microRNAs (miRNAs) — which are distinct in their biogenesis and cellular roles (Box 1). The studies[1–6] find that endo-siRNAs regulate transposons as piRNAs do; that, like miRNAs, they can arise from hairpins; and that, in flies, their processing involves a similar co-factor to the processing of miRNAs (Box 1).

This blurring of boundaries among different types of small RNA, together with the newly established links between siRNAs and pseudogenes, has interesting evolutionary implications. In plants, inverted duplications containing a protein-coding gene have been proposed[16] as a mechanism to create new miRNAs. Thus, one can imagine a gene being copied (either by duplication or retrotranscription) and this copy then being duplicated (again) in inverted fashion. Given the ubiquitous nature of genomic transcription, the copy and its inverted duplicate could potentially be transcribed to a hairpin precursor of endo-siRNAs to regulate the parent gene.

As the function of the hairpin no longer has anything to do with encoding protein, its sequence, still under selection, can acquire frameshifts and stop codons, making it seem pseudogenic. One could even imagine its sequence drifting further and becoming gradually transformed into a miRNA gene, the sequence of which is much less similar to the gene encoding its target mRNA. So pseudogenes encoding endo-siRNAs might provide a crucial intermediate link to understanding the evolution of miRNA-mediated regulation[17]. Although speculative, the plausibility of this theory is bolstered by a recent survey[18] of the genomic context of more than 300 human miRNA loci, which identified two that lie within pseudogenes. ■

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ATTOSECOND PHYSICS

An easier route to high harmony

Mark I. Stockman

The generation of ultrashort light pulses by atomic ionization and recombination doesn't come cheap. But by niftily exploiting the play of light on a nanostructured surface, it can be done on a table-top.

Extreme ultraviolet (EUV) radiation has great potential to be extreme not just in name, but in usefulness. It is the band of ultraviolet light with the shortest wavelength — around 5–50 nanometres, between 100 and 10 times shorter than that of visible light. In applications such as microscopy and lithography it can thus be used to probe and etch at tiny scales. What's more, this wavelength regime is that of many atomic resonances, making EUV light ideally suited for spectroscopic applications. On page 757 of this issue[1], Kim *et al.* detail a deft new way to produce EUV radiation — one that could be considerably more economical that previous approaches.

The way in which EUV radiation is currently generated is extremely fiddly. It starts with the amplification of light pulses from an oscillator, a source of laser light. These are used to drive the repeated ionization of noble-gas atoms. The electrons freed during this process are accelerated in the light field and, because the sign of the field reverses after half a cycle, re-collide with their parent atoms[2,3], releasing the electrons' surplus energy as light. The result is a sequence of ultrashort (attosecond) pulses that are themselves useful tools for high-time-resolution metrology[4,5]. More detailed consideration of the process reveals that the spectrum of these pulses consists of a comb of 'high harmonics' — spectral lines at wavelengths equal to the wavelength of the driving field divided by some integer. (Owing to symmetries of the particular situation, only light corresponding to odd-integer divisors is generated in this case.) The highest-harmonic (shortest-wavelength) component of this spectrum can be selected by filtering to produce a single attosecond pulse at an EUV wavelength.

Things would be much simpler if EUV radiation could be produced directly from an oscillator — an ultrashort pulsed laser of relatively low intensity — without the need for sophisticated, complex and expensive amplifiers to produce a high-intensity optical field. Kim *et al.*[1] provide a distinct glimmer of an indication that such an approach could be viable. They illuminate an intricate, nanoscale gold antenna structure with light from a standard titanium–sapphire laser, with a wavelength of 800 nm. The interaction of the light with the antennas produces high harmonics right up to the 17th harmonic — whose wavelength of 47 nm lies within the EUV range. The optical intensity required to generate this light is, at 10^{11} W cm^{-2}, about 100 times less than in the traditional approaches.

