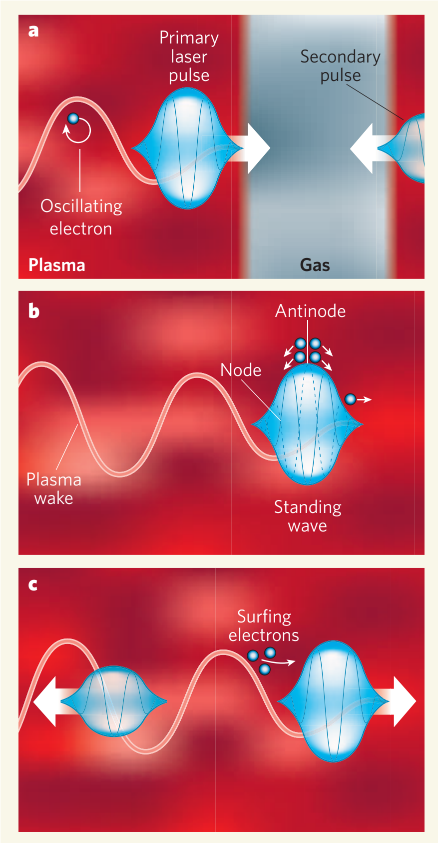

Figure 2 | Surfing in a plasma wakefield. **a**, In Faure and colleagues' experimental scheme[1], the primary laser wakefield pulse ionizes helium gas to a plasma. If the parameters of pulse and plasma are chosen appropriately, the electrons of the plasma oscillate about a fixed spot. **b**, If a second 'tow-in' pulse travelling in the opposite direction crosses the first, a standing wave forms. Electrons are pushed left and right in the standing wave from the antinodes to the nodes. **c**, Some electrons — those pushed to the right — gain enough speed to get caught up in the following wave crest and are accelerated forwards. The energy gain of the electrons is determined by how far they have to surf through the plasma, and so by where exactly along the plasma the two laser pulses cross.

initial laser pulse to keep the amplitude of the plasma waves just below the threshold for wave breaking. This means that no plasma electrons move fast enough to ride the waves. Instead, they just oscillate back and forth, as do water molecules in an ocean wave far from the beach. But when a second pulse is added, propagating in the opposite direction to the first, a temporary standing wave is formed with fixed maxima and minima, known as antinodes and nodes (Fig. 2). The radiation pressure caused by the momentum of the light pushes electrons at the antinodes of the standing wave towards the nodes. This slight extra push is enough to force some electrons into the wake of the first laser, where they become surfers at nearly the speed of light. The location of the overlap of the two lasers determines where along the plasma axis electrons first catch the wave, so the length of their ride, and hence their energy gain, can be easily controlled by adjusting the timing between the two lasers.

This idea of using a second laser pulse to slingshot electrons into a plasma wake dates back to 1996 (ref. 6) — not long after Hamilton and Kerbox were experimenting with jet skis to sling themselves into ocean waves. Several groups have attempted variations on the original idea, but Faure *et al.*[1] are the first to demonstrate high-quality beam injection. Interestingly, they succeed with the simplest of the schemes proposed so far.

The first idea was to cross two lasers at 90° and use the transverse radiation pressure of the second laser to inject electrons into the main laser's wake. But simulations indicated that it was the second laser's wake, rather than its radiation pressure, that caused injection[7]. The simultaneous use of counter-propagating and co-propagating secondary lasers for injection was then proposed[8]. It was thought that two lasers of frequencies differing by an amount matched to the resonant frequency of electrons in the plasma would be needed to create a slow plasma wave that would push electrons into the main wake. But further simulations[9] seemed to imply that radiation pressure from the standing field pattern produced with a single counter-propagating secondary laser could be sufficient. It is indeed this last and simplest scheme that has worked to such positive effect.

The approach does have limitations. The charge that can be accelerated in a single bunch amounts to just tens of picocoulombs, which is ten times less than the quantities typically accelerated without a stabilizing second laser. Although this much charge is adequate for many proposed applications[10–12], other groups in Britain, the United States and Japan are working with considerable success to stabilize the energy gain at higher charge levels using more precise control of the laser and gas conditions.

The rapidity with which barriers have continued to fall in the two years since the breakthrough[2–4] for monoenergetic acceleration of electrons in laser wakefields is astounding. Monoenergetic beams of ions have now been produced by laser irradiation of specially designed foil targets[13,14], rather than of gaseous targets as used for electron production. Work is also progressing towards showing that the plasma mechanisms can be scaled to higher energies[15,16], and particularly to the stringent requirements of a high-energy collider.

