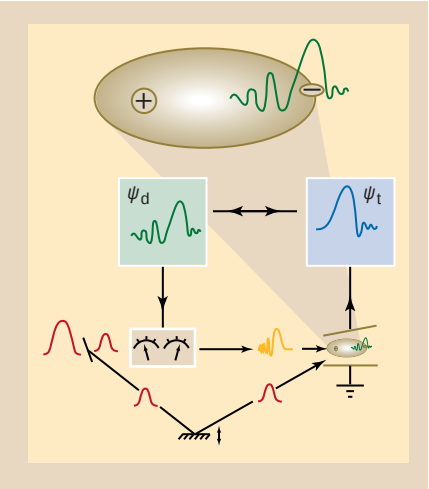

Figure 1 **Sculpting an electronic wavefunction in an atom as described by Weinacht *et al.*[4]. The goal is to prepare the electron in a caesium atom (detail; top) in a desired wavefunction ψ_d (green). For this purpose they use two laser pulses (red and yellow) to first prepare a trial wavefunction ψ_t (blue) then reconstruct it and compare it to the desired state ψ_d. When the two differ they adjust the parameters of the preparation device (box with dials) and prepare a new trial state. The iteration of this cycle of preparation, readout and comparison leads to the desired wavefunction.**

tion of the object wavefunction in amplitude *and* phase from the measured data.

However, before we can make a measurement of a quantum state we have to prepare that state. In the case of the caesium atom this job was done by the first object pulse. Can we prepare any desired state, that is, a target state? This is an issue that arises in many disciplines — ranging from physical chemistry, through atomic physics, to quantum optics — and many ways of tackling it have been suggested[3]. In the technique known as coherent control[8], one tries to find the appropriate sequence of laser pulses needed to break a specific chemical bond, and in quantum state engineering one attempts to prepare quantum states of the radiation field or vibrational modes of an ion in a trap. Both approaches are central to recent proposals for quantum computers[9].

How can we prepare a prescribed wavepacket of an electron orbiting the nucleus? The tools are short laser pulses. We therefore have to find the right shape and sequence of laser pulses to steer the quantum state to the target state. Usually the Schrödinger equation is used to calculate the quantum state that results after applying a sequence of laser pulses. However, in the case of coherent control, we concentrate on the inverse problem: we start from the target state and a rather simple initial state, and try to find the laser pulses that would lead to the desired state.

In their latest work, however, Weinacht *et al.*[4] pursue a different approach and combine quantum state preparation and measurement with feedback. The first laser pulse (yellow in Fig. 1) prepares a trial wavefunction, ψ_t (blue), and with the help of the second reference pulse (red) they reconstruct the trial state. The authors compare the reconstructed trial wavefunction ψ_t to the desired wavefunction ψ_d (green). When the two wavefunctions do not agree they readjust the dials on the pulse shaper so as to create a more appropriate laser pulse. This process is repeated until the desired wavefunction ψ_d emerges — usually within two cycles of the feedback loop.

The sculpting of wavepackets described by Weinacht *et al.*[4], and the coherent control of electrons in a solid-state quantum well[10] reported last year, are two impressive examples showing that the field of quantum control has entered a new era. It has broadened out beyond chemical reactivity and now allows encoding and decoding information on wavepackets. Moreover, the Weinacht procedure shows that it is possible to address and control individual quantum units. This feature is crucial for the implementation of various suggestions for quantum computation and coherent information processing and transfer. The long-held dream of coherent control and quantum state engineering has become reality. □

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Stress responses

Translational control perks up

Robert H. Silverman and Bryan R. G. Williams

The ability to respond to a variety of threats — from nutrient deprivation and viruses to chemical insults — is an essential property of cells. But how did primitive organisms survive these challenges, enabling them to evolve into complex animals? Stress responses are often linked to protein synthesis and folding which, in the budding yeast *Saccharomyces cerevisiae*, are controlled by two different kinds of gene, *GCN2* and *Ire1*. On page 271 of this issue, Harding *et al.*[1] describe a newly discovered mammalian gene with features from both of these yeast genes.

In yeast, amino-acid starvation is sensed by the GCN2 protein, which phosphorylates a conserved serine residue on the α-subunit of the eukaryotic initiation factor-2 (eIF2α)[2]. Phosphorylation of eIF2α suppresses translation from short upstream open reading frames within the messenger RNA for GCN4. The result is increased translation of GCN4, which activates transcription of the enzymes that synthesize amino acids.

Unfolded proteins in the yeast endoplasmic reticulum (ER) are sensed by Ire1, which is both a protein kinase and an endoribonuclease — an enzyme that cuts RNA molecules at internal sites[3,4]. When unfolded proteins accumulate in the ER, Ire1 probably self-associates (oligomerizes) in the ER membrane, phosphorylates itself, then cuts an intron out of the precursor mRNA for a transcription factor, HAC1. After splicing and translation, the HAC1 protein induces the transcription of several genes for proteins in the ER that mediate protein folding and modification.

GCN2 and Ire1 both need to be able to recognize RNA and phosphorylate other proteins. Compelling evidence from sequence analysis, backed up by experiment, indicates that during evolution the functional segments of the corresponding genes have been shuffled, allowing animals to cope with many different types of stress. In other words, GCN2 and Ire1 have evolved into a diverse family of mammalian stress-response proteins (Fig. 1).