The secret of the authors' success is the nanoscale behaviour of 'quasiparticles' known as surface plasmons. These packets of optical energy represent rapid oscillations of electron density that spring up in the surface regions of metal nanoparticles when bathed in an incident light field. If this incident light is of the right frequency, the surface plasmons can enter resonance, greatly increasing the local field intensity over that of the excitation wave. This phenomenon has a central role in, for example, surface-enhanced Raman scattering[6], a spectroscopy and imaging technique that is sensitive enough to detect the presence of individual molecules adsorbed on a metal surface.

The extent of this field enhancement is determined by the nanoparticles' plasmonic resonance properties, which in turn depend mostly on the resistivity of the metal at the frequency of the optical light. Additional magnitude comes from geometric effects[7–9], both in narrow gaps between particles where there is a significant localization of optical energy, leading to the formation of 'gap plasmons', and also similarly around sharp tips, a phenomenon known as the lightning-rod effect. Nanoparticles have been specifically engineered in

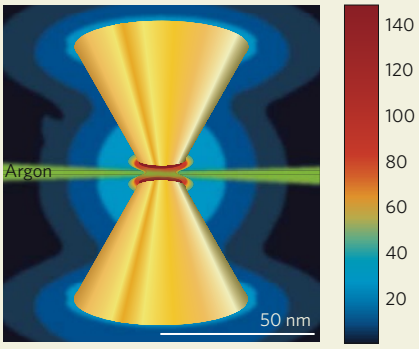

Figure 1 | Stripping on the table-top. The bow-tie-shaped gold nanoantennas used by Kim *et al.*[1] develop electric-field strengths in the gap through interactions with quasiparticles known as surface plasmons. (The field strength *E* is colour-coded; note that intensity is proportional to the square of the field strength.) When a beam of argon atoms (green) is directed towards the gap, the field strips them of electrons, which subsequently recombine — a process that results in the generation of high harmonics of the original light, including the sought-after extreme ultraviolet radiation. (Data and calculations courtesy of J. Aizpurua.)

configurations such as nanolenses[10] and bow-tie nanoantennas[11] to take advantage of all three mechanisms: resonance, gap plasmons and the lightning-rod effect.

The context for Kim and colleagues' experiments[1] is an array of gold bow-tie nanoantennas on a sapphire substrate. In the nanoscale gaps of the bow-tie, the local optical intensity can be enhanced in an idealized case by up to 10,000 times (Fig. 1). In reality, the enhancement is limited by intrinsic optical losses in gold, imperfections in the structure's geometry, and the defects and polycrystalline nature of the gold's crystal lattice. But if the local field intensity is increased by just 100 times, it reaches 10^{13} W cm^{-2}, sufficient for relatively efficient generation of EUV radiation. Because this field is extremely locally concentrated in the gaps, it does not damage the sapphire substrate. Equally, the high dielectric permittivity of the gold nanoparticles means that the field cannot penetrate far into their surface.

The authors immerse their bow-tie assembly in a jet of argon gas. From this point, everything proceeds broadly analogously to the traditional production of EUV light. First, the high local field created by the plasmonic enhancement detaches an electron from the argon atoms as they pass through the bow-tie gaps. This electron is accelerated by the optical fields along its trajectory, and collides and recombines with the atom. The oscillating optical field causes the collisions to repeat periodically, releasing energy at high-harmonic frequencies of the original light.

There are two principal distinctions between this process and the generation of high harmonics by intense optical pulses. First, the intensity threshold is considerably lower, as touched on earlier. Second, the incident optical pulses are relatively tightly focused, and so the EUV light is generated in just one or a few nanogaps of the array and is not highly directed. (Directedness would stem from the interference of radiation from many bow-ties.)

This new method of short-wavelength light generation will open doors in imaging, lithography and spectroscopy on the nanoscale. It could expand the range of techniques that exploit local-field enhancement, such as near-field scanning optical microscopy, from the infrared and optical wavelengths to the EUV and, ultimately, as the plasmonic quality of the nanoantennas improves, X-ray range. This much shorter wavelength will benefit techniques such as core spectroscopy and nanoscale X-ray crystallography.

