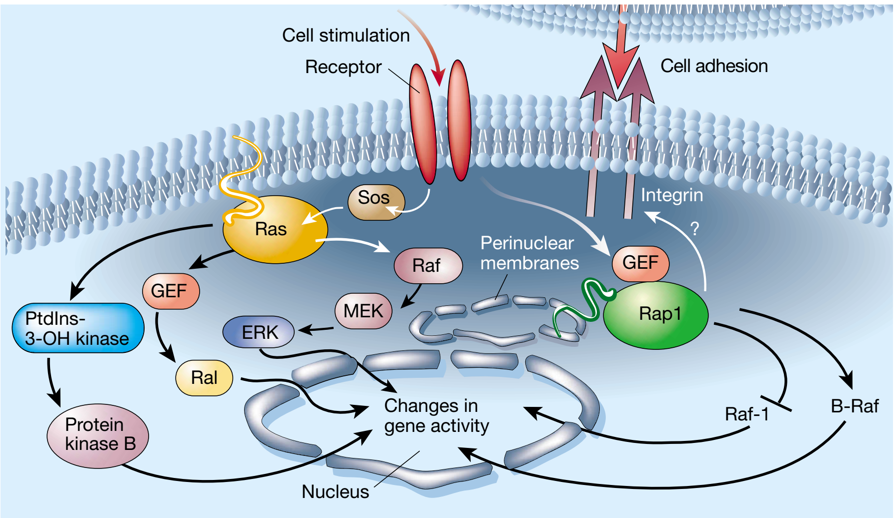

Figure 2 **Ras and Rap1 are active in different parts of the cell. Mochizuki *et al.*[1] find that, in response to cell stimulation, Ras is active near the cell membrane, whereas Rap1 is switched on near the membranes around the nucleus. This may reflect the involvement of these proteins in signalling pathways that lead in opposite directions, either into (Ras) or out of (Rap1) the cell. The molecules involved in some of these pathways are shown. GEF, guanine-nucleotide-exchange factor; PtdIns-3-OH kinase, phosphatidylinositol-3-OH kinase.**

provided as Supplementary Information (http://www.nature.com/nature). When the authors stimulated Cos cells with epidermal growth factor, they first detected activated Ras at the nearby plasma membrane. Active Ras then rapidly spread into the body of the cell, probably reflecting the internalization of a signalling complex composed of Ras, a guanine-nucleotide-exchange factor and perhaps the receptor. In PC12 cells that were induced to differentiate with nerve growth factor, active Ras was also detected near the plasma membrane, and persisted particularly at the tips of the extensions (neurites) sent out by the differentiated cells. This persistence was presumably due to continuous activation of Ras — the fluorescent signal was rapidly restored after being inactivated by photobleaching.

In contrast, the activation of Rap1 began just outside the nucleus and spread outwards. This implies that information from cell-surface receptors is transduced into the cell before Rap1 is activated. Indeed, the activation of Rap1 requires, for instance, the internalization of cell-surface receptors[1,4], or messenger molecules such as calcium that move freely in the cell (reviewed in ref. 5).

For Ras, these results are expected. Generally, a guanine-nucleotide-exchange factor, Sos, interacts (through connecting proteins) with receptors soon after they are activated. Sos then switches on Ras, which in turn activates several signalling pathways (Fig. 2), the end point of which is usually the control of gene expression[3]. The observations of Rap1, however, are more surprising. This protein is rapidly activated by several extracellular stimuli and, depending on the cell type, is implicated in either positive or negative control of a pathway that ultimately regulates gene expression. Rap1 has also been proposed to coordinate some functions of the plasma membrane, such as cell–cell adhesion, but little is known about how it regulates these processes[5].

The results of Mochizuki *et al.*[1] give a twist to our thinking about Rap1. It seems that the Rap1 signalling pathway responds to extracellular stimuli but begins inside the cell and directs signals outwards, for instance towards the plasma membrane. Why should Rap1 be activated near the nucleus to control events at the plasma membrane? This protein is often found near the nucleus in organelles known as endosomes[6], one of the functions of which is to sort proteins that are destined for different locations in the cell[7]. Rap1 may therefore be involved in protein sorting. It is also found in membranous packets of proteins that are destined to move outwards[8], and may even be needed to regulate secretion, as suggested by the involvement of one of its exchange factors in this process[9]. Finally, Bud1, the budding-yeast counterpart of Rap1, is involved in assembling protein complexes at the place on the plasma membrane where a bud will form[10].

