stereotypic response — the behavioural correlates of fear. After one or several pairings, a robust memory of the CS–US relationship is formed. So the CS alone can elicit the full behavioural repertoire that was previously produced only by the US. Conditioning is thought to require changes in the pathway that mediates the CS, due to the convergence of inputs from the US (ref. 7).

The lateral amygdala (LA) is thought to be the critical structure in which information from the CS and US converge (Fig. 1)[8]. Because the CS is a simple sensory stimulus, the afferents that carry the CS information into the LA can be defined. This connection between the auditory thalamus and LA can express LTP (ref. 9) which, when induced with electrical stimulation, causes an increase in the response of the LA to auditory stimulation[10]. The processing of natural stimuli can, therefore, use the mechanisms set up by artificially induced LTP.

But does LTP occur at thalamo-LA synapses during fear conditioning? To address this, Rogan *et al.*[2] monitored the extracellular potential in the LA, in response to the CS tones while a rat was trained. As the CS and US were paired, and the animal learned to respond to the CS with a behavioural correlate of fear, the response in the LA to the CS alone grew, and remained at a high level. Further presentations of the CS alone extinguished the behavioural response (that is, the memory), and the auditory-evoked potential returned to baseline. Importantly, when the CS and US were unpaired — so no learning occurred — there was no significant growth in the auditory-evoked potential.

These data compellingly show that there was a change in the pathway which processes the CS as the animals learned to associate the CS and US. Enhancement of the auditory-evoked LA response was identical to that elicited by electrical induction of LTP in the thalamo-LA path[10]. So the authors propose that the critical change occurred at the synapses in the LA. However, changes in other auditory processing stations, or in the intrinsic electrical properties of LA neurons, may have caused the behaviourally induced changes. Furthermore, the increase in the auditory-evoked response was not shown to be specific for the CS, as opposed to reflecting some general increase in LA responsiveness.

By preparing *in vitro* slices of the LA from fear-conditioned rats, McKernan and Shinnick-Gallagher[3] examined the synaptic responses of LA neurons to stimulation of afferents from the auditory thalamus. These responses were consistently larger than those recorded from LA slices prepared from control animals that had undergone unpaired CS–US training. Furthermore, the synaptic responses of LA neurons to an independent input that was not involved in fear conditioning remained unaltered. The compelling conclusion is that fear conditioning caused an increase in synaptic efficacy (for example, LTP), specifically at the synapses that process the CS. The authors also suggest that this behaviourally induced increase in synaptic strength may be due, at least in part, to presynaptic modifications, because it was accompanied by a change in one form of short-term presynaptic plasticity.

Is the LTP–memory connection — at least for one form of learning — now established enough to silence the sceptics? Rogan *et al.*[2] point out several features common to fear conditioning and hippocampal LTP, including their dependence on NMDA (*N*-methyl-D-aspartate) receptors[11,12]. Nevertheless, it remains to be shown that the mechanisms responsible for the behaviourally induced synaptic changes are the same as those underlying electrically induced LTP. But the new reports[2,3] indicate that attempts to study LTP have not simply been an intellectual exercise, and that progress continues towards a comprehensive understanding of the mechanisms that underlie learning and memory. □

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Genome sequencing

New tricks of tick-borne pathogen

Alan G. Barbour and Wolfram R. Zückert

Lyme disease is the most common vector-borne disease in Europe, the United States and parts of Asia[1,2]. In North America, the infection is transmitted by deer ticks between small mammals or, inadvertently, to people (Fig. 1). Like HIV and other emerging infections of the late twentieth century, the aetiologic agent — *Borrelia burgdorferi* — was unknown to the last generation of microbiologists and physicians. Now, before we are even close to understanding the pathogenesis of Lyme disease, Fraser *et al.*[3] report the near-complete sequence of the *B. burgdorferi* genome on page 580 of this issue. These findings are a first in several respects: this is the first genome from the eubacterial phylum of spirochaetes, with their peculiar morphology, physiology and behaviour; it is the first genome of a parasite that infects both invertebrates and vertebrates; and it is the first genome of a prokaryote with several genetic elements, most of which are linear.

