

6. Marshall, L., Helgadottir, H., Mölle, M. & Born, J. *Nature* **444**, 610–613 (2006).
7. Fogel, S. M. & Smith, C. T. *J. Sleep Res.* **15**, 250–255 (2006).
8. Stickgold, R., Whidbee, D., Schirmer, B., Patel, V. & Hobson, J. A. *J. Cogn. Neurosci.* **12**, 246–254 (2000).
9. Sejnowski, T. J. & Destexhe, A. *Brain Res.* **886**, 208–223 (2000).
10. Plihal, W. & Born, J. *NeuroReport* **10**, 2741–2747 (1999).

DEVICE PHYSICS

A terahertz modulator

Daniel Mittleman

Tiny metal resonators can be used to create a material with tunable responses to an applied voltage. Combined with a semiconductor substrate, they can be used to control technologically promising terahertz radiation.

Electromagnetic radiation with frequencies lying between the microwave region and the infrared — so-called terahertz radiation — holds great promise for imaging and sensing applications. It is non-ionizing, and therefore causes less damage to biological tissue than conventional, higher-energy X-rays. It penetrates plastics and clothing, but not metal, and so is ideal for security screening and non-contact testing or inspection. But to realize the full potential of terahertz radiation, more sophisticated techniques for its generation, manipulation and detection are required. In this issue, Chen *et al.* (page 597)¹ fill an important gap in our capabilities. They report the development of an efficient, electrically driven modulator for terahertz signals that functions at room temperature.

This work builds on exciting developments in the field of metamaterials. These are materials engineered to have electromagnetic responses that are impossible in naturally occurring materials, such as a negative refractive index. The refractive index of a material, n , is a measure of the speed of light in the material, and is given by $n = (\mu\epsilon)^{1/2}$, where μ is the material's 'permeability' to magnetic fields, and ϵ its 'permittivity' to electric fields. All naturally occurring materials have positive μ ; transparent materials have positive ϵ , too. In these normal materials, therefore, the refractive index is a real and positive number.

In 1968, the Soviet physicist Victor Veselago showed² that a hypothetical material with negative ϵ and μ would also have a real refractive index, meaning that light waves could propagate through the material, but would behave as though its refractive index were negative. This material would have unusual and potentially valuable properties. A flat slab of negative-index material, for example, would focus light in much the same way as a curved slab of ordinary material (a lens), but with a smaller focal spot.

Although negative-index materials do not violate any laws of physics, the absence of a medium with negative μ confined the idea to the realm of speculation. But in the late 1990s, John Pendry found that, by assembling a collection

of appropriately designed metallic structures, a material can be fabricated that has both negative ϵ and negative μ for incident electromagnetic radiation of a particular frequency^{3,4}. Furthermore, if the metal structures are each much smaller than the wavelength of the incident radiation, the radiation interacts with them not individually, but collectively, according to their average properties. These are the engineered materials now known as metamaterials.

Engineering a material with negative ϵ was easy: this equates to opacity, a property of all metals for incident radiation below a certain frequency. It was necessary to show only that a discrete set of thin metallic structures could mimic this property of the bulk metal⁵. The more difficult task was achieving a negative μ . It turned out that this could be done using a pair of concentric metallic rings with gaps that prevent current from circulating. Because these rings are both capacitors (they store electric charge) and inductors (they induce magnetic fields that self-sustain any current flowing through them), the presence of gaps leads to a resonant response, with charge accumulating alternately on one side of the gap and then the other, sloshing back and forth through the rings rather as a mass vibrates back and forth on a spring. At frequencies near the characteristic frequency of this resonant electron flow, ϵ and μ can vary dramatically as a function of frequency. Indeed, either one can become negative if the resonance is strong enough⁴.

The development of the split-ring-resonator concept was significant not only because it permits a negative refractive index, but more generally because it represents a new technique for 'designing' the optical response of a medium. The first experimental demonstration of a negative index⁵, along with nearly all research into metamaterials until now, was performed in the microwave regime. This region encompasses gigahertz frequencies below the terahertz regime, with wavelengths of several millimetres or longer. It was almost immediately recognized, however, that the approach could be extended into the shorter-wavelength, terahertz regime simply by shrinking