The implication of all of these results is that Rap1 is involved in collecting together proteins for transport to the plasma membrane. I predict that Mochizuki *et al.*'s technique[1], together with methods for determining the precise membranes in which active GTPases are found, will be invaluable in tackling this and related problems. ■

Johannes L. Bos is in the Department of Physiological Chemistry, Utrecht University, Universiteitsweg 100, NL-3584 CG Utrecht, The Netherlands.
e-mail: j.l.bos@med.uu.nl

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Communications technology

A bottleneck for optical fibres

Joseph M. Kahn and Keang-Po Ho

Optical fibres carry light signals at extremely high frequencies, and offer enormous bandwidth for transmitting data. But nonlinear effects may limit their capacity to carry information.

Over the past decade, the flow of Internet traffic and other digital information has increased explosively. Optical fibres made of silica offer the highest capacity of any communications medium, making them the most cost-effective choice for data transmission over all but the shortest distances (under about 1 km). Even so, transmitting and receiving light signals also requires electronic systems that convert electricity into light and vice versa. These conversion processes tend to limit the rate at which information can be carried on an optical fibre using a single frequency or wavelength. But dramatic increases in the capacity of optical fibres have been achieved since the mid-1990s by sending numerous signals along a single fibre, each with a different wavelength.

Commercial versions of this technology, called dense wavelength-division multiplexing (DWDM; Fig. 1, overleaf), achieve data transmission rates as high as 1.6 terabits per second by combining 160 signals that each carry 10 gigabits per second (Gbit s^{-1}). These systems transmit signals at infrared wavelengths between 1.53 and 1.60 μm. Optical amplifiers, placed at intervals of 60 to 100 km, simultaneously amplify signals at many wavelengths, allowing them to propagate over thousands of kilometres. On page 1027 of this issue, Mitra and Stark[1] calculate the fundamental information capacity of typical optical fibres, which is ultimately

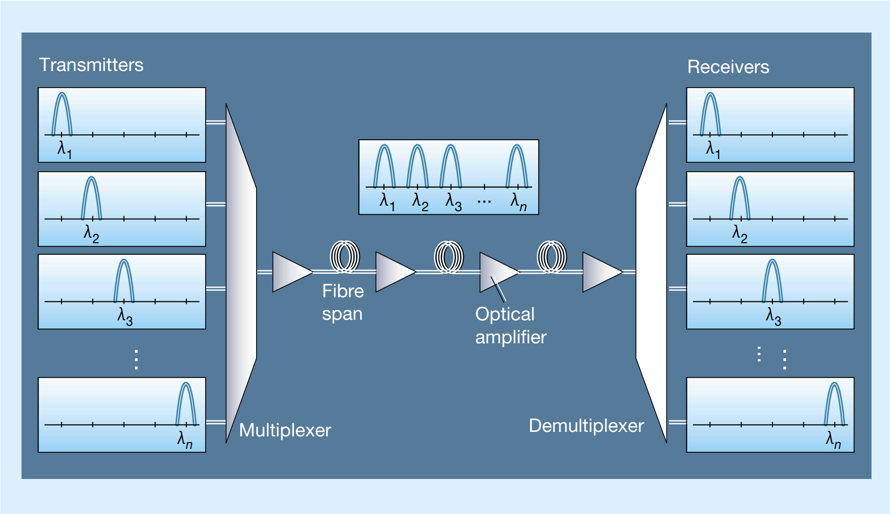

Figure 1 **Dense wavelength-division-multiplexed (DWDM) optical-fibre system. Optical signals can be transmitted over very long distances when lengths of fibre (fibre spans) are interspersed with optical amplifiers to boost the signal. The most common amplifiers are made of erbium-doped silica fibres, and provide gain for wavelengths between 1.53 and 1.60 μm. Newer technologies can provide amplification over the entire fibre bandwidth between 1.2 and 1.6 μm. Numerous optical signals at different wavelengths can be combined (by passing them through a multiplexer), transmitted along a common fibre, and separated at the receiving end (using a demultiplexer). The multiplexer and demultiplexer are special types of optical filters. Each signal conveys data at a bit rate R (in bit s^{-1}) and the spacing between adjacent signal wavelengths is $\delta\nu$ (in Hz). The spectral efficiency $R/\delta\nu$ (in bit s^{-1} Hz^{-1}) measures how efficiently bandwidth is used. Calculations by Mitra and Stark[1] show that fibre spectral efficiency is limited by the noise in the optical amplifiers, and ultimately by the nonlinear properties of the optical fibre.**

limited by optical-amplifier noise and by the nonlinear response of the fibre. The effect of the nonlinear response of optical fibres on information capacity has been difficult to evaluate, but Mitra and Stark have succeeded in estimating this fundamental limit.

