J. Zysman, A. Newman, Eds. (Stanford Univ. Press, 2006), pp. 361–378.

- L.-E. Cederman, A. Wimmer, B. Min, World Polit. 62, 87–119 (2010).
- R. Hodler, P. A. Raschky, *Q. J. Econ.* **129**, 995–1033 (2014).
- International Telecommunications Union, World Telecommunication/ICT Indicators Database (2013); www.itu. int/en/ITU-D/Statistics/Pages/publications/wtid.aspx.
- Demographic and Health Surveys Program, http:// dhsprogram.com/.
- S. Benitez-Baleato, N. B. Weidmann, P. Gigis, X. Dimitropoulos, E. Glatz, B. Trammell, in *Proceedings of the Passive and Active Measurement Conference*, J. Mirkovic, Y. Liu, Eds. (Springer, 2015), pp. 220–231.
- 12. A. Dainotti et al., Comput. Commun. Rev. 44, 99-100 (2014).
- 13. University of Oregon Route Views Project, www.routeviews.org.
- 14. MaxMind, GeoIP2 Databases; www.maxmind.com/en/geoip2databases.
- B. Huffaker, M. Fomenkov, K. Claffy, "Geocompare: A comparison of public and commercial geolocation databases" (CAIDA Tech Report, Center of Applied Internet Data Analysis, 2011); www.caida.org/publications/papers/2011/geocomparetr/geocompare-tr.pdf.
- J. Wucherpfennig, N. B. Weidmann, L. Girardin, L.-E. Cederman, A. Wimmer, Conflict Manage. Peace Sci. 28, 423–437 (2011).
- W. D. Nordhaus, Proc. Natl. Acad. Sci. U.S.A. 103, 3510–3517 (2006).
- J. V. Henderson, A. Storeygard, D. N. Weil, Am. Econ. Rev. 101, 194–199 (2011).
- X. Chen, W. D. Nordhaus, Proc. Natl. Acad. Sci. U.S.A. 108, 8589–8594 (2011).
- N. B. Weidmann, S. Schutte, J. Peace Res. 10.1177/ 0022343316630359 (2016).
- J. G. Altonji, T. E. Elder, C. R. Taber, J. Polit. Econ. 113, 151–184 (2005).
- 22. S. Tarrow, Power in Movement: Social Movements, Collective Action and Politics (Cambridge Univ. Press, 1994).
- J. Earl, K. Kimport, Digitally Enabled Social Change: Activism in the Internet Age (MIT Press, 2011).
- The World Bank, World Development Report 2016: Digital Dividends (The World Bank, 2016); www.worldbank.org/en/ publication/wdr2016.
- M. G. Marshall, T. R. Gurr, K. Jaggers, "Polity IV Project: Political regime characteristics and transitions, 1800–2015" (2015); www.systemicpeace.org/polity/polity4.htm.
- The World Bank, World Development Indicators (2016); http://data.worldbank.org/data-catalog/world-developmentindicators.

## ACKNOWLEDGMENTS

We acknowledge financial support from the Alexander von Humboldt Foundation (Sofia Kovalevskaja Award to N.B.W.). We are grateful to M. Baum, M. Becher, L.-E. Cederman, D. Lazer, A. Little, and P. Selb for comments. We do not have any real or apparent conflicts of interest. Data for replication are available at http://dx.doi.org/10.7910/DVN/Y3VPIG. There are two restrictions. First, we cannot share the active subnetworks data because these are computed from traffic traces (netflow) captured from an Internet service provider. These traces were made available to us under a strict nondisclosure agreement that prevents further sharing or public release. However, we share the complete list of routed subnetworks (annual observations) because they were derived from a public source. The second restriction concerns the spatial coordinates for each subnetwork. MaxMind does not permit the publication of any information contained in their database, so we share a random sample of 5% of the routed subnetworks with truncated geographic coordinates, but without IP addresses, along with code that executes the spatial aggregation to the group polygons in SQL (structured query language).

### SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/353/6304/1151/suppl/DC1 Materials and Methods Supplementary Text Figs. S1 to S3 Tables S1 to S8 References (27–43)

29 February 2016; accepted 27 July 2016 10.1126/science.aaf5062

# **ANIMAL BEHAVIOR**

# **Optic flow odometry operates independently of stride integration in carried ants**

Sarah E. Pfeffer and Matthias Wittlinger\*

*Cataglyphis* desert ants are impressive navigators. When the foragers roam the desert, they employ path integration. For these ants, distance estimation is one key challenge. Distance information was thought to be provided by optic flow (OF)—that is, image motion experienced during travel—but this idea was abandoned when stride integration was discovered as an odometer mechanism in ants. We show that ants transported by nest mates are capable of measuring travel distance exclusively by the use of OF cues. Furthermore, we demonstrate that the information gained from the optic flowmeter cannot be transferred to the stride integrator. Our results suggest a dual information channel that allows the ants to measure distances by strides and OF cues, although both systems operate independently and in a redundant manner.

he navigational skills of insects have engaged scientists for decades. Cataglyphis ants are one of the major model organisms used to study path integration, a navigation feat in which angles steered and distances travelled are combined to provide a direct link to the point of origin, a so-called home vector (1). While celestial cues are the main source for angular or compass information (2), distance information is derived from a pedometer, a stride integrator that accounts for stride number and the respective stride length (3, 4). It is well-known that optic flow (OF) is the means of estimating travel distance in flying hymenopterans, like bees or wasps (5-7). In ants, however, which are phylogenetically closely related, ventral OF has been shown to play only a minor role (8). Ants are walkers after all, so stride integration and OF integration are difficult to tease apart from each other experimentally (8, 9).

Social carrying behavior (10-13) gives us an opportunity to study how distance may be estimated without stride integration in nonwalking ants (Fig. 1). This behavior is common in Cataglyphis bicolor ants because of their polydomous nest structure, where the main nest with the single queen is surrounded by satellite nests. Experienced forager ants [here denoted as carrier (C) ants] frequently transport interior workers [here denoted as carried (Cd) ants] between the different nest sites. A C-Cd pair that is separated during transport will usually re-engage in social carrying behavior and continue its travel. However, if the Cd ant (which is inexperienced outside of the nest) stays lost, it can only use the path information acquired during transport to find its way back to the home nest. Cd ants do not locomote actively; therefore, the stride integrator will not receive any input. However, the visual

Institute of Neurobiology, Ulm University, 89081 Ulm, Germany. \*Corresponding author. Email: matthias.wittlinger@uni-ulm.de motion pattern generated during displacement can be exploited to gain information about the distance travelled.

In our first experiment, the OF experiment, we connected two nest entrances of neighboring nests with a walking channel. After a C-Cd pair had covered a distance of 10 m in the channel, we captured it and separated both ants carefully. The transported ant was then released in a distant test channel aligned in parallel, and its search behavior was examined. We recorded the search behavior as consecutive 180° turning points in the test channel (4, 6, 14). A Cd ant that fully exploits OF for odometry should be able to estimate the length of the travelled path and hence walk back to the nest from which it had departed. Our experiments show that Cd ants are able to gauge the distance to the nest (Fig. 2). After an initial search around the release point in the test channel (Fig. 2C), presumably to locate the absent C ant, the Cd ants eventually set out for the home nest and searched back and forth around the anticipated nest position [peak of second search phase at 9.6 m (Fig. 2C); peak of differential search at 9.7 m (Fig. 2D)].

To ensure that it is indeed the experienced OF mechanism that enables the Cd ants to estimate



Fig. 1. Body posture of a carrier-carried pair.



Fig. 2. Optic flow experiment. Distance was measured exclusively with OF cues. (A) Experimental procedure. Carrier-carried (C-Cd) pairs travel between two nests (N1 to N2) and were caught and separated at a walking distance of 10 m. The Cd ants were then released in the test channel, and their search behavior was recorded. (B) Relative search density (RSD). The performance of the OF group (n = 21 ants) is depicted in blue and that of the BF group (n = 26) is shown in shaded red. The ants of the BF group were prevented from perceiving OF cues during carrying and homing. (C) First and second search phases of the OF and BF groups. For the analysis of the two search phases, see (14). (**D**) Differential search density (DSD). The purple line indicates BF group data subtracted from that of the OF test group.

distances, we blindfolded the ventral part of the compound eyes of a separate test group. It has already been shown that ventral eye caps do not interfere with proper homing behavior in walking ants and thus ventral blindfolding does not affect correct distance estimation (9). The Cd ants of the blindfolded test group (BF group) did not obtain any distance information in the outbound journey because visual input was eliminated (covered eyes) and the stride integrator was also not effective