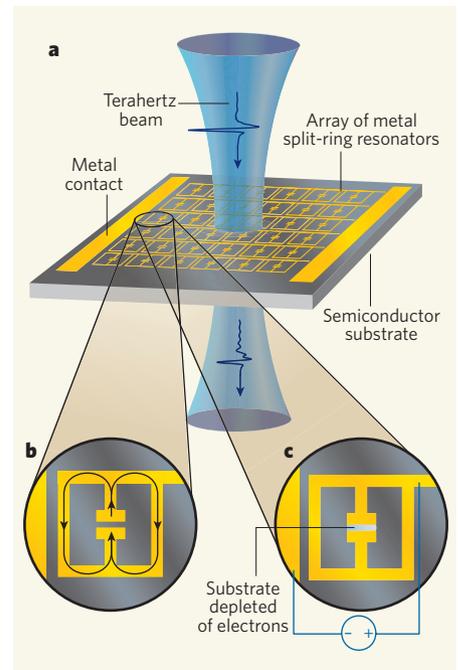


Figure 1 Chen and colleagues' resonant metamaterial modulator¹. **a**, The tunable resonant response of an array of metallic split-ring resonators on a thin semiconductor substrate can be exploited as a modulator, letting more or less of an incident radiation beam through. **b**, When no external voltage is applied, the doped semiconducting substrate conducts. Current circulates around the two lobes of the resonator in response to the applied terahertz field. **c**, When an external voltage is applied, the semiconductor ceases to conduct. Current can no longer flow through the ring gap; this gap instead behaves as a capacitor, storing up charge. The capacitance gives rise to a resonant behaviour at a frequency in the terahertz range, in which the electrons slosh back and forth between the upper and lower gap electrodes. The incident terahertz radiation drives this resonance efficiently, leading to the transfer of more energy from the beam to the electrons of the substrate. Thus, less radiation is transmitted through the device.

the size of the individual metallic components so that they remained smaller than the incident radiation's wavelength. At 1 THz, this is 300 μm , so the fabrication of a negative-index medium requires the technically challenging construction of three-dimensional objects with micrometre-scale features. Two-dimensional patterns on that scale, on the other hand, can be easily generated using conventional photolithography, and these patterns can be designed to exhibit a strong resonance in either ϵ or μ at any frequency of interest.

Chen *et al.*¹ use the split-ring-resonator concept as the basis for a metamaterial that provides a resonant response in ϵ — although not a negative refractive index — in the terahertz range. Furthermore, they have shown that this resonance can be externally controlled, and therefore can be exploited as a modulator for controlling the transmission of terahertz electromagnetic radiation.

The principle of this device's operation is simple and elegant (Fig. 1). An array of sub-wavelength metallic ring resonators is deposited on top of a thin, lightly doped semiconductor layer and illuminated with a beam of terahertz radiation. The electrons in the semiconductor substrate effectively short-circuit the gap in the split rings, driving the capacitance of the rings to zero and damping their normal resonant response. But when a negative voltage is applied to the metal structures, the electrons in the substrate beneath are repelled away from the gap. As electrons become depleted in the gap, current can no longer flow effectively and the gap behaves as a capacitor, storing electric charge. In this case, the resonance of the ring structure re-emerges, which gives rise to a pronounced change in the optical properties of the array at frequencies near its resonant frequency.

The authors' results¹ are impressive. At the design frequency, the on-off transmission ratio of this device is about 0.5 — more than ten times better than state-of-the-art, electrically operated modulators in this frequency range^{6,7}.

The new design is simpler to fabricate, and the modulator works at room temperature. This excellent performance comes from the exquisite sensitivity of a metamaterial's response to the precise properties of its resonant substructures. The ability to electrically switch the properties of a metamaterial by fabricating it on a semiconductor substrate provides a new method for active control of terahertz devices.

Naturally, challenges remain. Most obviously, larger on-off transmission ratios will be required for many applications. The modulation speed, which is only a few kilohertz, must be increased significantly. The authors point out that both of these difficulties can be addressed by optimizing both the pattern of the metal structures and the properties of the substrate. The properties of the device are also dependent on the direction of the electric-field vector (the polarization) of the incident radiation: the resonant behaviour of the split rings relies on this electric field driving current across the gaps, all of which are oriented in one particular direction. Designs of future

devices may seek to eliminate or alternatively exploit this polarization sensitivity. Finally, one can imagine a structure for which not only the transmitted intensity, but also the resonant frequency, is externally controllable.

