

## NANOTECHNOLOGY

# Nano-oscillators get it together

Pritiraj Mohanty

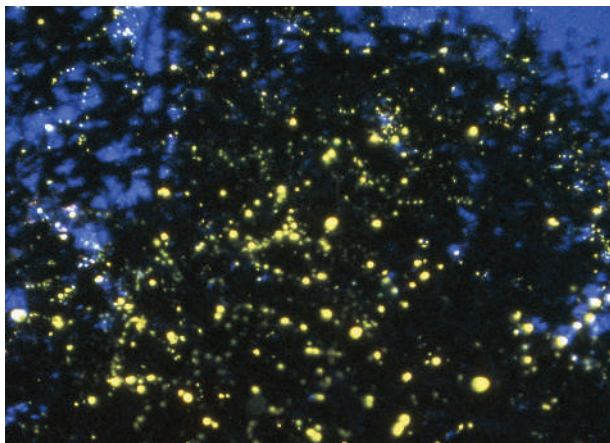
**Synchronized radiation from arrays of oscillators is widely used in microwave and wireless communications. Phase-locked oscillations produced at the atomic level now pave the way for devices on the nanoscale.**

Seen in southeast Asia, it is one of the most dazzling natural visual effects known: large congregations of fireflies blinking on and off in unison (Fig. 1). They orchestrate their flashing in almost perfect rhythm, and at a constant tempo. Each firefly maintains its steady beat through an internal clock, essentially a tiny oscillator inside its brain. Following outside stimuli, this oscillator begins to lock phase, or synchronize, with the firefly congregation<sup>1</sup>. A similar thing happens in the human heart: there, a cluster of pacemaker cells, known as the sinoatrial node, generates a synchronous oscillation that commands the rest of the heart to beat, in rhythm, for the duration of a life — typically some three billion pulses. Writing in this issue, Kaka and colleagues (page 389)<sup>2</sup> and Mancoff and colleagues (page 393)<sup>3</sup>

report the first demonstration of synchronized oscillation on the nanoscale: the phase-locking of two nano-oscillators in close proximity, through what is known as the spin-torque effect.

Spin is an intrinsic property of a particle or atom, and it is associated with angular momentum. A change in spin state therefore generates a change in angular momentum, resulting in a torque<sup>4</sup>. Use of this phenomenon to find the angular momentum of the photon was proposed by Albert Einstein and Wander de Haas<sup>5</sup> in 1915, and was achieved experimentally by Richard Beth 20 years later<sup>6</sup>. Since then, various fundamental measurements — notably those of the ratio of angular momentum to magnetic moment (the gyromagnetic ratio) of a metal<sup>7</sup>, and the quantum of superconducting flux<sup>8</sup> — have relied on spin-torque effects. New approaches to spin-based electronics using mechanical nano-oscillators have been proposed on the strength of the idea<sup>9</sup>. And spin-torque effects have also been discovered<sup>10,11</sup> in nanoscale magnetic multilayers, allowing steady microwave power to be generated in response to a direct current.

The operational principle of the spin-transfer device used by Kaka *et al.*<sup>2</sup> and Mancoff



**Figure 1 | Fireflies, fireflies burning bright.** In the forests of the night, certain species of firefly flash in perfect synchrony — here *Pteroptyx malacciae* in a mangrove apple tree in Malaysia. Kaka *et al.*<sup>2</sup> and Mancoff *et al.*<sup>3</sup> show that the same principle can be applied to oscillators at the nanoscale.

*et al.*<sup>3</sup> is well known. This device consists of an electrical point contact linked to multiple thin layers of magnetic material. When a direct current is applied to this contact, torque from the spins of the electrons in the material causes the direction of magnetization to oscillate at microwave frequencies. A spin-transfer oscillator would be expected to produce 'spin-waves', emanating from the region beneath the point contact as each layer of the material influences the next. A second point contact, or a spin-transfer device in close proximity, should experience this spin-wave, leading to phase-locking of the two oscillators — in much the same way that two pendulum clocks coupled through a wall will lock phase, a fact first noted by Christiaan Huygens in the seventeenth century<sup>12</sup>.