But those who were expecting to find in *B. burgdorferi* a rich vein of gold in which to mine virulence determinants have to be disappointed. The sequence is as notable for what it does not contain as for what it does. Instead of finding many orthologues[4] of toxin and invasion genes, global regulatory systems, two-component signal-transduction pathways and bacteriophages of other pathogenic bacteria, the authors found an almost bewildering array of duplicated lipoprotein genes, unique to *Borrelia* spp. and of unknown function. These genes are located on extrachromosomal stretches of

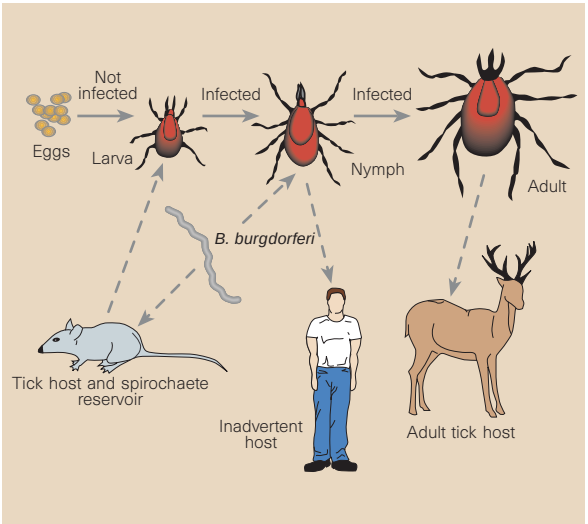

Figure 1 **Life cycle of *Ixodes* tick vectors of *Borrelia burgdorferi*, the spirochaete agent of Lyme disease that has now been sequenced by Fraser *et al.*[3]. Small rodents, such as mice, are reservoirs for *B. burgdorferi*. The tick becomes infected from feeding on a mouse and remains infected as it changes to nymph and then adult. The spirochaetes are transmitted by infected nymphs to other mice and to humans, which are inadvertent hosts. Deer are important hosts for adult ticks, but are not effective reservoirs for *B. burgdorferi*.**

DNA called plasmids. One of the lipoproteins, OspA, has already been crystallized and structurally characterized[5], and it is undergoing human field trials as a vaccine against Lyme disease, although no one yet knows what it does.

Discovery of the linear chromosome in *Borrelia*[6,7] challenged ideas of what a bacterial chromosome is. The findings of Fraser *et al.*[3] now provide further evidence that the distinction between a plasmid and chromosome is primarily a matter of size. The linear and circular plasmids of *Borrelia* spp. are equimolar with chromosomes[8,9], they contain genes that are usually found on chromosomes (for example, *guaA* and $tRNA^{Gly}$), and they have apparently undergone recombination with the chromosome. These elements could equally be examples of minichromosomes as of plasmids, and they seem to provide an opportunity and place for the organism to duplicate genes and rearrange them without much cost or damage. Moreover, by possessing several copies of highly similar genes on the same (and different) elements, there is the potential for diverse antigenic variation — and this has been observed in relapsing fever *Borrelia* spp.[10].