Whatever the next stage of development might be, the resonator structures described by Chen *et al.*¹ open a new and promising set of possibilities for the active control of terahertz radiation, with all the potential that it holds. ■

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1. Chen, H.-T. *et al.* *Nature* **444**, 597–600 (2006).
2. Veselago, V. G. *Sov. Phys. Uspekhi* **10**, 509–514 (1968).
3. Pendry, J. B., Holden, A. J., Stewart, W. J. & Youngs, I. *Phys. Rev. Lett.* **76**, 4773–4776 (1996).
4. Pendry, J. B., Holden, A. J., Robbins, D. J. & Stewart, W. J. *IEEE Trans. Microwave Theory Tech.* **47**, 2075–2084 (1999).
5. Shelby, R. *et al.* *Science* **292**, 77–79 (2001).
6. Kleine-Ostmann, T., Dawson, P., Pierz, K., Hein, G. & Koch, M. *Appl. Phys. Lett.* **84**, 3555–3557 (2004).
7. Kersting, R., Strasser, G. & Unterrainer, K. *Elec. Lett.* **36**, 1156–1158 (2000).

SYSTEMS BIOLOGY

Many things from one

John R. S. Newman and Jonathan S. Weissman

Cells of the same type can generate diverse sets of physiological traits from a single set of genes. Part of this diversity could stem from 'noise' that arises from variations in the way proteins are expressed.

The census bureau will tell you that the typical American family has 2.1 children, but there are no families (we hope) that precisely match this mean. Similarly, biologists have come to realize that population-based measurements can obscure critical information about cell-to-cell diversity. The use of fluorescent proteins as tags to look at the abundances of proteins in single cells has revealed that, at least for microorganisms, individual protein levels can vary considerably, even for genetically identical populations grown under uniform conditions.

On page 643 of this issue, Sigal and colleagues¹ present a view of what protein variation may look like in human cells*. They reveal that this variation (or 'noise') can persist over several cell generations. Additionally, for proteins belonging to the same biochemical pathway, variation seems to be larger between cells than within cells. To the extent that protein abundance and activity are correlated, this variation might contribute to the ability of cells to generate a diversity of behaviours from a single set of genes (genotype).

Variation has attracted considerable interest,

*This article and the paper concerned¹ were published online on 19 November 2006.

particularly because it can affect cells differentially. It can be an obstacle to the precise functioning of cells, by causing levels of biological molecules to deviate from their optima, and can degrade biological signals. But noise can also be exploited by allowing cells to switch between expression states, or, more speculatively, by generating diversity in physiological characteristics (phenotypes).

Studies using microorganisms have identified at least two types of noise. Extrinsic noise results from intercellular variations in the levels of components of the pathways that regulate gene expression. Intrinsic noise, however, arises from the random production and/or destruction of messenger RNAs and proteins that is due to chance interactions occurring in cells. These interactions would persist even if every cell were otherwise identical. Extrinsic noise tends to dominate for proteins present in high amounts in a cell, whereas intrinsic noise dominates when proteins, and their corresponding mRNAs, are present in low copy number. In contrast to our understanding of variation in microorganisms, much less is known about the origins and consequences of variation in the cells of multicellular organisms. A priori one might speculate that, in

these cells, the cost of noise might be greater because of the interdependence of cells within tissues or organs. This, together with the fact that there are higher numbers of mRNA molecules per cell, which tends to average out the randomness of the production and destruction of individual messages, suggests that total noise might be lower than that observed in microorganisms.

To explore this issue directly, Sigal and colleagues¹ created a series of strains of a human cancer cell line in which DNA encoding yellow fluorescent protein (YFP) was inserted into the genome in the middle of genes encoding various proteins (one insertion per strain). The genes therefore maintained their natural regulation, but encoded fluorescent fusion proteins. As the cells grew, time-lapse microscopy was used to monitor their overall fluorescence (and thus the abundance of the respective protein). The images were 'synchronized' with respect to cell divisions, eliminating a major source of variation that was not pertinent to these studies. The authors found that the coefficient of variation (standard deviation/mean) is 10–30%, similar to measurements in microorganisms².

To explore the level of intrinsic and extrinsic noise, the authors succeeded in obtaining a strain in which both copies of the gene that encodes the RPL5 protein were tagged, one with the DNA encoding YFP and one with DNA encoding a red fluorescent protein (RPL5 is found in a multi-subunit complex called the ribosome, which is involved in protein synthesis). Such a strain is useful because it makes it possible to distinguish between extrinsic and intrinsic noise (observed as intercellular and intracellular differences in fluorescence,