That energy frontier is still a long way off for laser-plasma technology. But thanks to work such as that of Faure and colleagues[1], the widespread use of compact plasma accelerators for medicine, industry and research may be much closer than we think. ■

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1. Faure, J. *et al. Nature* **444,** 737–739 (2006).
2. Mangles, S. *et al. Nature* **431,** 535–538 (2004).
3. Geddes, C. G. R. *Nature* **431,** 538–541 (2004).
4. Faure, J. *et al. Nature* **431,** 541–544 (2004).
5. Dawson, J. M. *Phys. Rev.* **113,** 383–387 (1959).
6. Umstadter, D., Kim, J.-K. & Dodd, E. *Phys. Rev. Lett.* **76,** 2073–2076 (1996).
7. Hemker, R. G., Tzeng, K.-C., Mori, W. B., Clayton, C. E. & Katsouleas, T. *Phys. Rev. E* **57,** 5920–5928 (1998).
8. Esarey, E., Hubbard, R. F., Leemans, W. P., Ting, A. & Sprangle, P. *Phys. Rev. Lett.* **79,** 2682–2685 (1997).
9. Fubiani, G., Esarey, E., Schroeder, C. B. & Leemans, W. P. *Phys. Rev. E* **70,** 016402 (2004).
10. Brozek-Pluska, B., Gliger, D., Hallou, A., Malka, V. & Gauduel, Y. A. *Radiat. Chem.* **72,** 149–159 (2005).
11. Glinec, Y. *et al. Med. Phys.* **33,** 155–162 (2006).
12. Glinec, Y. *et al. Phys. Rev. Lett.* **94,** 025003 (2005).
13. Hegelich, B. M. *et al. Nature* **439,** 441–444 (2006).
14. Schwoerer, H. *et al. Nature* **439,** 445–448 (2006).
15. Leemans, W. *et al. Nature Phys.* **2,** 696–699 (2006).
16. Hogan, M. J. *et al. Phys. Rev. Lett.* **95,** 054802 (2005).

EVOLUTIONARY BIOLOGY

Caught right-handed

A. Richard Palmer

Are two penises better than one? Not so, implies a study of doubly endowed earwigs. An ancestral behavioural preference for the right penis might have facilitated the loss of the left in species that arose later.

Human males may sometimes wonder about the size of their penis, but they rarely fret about which one to use. Not so for many arthropods, among them fairy shrimp[1], dragonflies[2] and spiders[3], some of which face a delicate choice before each tryst: "Left or right tonight?" Doubly endowed lizards[4] and snakes[5] seem ambivalent, although they tend to alternate between the right and left of their two members. Males of two theridiid spider genera (*Tidarren* and *Echinotheridion*) have a particularly radical solution to their quandary: they voluntarily rip off a palp at random and eat it, leaving only one behind.

Writing in the *Journal of Morphology*[6], Yoshitaka Kamimura describes his investigations of the private life of the doubly endowed male of the earwig species *Labidura riparia* (Fig. 1a). He shows that this earwig has a strong preference for its right penis: nearly 90% of field-collected and laboratory-reared males hold their intromittent organs in the 'right-ready'