Fig. 3. Interodometer transfer experiment. No OF information was transferred to the stride integrator. (A) Experimental procedure. C-Cd pairs travel between two nests (N1 to N2) and were caught and separated at a walking distance of 10 m. The Cd ants were ventrally blindfolded and then released in the test channel, and their search behavior was recorded. (B) Relative search density (RSD). The performance of the IT group (n = 25 ants) is depicted in green and that of the BF group (n = 26)is shown in shaded red. The ants of the BF group were prevented from perceiving OF cues during carrying and homing. Thus, their search behavior did not extent beyond the point of release (0 m) (compare with fig. S1). (C) First and second search phases of the IT and BF groups. For the analysis of the two search phases, see (14). (D) Differential search density (DSD). The purple line indicates BF group data subtracted from that of the IT test group.

(carried mode). The blindfolded ants did not head for the home nest; their search was concentrated around the releasing point (Fig. 2). For additional experimental and control groups, see fig. S1.

*Cataglyphis* carry their conspecifics in a stereotyped formicine fashion where both ants are facing each other, with the Cd ant in a "pupal" posture (*10*) (Fig. 1 and movie S1). As such, the



Fig. 4. Statistical comparison of odometer performance. Distributions of the search centers (medians of all turning points) of each test group (entire searches) are shown as box-and-whisker plots [OF experiment: median = 4.28 m, interquartile range (IQR) = 2.25 m; IT experiment: median = 0.30 m, IQR = 2.32 m; BF group: median = 0.42 m, IQR = 1.80 m]. The OF and the BF groups differ significantly (*U* test; \*\*\*P  $\leq$  0.001). We found no significant (ns) difference between the IT and BF groups (*U* test; *P* = 0.742).

orientations of the head and visual field of both ants are similar (*12*); however, the Cd ant's view is flipped anterio-posteriorly, and it experiences reversed image motion (for head angles, see fig. S2). Our data show that the Cd ants cope well with this situation, suggesting the use of the absolute value of the perceived OF amount as odometer information. In two earlier papers, Duelli (*11*, *12*) reports that the celestial compass system keeps the ants on track even though the compass input was reversed during transport and that, at least qualitatively, the ants have some idea about distance. In general, the reversing of celestial compass cues during homing does not seem to be a problem for navigating desert ants (*15*).

In a second experiment, the interodometer transfer (IT) experiment, we further investigated whether the distance information gained by the optic flowmeter can be used and exploited by the stride integrator. By using the term "interodometer transfer," we do not necessarily mean that information is directly transferred from one system to another. Rather, information acquired by one system could be read off of some downstream integration stage by another system. At some stage, a transfer of information occurs (16). After 10 m of carrying, where the Cd ant visually perceived the transport, we disengaged the C-Cd pair. The ventral part of the Cd ant's eyes were then occluded, and we tested its ability to gauge the homing distance. Thus, after it was released into the test channel, the walking but blindfolded ant had no chance of running off its vector with the optic flowmeter but instead had to rely on the alternative odometer, the stride integrator, available for the homing task. If the stride integrator could make use of OF distance information, we would expect the Cd ants to exhibit a search peak at the virtual nest position. However, we saw no evidence of such IT (Fig. 3). Rather, the ants in this experiment seemed to be lost, pacing back and forth around the point of release, basically exhibiting just one distinct search phase.

The box-and-whisker plots of Fig. 4 contain the entire search phases of each experiment. Note that in the case of the OF group, as opposed to the IT and BF groups, two distinct search phases exist (compare Figs. 2 and 3). The first is centered on the point of release and the second on the position of the nest location. Because both contribute to the entire data distribution, the median value lies around roughly half the distance between the releasing point and the nest position. The IT and BF groups do not show such a distinct second search phase; thus, the data are distributed around the point of release.

Our experiments show that the exclusive use of OF cues is sufficient for the ants to measure travel distances. Furthermore, active locomotion is not a prerequisite for distance estimation or path integration, provided that the transport happens in a naturally occurring behavior (17). There is ample evidence that the stride integrator can function without visual input. Ants walking in complete darkness (18), or with the ventral halves of their eyes covered (8, 9), are still able to gauge homing distance correctly. However, our results show that two separate and independent systems of distance measurement exist and operate redundantly.

