prevents others from following.
  - Short dead ends are completely avoided: attractant gradients are dissipated before cells even arrive.

Maze Navigation:

- Cells navigate mazes successfully even with uniform attractant concentration.
- Longer dead ends reduce decision fidelity.
- Decision-making improves over time due to attractant depletion in dead ends.
- Slower cell speeds (in simulation) improve accuracy, though this does not generalize to slower-moving cancer cells, likely due to differences in attractant diffusivity.
- Dead ends with widening or branching structures can create "chemotactic mirages" and attract cells.

Key Conclusions:

- Attractant flux (rate of change) is more critical for cell decisions than attractant concentration.
- Maze geometry, especially dead end length, affects gradient strength and navigational accuracy.
- Ligand breakdown is rarely modeled but is biologically significant and should be incorporated in future models.
- Implications for understanding complex migration phenomena, including:
  - Neutrophil extravasation,
  - Melanoblast migration in embryonic dermis,
  - Glioblastoma metastasis along white matter tracts.

Modeling Details:

- Simulations were implemented in Java.
- Diffusion was simulated using the semi-implicit DuFort-Frankel method in a complex environment.
- Cells followed a persistent, biased random walk informed by local gradient sensing.
- Gradient direction was estimated from grid points within 6 μm of the cell centroid.
- Attractant degradation followed Michaelis-Menten kinetics, with rate $r = v_{\max}\frac{c}{c+K_m}$, where c is the local concentration and k_m is the Michaelis constant.

Note: This form of chemotaxis is fundamentally different from that used by *Physarum polycephalum*, which explores all paths and later prunes the least successful.

[6] J. D. Wheeler and K. Y. K. Chan, "The Whole is Greater Than the Sum of Its Parts: Large-scale Phenomena Arising from Small-scale Biophysical Processes," *Integrative and Comparative Biology*, vol. 63, no. 6, pp. 1399–1404, December 2023.

Annotation here.