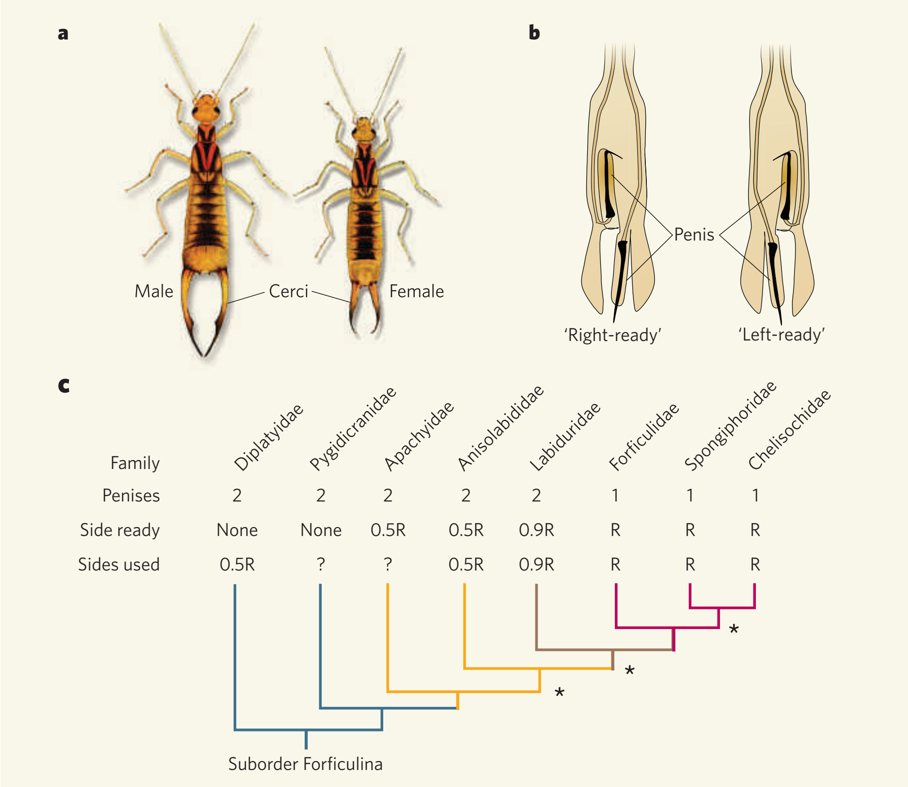

Figure 1 | Earwig penis number, orientation and evolution. **a**, A male and female *Labidura riparia*, the object of Kamimura's studies[6], showing the pronounced cerci for which earwigs are best known. **b**, The genitalia of the doubly endowed male *L. riparia* earwig showing two different penis orientations while at rest (not mating): 'right ready' (left penis folded anteriorly) and 'left-ready' (right penis folded anteriorly). Nine out of ten *L. riparia* prefer right-ready. (Figure modified from ref. 6.) **c**, Tentative phylogenetic relations among the families of the earwig suborder Forficulina[7,8], with asterisks indicating nodes with weak or inconsistent support. The inconsistencies are resolved here following ref. 7. Number of penises, and 'ready' and 'used' side is shown (0.5R = right-side penis ready or used in 50% of cases, and so on; data from ref. 6). The coloured lines represent different combinations of behaviours as indicated by the data above each line.

state (right side extended backwards, ready to mate; Fig. 1b) when not mating, as well as when *in flagrante delicto*. Curiously, the earwig's two penises are morphologically indistinguishable and fully functional. They connect to equivalent testes, and individuals with an injured or experimentally ablated right penis readily revert to using the left one. This right-ready asymmetry is therefore largely — if not entirely — behavioural.

On its own, right-handed penis preference in doubly endowed earwigs would qualify only as amusing natural history. But two other observations noted by Kamimura[6] increase its significance. The first is that not all earwig taxa have two penises. Some have only one, and it is indeed on the right side. The second is that not all earwigs with two penises have a right-side preference. Some (such as certain species of the families Diplatyidae and Anisolabididae) use the right or left indifferently.

It is the evolutionary relations among these earwigs[6–8] that elevates a genitalic curiosity to a higher plane (Fig. 1c). First, the earliest two lineages of the earwig suborder Forficulina, the families Diplatyidae and Pygidicranidae, have two penises, both of which point forward in the 'not-ready' position when not mating. Second, the three families Apachyidae, Anisolabididae and Labiduridae, in which doubly endowed males always hold one penis, either left or right, in the 'ready' position when at rest, are closely related, and lie evolutionarily between the primitive doubly endowed earwigs and the more recently evolved singly endowed earwigs. Third, these later earwigs (the three families Forficulidae, Spongiphoridae and Chelisochidae) that possess only one penis — the right — form a monophyletic group (they are all descendants of a common ancestor) derived from doubly endowed earwigs. Although morphological[7] and molecular[8] data yield somewhat different placements, the family Labiduridae, to which the right-leaning *L. riparia* belongs, is closely related to this common ancestor of single-penis earwigs.

Kamimura suggests[6] an intriguing evolutionary scenario that stems from these phylogenetic relations. Male earwigs evolved from a primitive state with both penises held in the 'not-ready' orientation when not mating, first through a stage where they always held one penis — either the right or left at random — in the 'ready' orientation. The next evolutionary step was males that still possessed two morphologically indistinguishable penises, but which preferentially held the right in the 'ready' orientation. Finally, the less-preferred (left) penis disappeared altogether, leaving only traces of a closed, non-functional ejaculatory duct. Thus, a purely behavioural asymmetry might have facilitated the evolution of a fully-blown morphological asymmetry.