And here lies the exciting aspect of the latest experiments<sup>2,3</sup>. Mancoff and co-workers<sup>3</sup> vary the distance between the contacts of two identical spin-transfer oscillators and find that, when it is less than roughly 200 nanometres, the oscillators synchronize at a single resonance-peak frequency. Oscillators with a larger inter-contact spacing (typically 400 nanometres) produce two separate resonance peaks, one for each oscillator. The power

radiated from the two locked oscillators is twice that produced from two oscillators at a greater separation radiating independently. Such an enhancement of output power, proportional to the square of the number of oscillators ( $N^2$ ), is the tell-tale sign of coherent radiation (in the incoherent case, the dependency is on  $N$ ).

Kaka and co-workers<sup>2</sup> also find that the power radiated from their device, which consists of two phase-coupled oscillators with different individual power outputs, is consistent with that expected for two phase-coherent signals interfering constructively. Again, this is almost twice that expected from two oscillators radiating at the same frequency but out of phase. In a further testimony to the phase coherence between the

oscillators, the authors find that, as expected, the spread in frequency of the oscillation is reduced in the phase-locked state.

Such phase-locked nano-oscillators<sup>2,3</sup> have major implications for the use of nanoscale spin-transfer devices. The output power of a single device is small (typically less than a millionth of a milliwatt), but connecting two or more phase-locked devices together could quickly increase the output to a useful level of the order of microwatts or even milliwatts at gigahertz frequencies. The radiation pattern produced by an array of oscillators vibrating in phase is highly directional, making them useful as beam-steering devices in wireless communications — as either transmitters or receivers. Before such a device can be used on the nanoscale, however, phase-locking among many nano-oscillators must be demonstrated.

Finally, the significance of the oscillators' spatial distribution adds an exciting dimension to the problem. It creates the potential for probing synchronization and chaos at the nanoscale, an active field of research in applied mathematics and neuroscience. Motivation for future work here can once again be found in the stunning visual patterns of the spatial temporal dynamics of fireflies. Nature never fails to inspire. ■

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## GENOMICS

# Massively parallel sequencing

Yu-Hui Rogers and J. Craig Venter

**A sequencing system has been developed that can read 25 million bases of genetic code — the entire genome of some fungi — within four hours. The technique may provide an alternative approach to DNA sequencing.**

Since the publication of the first complete genome sequence of a living organism<sup>1</sup> in 1995, the field of genomics has changed dramatically. Fuelled by innovations in high-throughput DNA sequencing, high-performance computing and bioinformatics, genomic science has expanded substantially and the rate of genomic discovery has grown exponentially. To date, the genomes of more than 300 organisms have been sequenced and analysed, including those of most major human pathogens, diverse microbes — and, of course, our own genome<sup>2,3</sup>. These advances have profoundly altered the landscapes of biological science and medicine. In this issue, Rothberg and colleagues (page 376)<sup>4</sup> describe a sequencing system that offers a much higher throughput than the current state-of-the-art methods. The system has some limitations to overcome before it can be used for all sequencing applications, but it is nonetheless one of the most promising sequencing technologies to have emerged in recent years.