Determination of the *B. burgdorferi* genome has opened doors for investigation and closed just as many. By understanding the biosynthetic and transport limitations of *B. burgdorferi*, we may be able to develop a medium in which to grow as-yet uncultivable *Borrelia* spp. The results encourage study of a more metabolically competent spirochaete, such as the free-living *Spirochaeta aurantia*, for a better understanding of how this ancient group of bacteria evolved, and to identify catalytic molecules of industrial importance. But the sequence does not explain the persistence of the disease in some people yet not in others; the differential expression of surface proteins in the tick and in the mammal; or migration of the spirochaetes from the midgut to the salivary gland of the tick, or from the skin to the brain of the mammal. These explanations will require taking the hints (and primers) from the genome and returning to animal models and the clinics. □

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Stellar astronomy

Clocks within the hourglass

Mario Livio

Rarely in astronomy can a stellar cataclysm be predicted in advance. It is also rare that an extremely well-studied object suddenly reveals a previously undetected periodicity. But both of these things are true for one of the most famous stars in the sky, the luminous blue variable Eta Carinae. On page 587 of this issue[1], Corcoran *et al.* report the discovery of small-scale X-ray outbursts from this source, which repeat every 85 days, superimposed on an overall increase in the mean X-ray flux, which may herald a dramatic 'event' in January.

Luminous blue variables (LBVs) represent a short-lived phase in the evolution of massive stars, during which the star occasionally erupts, changing markedly in its brightness and spectrum. The variations typically fall into three categories: 'micro' variations, up to a few tenths of a magnitude (one magnitude is a factor of about 2.5) on timescales of weeks to months; minor eruptions (increases in brightness by about one magnitude on timescales of years); and giant outbursts (increases by more than three magnitudes, with durations of decades[2]). LBVs may be an evolutionary stage between massive 'O-type' stars that are still burning hydrogen in their cores, and Wolf–Rayet stars, which have run out of hydrogen and must burn helium instead.

Eta Carinae is the most famous and the most spectacular LBV. But despite many observations, covering almost all wave bands, its exact nature remains a mystery. In particular, no satisfactory explanation exists for its huge outburst in the first half of the last century. (Some of the more promising mechanisms involve the action of strong radiation pressure on layers with high opacity.) That eruption resulted in the ejection of an hourglass-shaped bipolar nebula, now called the Homunculus[3] (Fig. 1, overleaf).

A remarkable recent discovery about Eta Carinae is a probable 5.5-year periodicity in its spectrum[4,5]. The discovery of a periodicity often leads to a detailed dynamical model of a system; and in the case of Eta Carinae, the 5.5-year period could either be the orbital period of a highly eccentric binary, or a timescale associated with the stability of a single star[6,7]. The local thermal timescale of some part of

100 YEARS AGO

Astronomy is, perhaps, among all physical sciences the one destined by its historical tradition, no less than by its present and future necessities, to second – nay, to promote and develop – the cosmopolitan tendency. The grand spectacle of the face of the heavens, ever before the eyes of all; the difference of phenomena according to the horizons, which carries with it the need of co-operation between the observers diversely situated with regard to the celestial sphere; in fine, the high and significant moral education that comes to astronomers from the continual contrast between the immensity of the heavens and the miserable narrowness of the limits traced out conventionally on the globe between one country and another; here are the causes through which a spirit superior to any narrow nationalism was soon breathed into our souls. Tycho Brahe, the proud Danish patrician, the founder of practical astronomy in the Renaissance, sings sternly –

Omne solum forti patria est, coelumque
Undique supra….

And his name, with those of Copernicus, Kepler, Galileo and Newton, form a constellation that shines not more for the sky of Denmark, than for that of Germany, Italy, or England!

From *Nature* 9 December 1897.

50 YEARS AGO

"Coconut Conference" – Because of the present world shortage of vegetable oils and fats, and the fact that the situation is one which will take years to remedy, particular interest is attached to oil-producing crops, their cultivation, conservation, potentialities and use. During this summer the Coconut Conference (Colombo, July 4, 1947) covered much useful ground, papers, chiefly of a directly practical nature, being devoted to the regeneration of plantations, the use of manures, the value of combining animal husbandry with coconut cultivation, problems of soil conservation, the control of insect pests, and problems of co-operation and marketing of coconut products. This report will undoubtedly prove of interest and value to scientific workers and members of the planting community in other tropical regions where the coconut is an important crop.

From *Nature* 13 December 1947.