With less-tight focusing, it will also become possible to generate EUV radiation in many nanoantennas simultaneously. The resulting spatially coherent, laser-like light could have applications in many areas: in macroscopic spectroscopies, in screening for structural defects in materials and, extended to X-ray and even γ-ray wavelengths, in the detection of minute amounts of fissile materials in the arenas of public security and defence. ■

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DEVELOPMENTAL BIOLOGY

Order in the lung

David Warburton

Given the lung's thousands of branching airways, its development might be expected to be a highly complex process. Yet a surprisingly simple picture now emerges of when, where and in what order these branches form.

Elaborate branching is everywhere in nature. From riverbeds to oilfields, from trees to blood vessels, branching connects the large to the small. The lung is also a prime example of a reproducible branching system, allowing gas to be transported from the air to tissues deep within an animal. Without it — or without the simpler branched ducts found in less complex organisms — oxygen transport by diffusion probably would have limited the evolution of terrestrial animals to less than one millimetre in size. But how does such a sophisticated network develop? Metzger *et al.*[1] (page 745 of this issue) provide a remarkable, yet simple picture that explains the orderly development of the more than a million branches in the mammalian lung.

In mammals, air enters through the nasal and oral cavities and passes through the larynx and trachea before reaching the lung. The trachea branches into two primary bronchi, which, within the lung, further branch into secondary and tertiary bronchi and finally into bronchioles. To investigate the sequence of events leading to this complex, yet highly reproducible network of branches, Metzger *et al.* studied the early bronchial tree in three dimensions by examining chemically fixed lung tissue from mouse embryos using microscopy.

The authors parse bronchial branching beyond the primary branch into three geometrical modes, which they call domain branching, planar bifurcation and orthogonal bifurcation. In domain branching, daughter branches form in rows along the parent branch, like bristles on a bottle brush. This branching mode forms the main secondary branches. Next, planar bifurcation is used for the formation of tertiary and later-generation branches; this mode is characterized by the splitting of a branch tip into two. Finally, orthogonal bifurcation involves two rounds of branching. Both rounds involve

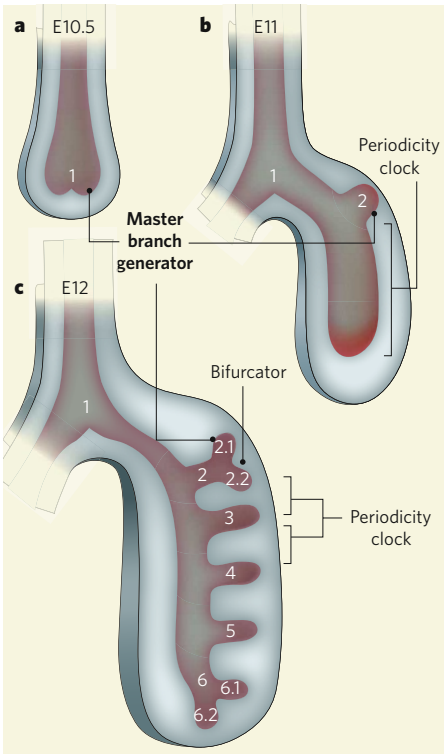

Figure 1 | A master and three slaves. Studying early lung morphogenesis in the mouse embryo, Metzger *et al.*[1] show that this organ's airways form in a sequential manner in three series of events, or subroutines, which are all driven by one master branch generator. **a**, At embryonic day (E) 10.5, the primary bronchial branch (1) forms, followed by (**b**) the development of the left upper-lobe branch (2) by E11. **c**, The first two segmental branches of the left upper-lobe branch (2.2 and 2.3) and the subsequent formation of branches 3–6 occur at E12. The master branch generator is active throughout these events, and the inferred sites of action of the periodicity clock and bifurcator subroutines are shown. At E12, the rotator subroutine has not yet begun to function.