#### **REFERENCES AND NOTES**

- M. Müller, R. Wehner, Proc. Natl. Acad. Sci. U.S.A. 85, 5287–5290 (1988).
- R. Wehner, M. V. Srinivasan, in *The Neurobiology of Spatial Behaviour*, K. J. Jeffrey, Ed. (Oxford Univ. Press, 2003), chap. 1, pp. 9–30.
- M. Wittlinger, R. Wehner, H. Wolf, Science 312, 1965–1967 (2006).
- M. Wittlinger, R. Wehner, H. Wolf, J. Exp. Biol. 210, 198–207 (2007).
- H. E. Esch, J. E. Burns, *Naturwissenschaften* 82, 38–40 (1995).
- M. V. Srinivasan, S. Zhang, M. Altwein, J. Tautz, Science 287, 851–853 (2000).
- 7. A. Ugolini, Anim. Behav. 35, 590–595 (1987).
- B. Ronacher, R. Wehner, J. Comp. Physiol. A 177, 21–27 (1995).
- 9. M. Wittlinger, H. Wolf, J. Physiol. Paris 107, 130-136 (2013).
- 10. M. Möglich, B. Hölldobler, Psyche 81, 219-236 (1974).
- 11. P. Duelli, Rev. Suisse Zool. 83, 413-418 (1976).
- 12. P. Duelli, Rev. Suisse Zool. 80, 712-719 (1973).
- A. Dahbi, J. Retana, A. Lenoir, X. Cerdá, J. Ethol. 26, 119–126 (2008).
  Materials and methods are qualiable as supplementary.
- 14. Materials and methods are available as supplementary materials on *Science* Online.
- S. E. Pfeffer, M. Wittlinger, J. Exp. Biol. 219, 2119–2126 (2016).
  F. Lebhardt, B. Ronacher, J. Comp. Physiol. A 201, 599–608
- T. Lebhardt, B. Kohachel, J. Comp. Physiol. A 201, 399–666 (2015).
  T. Seidl, M. Knaden, R. Wehner, J. Comp. Physiol. A 192
- 17. T. Seidl, M. Knaden, R. Wehner, J. Comp. Physiol. A 192, 1125–1131 (2006).
- M. Thiélin-Bescond, G. Beugnon, *Naturwissenschaften* 92, 193–197 (2005).

### ACKNOWLEDGMENTS

We thank H. Wolf for help during the initial experiments, discussions, and support; K. J. Kaiser and V. L. Wahl for help collecting data in the field; O. Stroh for measuring the head angles, and U. Seifert for editing the text. The University of Ulm provided financial support and infrastructure. M.W. developed the initial idea and concept. M.W. and S.E.P. planned and carried out the experiments, analyzed the data, and wrote the manuscript. Data are available on Dryad (doi: 10.5061/dryad.r8h3n).

#### SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/353/6304/1155/suppl/DC1 Materials and Methods Supplementary Text Figs. S1 and S2 References (19–21) Movie S1 28 April 2016; accepted 17 August 2016

10.1126/science.aaf9754

## **CELL MIGRATION**

# **Collective cell durotaxis emerges from long-range intercellular force transmission**

Raimon Sunyer,<sup>1</sup> Vito Conte,<sup>1</sup> Jorge Escribano,<sup>2</sup> Alberto Elosegui-Artola,<sup>1</sup> Anna Labernadie,<sup>1</sup> Léo Valon,<sup>1</sup> Daniel Navajas,<sup>1,3,4</sup> José Manuel García-Aznar,<sup>2</sup> José J. Muñoz,<sup>5</sup> Pere Roca-Cusachs,<sup>1,3\*</sup> Xavier Trepat<sup>1,3,6,7\*</sup>

The ability of cells to follow gradients of extracellular matrix stiffness—durotaxis—has been implicated in development, fibrosis, and cancer. Here, we found multicellular clusters that exhibited durotaxis even if isolated constituent cells did not. This emergent mode of directed collective cell migration applied to a variety of epithelial cell types, required the action of myosin motors, and originated from supracellular transmission of contractile physical forces. To explain the observed phenomenology, we developed a generalized clutch model in which local stick-slip dynamics of cell-matrix adhesions was integrated to the tissue level through cell-cell junctions. Collective durotaxis is far more efficient than single-cell durotaxis; it thus emerges as a robust mechanism to direct cell migration during development, wound healing, and collective cancer cell invasion.

he ability of living cells to migrate following environmental gradients underlies a broad range of phenomena in development, homeostasis, and disease (1, 2). The bestunderstood mode of directed cell migration is chemotaxis, the well-established ability of cells to follow gradients of soluble chemical cues (1). Some cell types are also able to follow gradients in the stiffness of their extracellular matrix (ECM), a process known as durotaxis (3–10). Durotaxis has been implicated in development (11), fibrosis (12), and cancer (13), but its underlying mechanisms remain unclear.