The classic theory of information developed by Claude Shannon sets fundamental limits on the efficiency of communication[2]. According to Shannon, the capacity of a communications medium is the maximum bit rate that can be transmitted without error, taking into account noise, available bandwidth and limited power. When light is amplified, noise is inherently added, following the principles of quantum mechanics. In addition to amplifier noise, fibre nonlinearities contribute to signal distortion and noise in DWDM systems. Conventional optical fibres have a higher refractive index in their core than in their outer shell, allowing them to guide light by total internal reflection. Fibre materials exhibit a nonlinear response to strong electric fields, such as those of optical signals confined within the small core. Optical amplifiers maintain these fields at high intensities over long distances, and the nonlinear response of the fibre leads to signal distortion and noise.

Mitra and Stark argue that the information capacity of optical fibres in DWDM systems is limited most fundamentally by a nonlinear effect called cross-phase modulation (CPM), in which each signal in the fibre perturbs neighbouring signals. In current DWDM systems, optical waves are intensity modulated, which means that the intensity (instantaneous power) is varied to encode information — in much the same way that radio waves are amplitude modulated (AM) or frequency modulated (FM). In DWDM systems the full optical bandwidth is occupied by numerous signals at different wavelengths, each of which is modulated separately. The degradation associated with CPM arises because the modulated intensity of each signal perturbs the refractive index of the fibre, thereby distorting the other signals.

Mitra and Stark show that the impact of CPM on the capacity of optical fibres is strongly dependent on a nonlinear intensity scale, I_0, which is fixed for a particular DWDM system design. When the power transmitted at each signal wavelength is well below I_0, increasing the power increases the capacity. As the transmitted power approaches I_0, however, CPM effects increase rapidly, causing the capacity to drop precipitously. So for a given I_0 there is a transmitted power for which the capacity is maximized. The nonlinear intensity scale, I_0, and the maximum capacity increase with the bandwidth of each signal and the spacing between adjacent signals, and decrease with the total number of signals and the total number of amplifiers. Mitra and Stark express the capacity of a DWDM system in terms of 'spectral efficiency', which is the bit rate per signal divided by the channel

100 YEARS AGO

● I have just tested the inherited powers of swimming in newly hatched pheasants. I find that when placed in tepid water, at the age of about thirty hours, they swim easily with well-coordinated leg-movements and show very little signs of distress.

● Among the many useful publications issued annually by the Royal Observatory of Belgium we draw special attention to "*Ephémérides météorologiques et naturelles*"... The absolute maximum shade temperature was 95.4 °F and the minimum 4.4 °F. The average annual rainfall amounts to 28.56 inches and the mean number of rainy days is 190. The relative humidity at noon is fairly uniform.

● "*Sunny Days at Hastings and St. Leonards*" is the title of a well-illustrated and well-printed little handbook for south-east Sussex, by Messrs. W. H. Sanders and P. Row. There is a 'six-inch' map of Hastings and St Leonards, and another map, on the scale of an inch to four miles, of the country as far as Seaford, Tunbridge Wells and Ashford — all for the price of 6d.

From *Nature* 27 June 1901.

50 YEARS AGO

Polypeptide chains in certain synthetic polymers, in fibrous proteins of the keratin–myosin–fibrinogen group, and also in haemoglobin, appear to be coiled or folded to about half the length of a fully stretched chain. Many different chain configurations have been proposed to account for the X-ray diffraction data, the latest being those of Pauling, Corey and Branson. Until now, however, the lack of any simple and decisive criterion in the X-ray diffraction pattern has made it difficult to test the validity of proposed models. This communication describes a new reflexion, not hitherto observed, which is given by the proteins mentioned above. The spacing at which this reflexion appears excludes all models except the 3.7 residue helix of Pauling, Corey and Branson, with which it is in perfect concord.

This model has two types of repeat: (*a*) the distance between successive turns of the spiral (5.55 A.), and (*b*) the spacing along the chain of successive amino-acid residues (1.5 A.). Thus there are in this model 3.7 residues per turn... I have found a new reflexion from planes perpendicular to the fibre axis at a spacing of 1.50 A. which corresponds to the repeat of the amino-acid residues along the chain. M. F. Perutz

From *Nature* 30 June 1951.

spacing, and has units of bits per second per hertz (bit s^{-1} Hz^{-1}).

Reaching the spectral-efficiency limits calculated by Mitra and Stark requires coherent optical detection, which involves interfering the received signal with a reference signal at an identical or slightly different frequency. Current systems use a simpler method, which detects the intensity of the received optical signal. In the absence of amplifier noise and nonlinearities, capacities of optical fibres can be calculated rigorously for systems using intensity detection[3,4]. We don't know what the limits are for a nonlinear amplified DWDM system using intensity detection, but in the linear regime the maximum spectral efficiency of a DWDM system using intensity detection[5] is roughly 1 bit s^{-1} Hz^{-1} less than half that with coherent detection (for example, 2 and 1 bit s^{-1} Hz^{-1} compared with 6 and 4 bit s^{-1} Hz^{-1}, respectively).