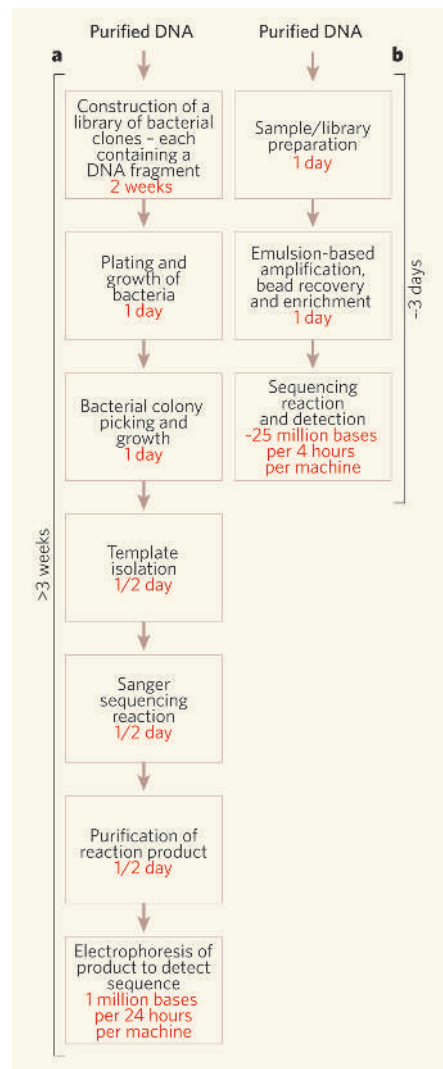
For more than a decade, Sanger sequencing<sup>5</sup> and fluorescence-based electrophoresis technologies<sup>6</sup> have dominated the DNA sequencing field. Continued improvements in these techniques and in instrumentation, paired with advances in computing and informatics, have reduced the cost of sequencing by roughly two orders of magnitude and transformed genome projects from decade-long endeavours to projects of mere months (for mammalian-sized genomes), or even weeks (for microbial genomes). However, it still costs an estimated US\$10 million to US\$25 million to sequence a single human genome<sup>7</sup> and \$20,000–\$50,000 to sequence a microbial genome. Only a handful of large genome centres worldwide have the resources and technical expertise to handle the sequencing of a mammalian-sized genome, perform large-scale sequencing of multiple organisms or conduct the resequencing of large numbers of genes. To ensure continued growth of genomic science and to enable more

labs to become involved in DNA sequencing, new approaches must decrease the cost and increase the throughput of sequencing significantly, while maintaining the high quality of data produced by the current approach.

Rothberg and colleagues<sup>4</sup> have developed a highly parallel system capable of sequencing 25 million bases in a four-hour period — about 100 times faster than the current state-of-the-art Sanger sequencing and capillary-based electrophoresis platform. The method could potentially allow one individual to prepare and sequence an entire genome in a few days (Fig. 1). The sequencer itself, equipped with a simple detection device and liquid delivery system, and housed in a casing roughly the size of a microwave oven, is actually relatively low-tech. The complexity of the system lies primarily in the sample preparation and in the microfabricated, massively parallel platform, which contains 1.6 million picolitre-sized reactors in a 6.4-cm<sup>2</sup> slide.

Sample preparation starts with fragmentation of the genomic DNA, followed by the attachment of adaptor sequences to the ends of the DNA pieces. The adaptors allow the DNA fragments to bind to tiny beads (around 28 µm in diameter). This is done under conditions that allow only one piece of DNA to bind to each bead. The beads are encased in droplets of oil that contain all of the reactants needed to amplify the DNA using a standard tool called the polymerase chain reaction. The oil droplets form part of an emulsion so that each bead is kept apart from its neighbour, ensuring the amplification is uncontaminated. Each bead ends up with roughly 10 million copies of its initial DNA fragment.

To perform the sequencing reaction, the DNA-template-carrying beads are loaded into the picolitre reactor wells — each well having space for just one bead. The technique uses a sequencing-by-synthesis<sup>8</sup> method developed by Uhlen and colleagues, in which DNA



**Figure 1 | Speeding up sequencing.** Flow diagrams for **a**, traditional microlitre-scale Sanger DNA sequencing and electrophoresis, and **b**, the massively parallel picolitre-scale sequencing developed by Rothberg *et al.*<sup>4</sup>. The traditional microlitre-scale approach requires a longer processing time per production cycle, substantially more support equipment, a larger facility and more labour than the picolitre-scale approach.

complementary to each template strand is synthesized. The nucleotide bases used for sequencing release a chemical group as the base forms a bond with the growing DNA chain, and this group drives a light-emitting reaction in the presence of specific enzymes and luciferin. Sequential washes of each of the four possible nucleotides are run over the plate, and a detector senses which of the wells emit light with each wash to determine the sequence of the growing strand.

This new system shows great promise in several sequencing applications, including resequencing and *de novo* sequencing of smaller bacterial and viral genomes. It could potentially allow research groups with limited resources to enter the field of large-scale DNA sequencing and genomic research, as it provides a technology that is inexpensive and easy to implement and maintain. However, this technology