Most of our understanding of directed cell migration has been obtained in single isolated cells. However, fundamental processes during development, wound healing, tissue regeneration, and some forms of cancer cell invasion are driven by directed migration of cell groups (*14–16*). Cell-cell interactions within these groups provide cooperative mechanisms of cell guidance that are altogether inaccessible to single cells (*14–20*). Here, we investigated whether cell groups undergo collective durotaxis and the cooperative nature of underlying mechanisms.

Using stencils of magnetic polydimethylsiloxane (PDMS), we micropatterned rectangular clusters (500  $\mu$ m in width) of human mammary epithelial cells (MCF-10A) on fibronectin-coated polyacrylamide gel substrates exhibiting either uniform stiffness or a stiffness gradient (56.6  $\pm$ 2.1 kPa/mm) (fig. S1) (*21, 22*). Upon removal of the PDMS stencil, clusters migrating on uniform gels displayed symmetric expansion (Fig. 1, A, C, E, and G; fig. S2A; and movie S1), whereas clusters migrating on stiffness gradients displayed a pronounced asymmetry characterized by faster, more persistent expansion toward the stiff edge (Fig. 1, B, D, F, and H; fig. S2, B to F; and movie S1). This result was also observed in clusters of Madin-Darby canine kidney epithelial cells (MDCK) and threedimensional spheroids of human epidermoid carcinoma cells (A431) (fig. S3).

Asymmetric expansion is not attributable to cell proliferation, because it was unaffected by inhibition of cell division and because the number of divisions in the cluster was independent of substrate stiffness (fig. S4). Importantly, it is not attributable to additive contribution of singlecell durotaxis either, because single MCF-10A cells did not durotax in isolation (Fig. 2, A to C and E, and movie S2). Taken together, these data establish an unanticipated mode of collective durotaxis driven by an emergent property of the cell cluster.

Even if single MCF-10A cells did not durotax in isolation, they exhibited faster randomly oriented velocity on stiffer gels (Fig. 2D) (13). In a close-packed system, this feature could explain collective durotaxis because volume exclusion would force cells to move persistently away from the cluster at a higher speed on the stiffer edge. To test the contribution of this mechanism, we perturbed cell-cell junctions independently of close packing by knocking down  $\alpha$ -catenin using small interfering RNA (siRNA). Like control cells,

\*Corresponding author. Email: rocacusachs@ub.edu (P.R.-C.); xtrepat@ibecbarcelona.eu (X.T.)

<sup>&</sup>lt;sup>1</sup>Institute for Bioengineering of Catalonia, 08028 Barcelona, Spain.<sup>2</sup>Aragon Institute of Engineering Research (I3A), University of Zaragoza, 50018 Zaragoza, Spain. <sup>3</sup>University of Barcelona, 08028 Barcelona, Spain. <sup>4</sup>Centro de Investigación Biomédica en Red en Enfermedades Respiratorias, 28029 Madrid, Spain. <sup>5</sup>Laboratory of Numerical Analysis (LaCàN), Polytechnic University of Catalonia (UPC- BarcelonaTech), 08036 Barcelona, Spain. <sup>6</sup>Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain. <sup>7</sup>Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina, 28029 Madrid, Spain.



Editor's Summary

**Optic flow odometry operates independently of stride integration in carried ants** Sarah E. Pfeffer and Matthias Wittlinger (September 8, 2016) *Science* **353** (6304), 1155-1157. [doi: 10.1126/science.aaf9754]

This copy is for your personal, non-commercial use only.

Article Tools	Visit the online version of this article to access the personalization and article tools: http://science.sciencemag.org/content/353/6304/1155
Permissions	Obtain information about reproducing this article: http://www.sciencemag.org/about/permissions.dtl

*Science* (print ISSN 0036-8075; online ISSN 1095-9203) is published weekly, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. Copyright 2016 by the American Association for the Advancement of Science; all rights reserved. The title *Science* is a registered trademark of AAAS.