Mitra and Stark[1] now show that for a typical nonlinear DWDM system, assuming coherent detection, the spectral efficiency limit exceeds 3 bit s^{-1} Hz^{-1}. For comparison, the next-generation commercial DWDM systems are expected to use 40 Gbit s^{-1} channels with 100-GHz spacing — equal to a spectral efficiency of only 0.4 bit s^{-1} Hz^{-1}. All current DWDM systems use 'on–off keying', a way of encoding bits by the presence or absence of light. Using a binary modulation technique such as on–off keying, spectral efficiency cannot exceed 1 bit s^{-1} Hz^{-1} (this limit is reduced to 0.67 bit s^{-1} Hz^{-1} by assuming more realistic system parameters). So a system approaching Mitra and Stark's spectral-efficiency limits would require a non-binary encoding technique, such as multilevel intensity or phase modulation.

When calculating the effects of CPM, Mitra and Stark have implicitly assumed a modulation technique involving time-varying intensity. It is already known that using a constant-intensity modulation technique, such as phase or frequency modulation, can eliminate CPM. The fibre's refractive index varies slightly with the wavelength of light, which tends to convert phase or frequency modulation to intensity modulation. This wavelength dispersion must be carefully compensated for to maintain constant intensity. If we follow the same calculations as Mitra and Stark, and constant intensity is maintained, then the spectral-efficiency limit should increase with transmitted power, in contrast with their results. In reality, as the power increases, spectral efficiency would eventually be limited by other nonlinear effects, such as four-wave mixing.

As Mitra and Stark point out, nonlinearities such as CPM can be cancelled out, in principle, by using a number of clever tricks[6,7]. Better optical fibres can also help — for example, hollow fibres with air cores have a reduced nonlinear response[8]. In ordinary optical fibres, light can propagate in two orthogonal polarizations — that is, with electric field lines along two perpendicular directions. A simple way to double spectral efficiency is to send two independent signals with these different polarizations and use polarization-resolved detection. Even without polarization-resolved detection, sending neighbouring signals with perpendicular polarizations is a well-known method to reduce nonlinearities.

Mitra and Stark's work is a useful step towards working out the limits to the spectral efficiency of optical fibres. Nonetheless, our understanding of the ultimate limits, and how to approach them in practice, will continue to evolve. ■

Joseph M. Kahn is in the Department of Electrical Engineering and Computer Sciences, University of California, Berkeley, California 94720, USA.
Keang-Po Ho is in the Department of Information Engineering, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong.
e-mails: jmk@eecs.berkeley.edu
kpho@ie.cuhk.edu.hk

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Immunology

T cells and tumours

Drew Pardoll

The immune system's response to new tumours is complicated but seems to depend on where and when tumours develop. This will have to be much better understood to enlist a patient's immune defences in fighting cancer.

Does the immune system see tumours more as 'self' or as 'foreign'? The answer is complex, as is plain from papers published here in April[1] and on page 1058 of this issue[2]. They show that the immune response probably depends on the location and properties of tumour cells early in their development.

Quantum engineering

Catch the atom

Two groups have independently succeeded in confining single atoms in microscopic traps (N. Schlosser *et al.*, *Nature* **411,** 1024–1027; 2001, and S. Kuhr *et al.*, *Science*, 14 June 2001, 10.1126/science.1062725). This feat opens the way to designing experiments in which various quantum-mechanical effects can be exploited. Several techniques already exist to manipulate individual particles, such as photons and ions, but it has been notoriously difficult to pin down neutral atoms.

The two groups developed methods to attract cooled-down atoms towards spots of high electric-field intensity in traps formed by laser beams. Schlosser *et al.* find that the individual rubidium atoms entering their traps scatter enough photons to image them with a CCD camera. The images show that the traps are occupied by either no atoms or just one at a time. Moreover, once an atom is caught, it can be kept trapped for up to 2 seconds — a veritable lifetime in quantum mechanics.

Kuhr *et al.* exerted their control over chilled caesium atoms and designed traps that can catch any desired small number of atoms. Intriguingly, they also found that these atoms can be catapulted into free flight from the trap, raising prospects of an 'atom on demand' delivery service.

As a final flourish, Schlosser *et al.* have positioned two traps, each containing a single atom, close to each other as shown here in the CCD image. In this set-up, the internal states of the two atoms can be intimately related to each other, or 'entangled'. Such entangled states can be used as logic elements for efficient computation tasks. **Liesbeth Venema**