The current view of the Forficulina phylogeny is in places tentative (Fig. 1c), as is the exact placing of *L. riparia* in its family, so the possibility that right-handed behaviour and left-side penis loss evolved independently cannot be discounted. Nevertheless, the observations seem to support a still controversial and underappreciated mode of evolution, known as the Baldwin effect, that was advanced more than a century ago[9,10]. This theory of 'organic selection', named after the experimental psychologist James Mark Baldwin, emphasized the impact of behaviour on evolution. Baldwin argued, as had Jean-Baptiste Lamarck nearly a century before[11], that new behaviours, learnt or otherwise, can expose an organism to novel conditions of growth to which it may then respond. But unlike Lamarck, Baldwin observed that altered behaviours can also yield altered morphologies through the inherent variation in possible outcomes (the 'plasticity') of an organism's development. If these behaviour-induced morphological differences affect performance positively, natural selection should favour genetic variants that increase or fix the plastic response.

Learnt handedness, coupled with developmental plasticity, provides an attractive mechanism for inducing right–left morphological asymmetries: excess use of one side of the body can induce its overdevelopment, as it does in the upper arm bones of professional tennis players[12]. The right-handed *L. riparia* seems to be one of those rare missing links where a right-side behavioural preference has been 'caught' genetically before any morphological differentiation. (As Kamimura shows[6], *L. riparia*'s right-side preference develops within four days of adult emergence, before any mating experience, so it involves no learning.)

The progression of the story would be deliciously complete if we also knew that individual males of the ambidextrous families Apachyidae and Anisolabididae actually learn to use one side preferentially with increased mating experience. Then the learnt handedness of an individual earwig would clearly have preceded evolutionarily the genetically captured handedness seen in *L. riparia*.

But a puzzling question remains: why a right-side preference? A minor anatomical asymmetry in the female *L. riparia* reproductive tract might favour right-handed males[6], rather as it does in birds. Most male birds lack an intromittent organ, and mate by pressing together their posterior opening, known as a cloaca, with that of the female. In two species, this 'cloacal kiss' comes most often from the left side[13,14], probably because the female's solitary ovary, and the opening to the oviduct, lie to the left[15]. But

50 & 100 YEARS AGO

50 YEARS AGO

The major part of the inaugural address as president of the Institution of Electrical Engineers, delivered by Sir Gordon Radley... was devoted to a consideration of world telecommunication, a subject particularly topical in view of the recent opening to traffic of the first trans-Atlantic telephone cable. The practical realization of inter-continental multi-channel telephone communication by submarine cable is, in Sir Gordon's view, revolutionary in its possibilities, because the traffic capacities of such cables are likely to exceed the existing demand for telegraph and telephone facilities on their routes... A new facility is planned for the trunk telephone network of Great Britain in the form of subscriber-dialling of long-distance calls. To render this practicable, it is necessary to have a nation-wide number scheme...
From *Nature* 8 December 1956.

100 YEARS AGO

To conclude, one may quote some admirable remarks... on the unfortunate result of ignorant European interference with Kafir customs... "In olden days there were regular courts of investigation, consisting of a dozen old women of the kraal. All the girls were medically examined by these women before and after large dances; and thus certain forms of vice were impossible as they would be so speedily detected. Nowadays the young women will not submit to such examination... [A]ncient restraints have been removed, and no new ones have been substituted by white men. The result is disastrous... The case of 'mixed bathing' of the children is another example of a somewhat similar thing. According to Western conceptions of morality this practice is indelicate and liable to lead to immorality. So missionaries advised natives to abandon it. The natives now declare that the abandonment of this custom has led to an increase of immorality, and say that it introduces new vices amongst the people."
From *Nature* 6 December 1906.

Kamimura shows that right-handed and left-handed *L. riparia* have equal mating success[6].

Alternatively, right-side penis preference might somehow be connected to the unknown factor that favours a stronger curvature of the right cerci in some related wingless earwigs, for example *Anisolabis* and *Euborellia*[16]. But the cerci in *L. riparia* are symmetrical (Fig. 1a), so the puzzle remains.

Clearly, the earwig penis system warrants more study. It could become a textbook example of how a possibly learnt lateralized behaviour bred a lateralized morphology evolutionarily. It already qualifies as a fine example of a phenotype-precedes-genotype mode of evolution because the right-ready and left-ready penis variants, which are equally common in evolutionary intermediates (Fig. 1c), and therefore probably not heritable[17], clearly existed before the genetically captured right-ready phenotype seen in *L. riparia*. Who would have ever thought you could learn so much from earwig penises? ■

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1. Rogers, D. C. & Fugate, M. *West. N. Am. Nat.* **61,** 11–18 (2001).
2. Bechly, G., Brauckmann, C., Zessin, W. & Groning, E. *J. Zool. Syst. Evol. Res.* **39,** 209–226 (2001).
3. Knoflach, B. & van Harten, A. *J. Nat. Hist.* **40,** 1483–1616 (2006).
4. Tokarz, R. R. & Slowinski, J. B. *Anim. Behav.* **40,** 374–379 (1990).
5. Shine, R., Olsson, M. M., LeMaster, M. P., Moore, I. T. & Mason, R. T. *Behav. Ecol.* **11,** 411–415 (2000).
6. Kamimura, Y. *J. Morphol.* **267,** 1381–1389 (2006).
7. Haas, F. & Kukalova-Peck, J. *Eur. J. Entomol.* **98,** 445–509 (2001).
8. Jarvis, K. J., Haas, F. & Whiting, M. F. *Syst. Entomol.* **30,** 442–453 (2005).
9. Baldwin, J. M. *Am. Nat.* **30,** 441–451 (1896).
10. Baldwin, J. M. *Am. Nat.* **30,** 536–553 (1896).
11. Lamarck, J. B. *Philosophie Zoologique* (Dentu, Paris, 1809).
12. Trinkaus, E., Churchill, S. E. & Ruff, C. B. *Am. J. Phys. Anthropol.* **93,** 1–34 (1994).
13. Nyland, K. B., Lombardo, M. P. & Thorpe, P. A. *Wilson Bull.* **115,** 470–473 (2003).
14. Petersen, A. D., Lombardo, M. P. & Power, H. W. *Anim. Behav.* **62,** 739–741 (2001).
15. King, A. S. in *Form and Function in Birds* Vol. 2 (eds King, A. S. & McLelland, J.) 107–148 (Academic, New York, 1981).
16. White, R. E., Borror, D. J. & Peterson, R. T. *A Field Guide to Insects: America North of Mexico* (Houghton Mifflin, Boston, 1998).
17. Palmer, A. R. *Science* **306,** 828–833 (2004).

CHEMICAL BIOLOGY

Renewing embryonic stem cells

Reka R. Letso and Brent R. Stockwell

Embryonic stem cells have great potential in medicine, but the current methods used to grow them prevent their therapeutic use. A dual-action compound has been discovered that may help solve this problem.

Last year, the International Stem Cell Forum stated that a reliable method for growing stem cells that does not depend on animal-derived products is a requirement for future work[1]. Reporting in *Proceedings of the National Academy of Sciences*, Chen *et al.*[2] describe their progress towards this goal. Using high-throughput screening, they have discovered a chemical that allows mouse embryonic stem (ES) cells to perpetuate themselves. This compound is a valuable tool for studying ES cell self-renewal, and may bring us closer to developing these cells for therapeutic purposes.

Great hopes have been raised that ES cells will one day be used to replace damaged cells, and to provide therapies beyond the reach of conventional drugs. However, a serious obstacle to their use is our lack of insight into the mechanisms that regulate a stem cell's behaviour — more specifically, whether it undergoes self-renewal or differentiates to become a more specialized type of cell. Furthermore, most human stem-cell lines, including all human ES cell lines approved for study with US federal funds, were grown using animal products, so the potential for cross-species contamination is too high for these lines to be developed for therapeutic purposes[3]. A synthetic compound that promotes ES cell self-renewal could help to address both of these issues.

Intriguingly, Chen and colleagues' compound — named SC1 — hits two targets in a protein network. Both of these targets are necessary to promote ES cell self-renewal. The authors discovered the compound by high-throughput screening of a chemical library[4] they had designed to target kinase enzymes; kinases pass on signals inside the cell. The authors tested their chemicals in mouse ES cells that were engineered to produce green fluorescent protein (GFP) only when they were perpetuating themselves. For the screen, the cells were grown under conditions that should cause them to stop self-renewing and to differentiate, a process that causes the levels of GFP to drop and the fluorescence to disappear. Chen *et al.* looked for compounds that had the ability to maintain fluorescence under these conditions.

Surprisingly, although the library was designed to target kinase enzymes, only one of the two targets of SC1 is a kinase. This illustrates an interesting notion in the design of chemical libraries: certain chemical groups