Harding *et al.*[1] and Shi *et al.*[5] have now cloned the gene for the newest player among these stress-response proteins, PERK (RNA-dependent protein kinase (PKR)-like ER kinase; also known as PEK, pancreatic eIF-2α kinase). PERK combines functional properties of both GCN2 and Ire1, and it has sequence similarity to two mammalian homologues of these proteins, PKR and Ire1β, respectively (Fig. 1). The domain related to Ire1β is believed to detect unfolded proteins, whereas the PKR-related sequence encodes a protein kinase that can regulate protein synthesis. The amino-terminal, Ire1-related portion probably resides within the lumen of the ER, with the kinase domain in the cytoplasm. When cells are subjected to stress — such as unfolded proteins in the ER — eIF2α is phosphorylated leading to a suppression of global protein synthesis, preserving energy and nutrients[6]. Harding *et al.* suggest that PERK, which is activated

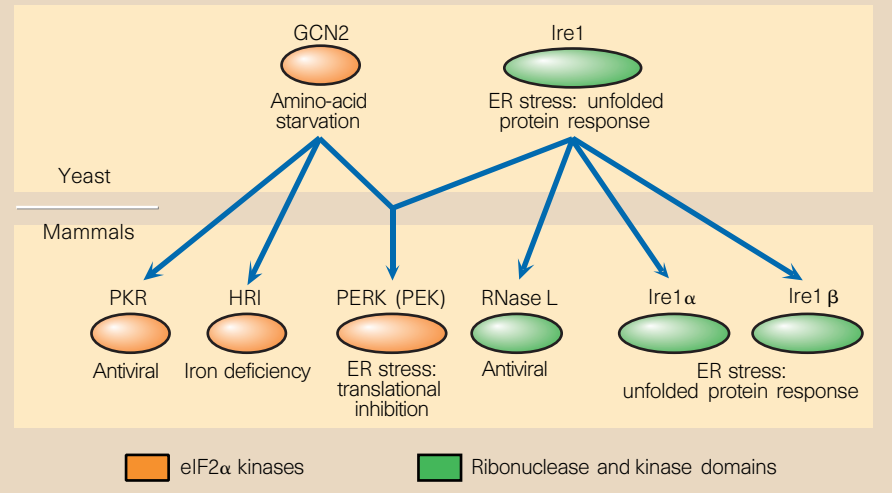

Figure 1 **Relationship of yeast and mammalian stress-response proteins. The eukaryotic initiation factor (eIF2α) kinase family originated with the yeast kinase GCN2, and shares homology with the mammalian RNA-dependent protein kinase (PKR), haem-regulated inhibitor (HRI), and the PKR-like ER kinase (PERK) cloned by Harding *et al.*[1] and Shi *et al.*[5]. Yeast Ire1 — both a kinase and an endoribonuclease — has homology with PERK, RNase L and the mammalian Ire1α and β. So PERK has features of both GCN2 and Ire1, and is a missing link in the pathways.**

during ER stress, is the protein most likely to be responsible for these effects.

Phosphorylation of eIF2α is a key point in the regulation of protein synthesis in mammalian cells. Two kinases known to phosphorylate eIF2α are PKR and the haem-regulated inhibitor (HRI) of erythroid cells[2,7]. With GCN2, these proteins form a small family of eIF2α kinases that contain a conserved eIF2α recognition motif, amino-terminal to the kinase subdomain V. They can all regulate the phosphorylation of eIF2α in yeast[2,7], a feature that Shi *et al.*[5] also attribute to the ER stress-response kinase, PERK. Some of the effects of PKR mutants are probably due to inhibition of PERK. For example, although the ER stress response is normal in fibroblasts that lack PKR[1], a *trans*-dominant PKR mutant in wild-type cells interferes with phosphorylation of eIF2α in response to ER stress[6]. Moreover, the transforming activity of PKR mutants[8] could implicate PERK in maintaining normal cellular homeostasis. Other properties of PKR may also apply to PERK. For example, PKR is targeted for inhibition by some viral proteins, allowing viruses to escape the antiviral effects of interferon[8]. The vaccinia virus *K3L* gene product contains regions of homology to eIF2α, allowing it to inhibit PKR by mimicking its substrate — this should also inhibit the activity of PERK.

PERK lacks the conserved ribonuclease domain that is essential in yeast Ire1 and in three mammalian proteins, Ire1α[9], Ire1β[10] and RNase L[11,12]. Ire1α and Ire1β are probably sensors and upstream effectors of the unfolded protein response. Why are there two Ire1 proteins in mammalian cells yet only one in yeast? It has been suggested that Ire1α and Ire1β might cleave at separate 5′ and 3′ splice sites in the RNA substrate, unlike the yeast Ire1 which excises an intron from HAC1 pre-mRNA by cleaving at both sites[3,9]. RNase L does an entirely different job. Type I interferons induce a family of proteins known as the 2′, 5′-oligo A synthetases. When stimulated by double-stranded viral RNA, these proteins produce short, 2′, 5′-oligoadenylates from ATP, which bind to inactive, monomeric RNase L, causing it to dimerize into its catalytically active form. The active RNase L digests single-stranded RNA, and RNA decay in interferon-treated cells attenuates viral replication[8].

Although activation of Ire1 and RNase L is driven by unfolded proteins and 2′, 5′-oligo A, respectively, both proteins oligomerize during activation. A functional link between RNase L, PKR and Ire1β is that they are involved in mediating apoptosis induced by a variety of stimuli[8,10]. Perhaps PERK may also be involved in apoptosis. Curiously, RNase L also has protein-kinase homology although, unlike Ire1, it lacks residues important for kinase function. Moreover, the amino-terminal regulatory regions of RNase L and Ire1 are unrelated, with ankyrin repeats and P-loop motifs in the 2′, 5′ oligo-A-binding domain of RNase L[11], and intralumenal and transmembrane domains in Ire1. Also, although the Ire1 proteins are highly specific RNases, RNase L has a broader specificity for UU and UA[8].

By connecting two protein families involving eIF2α kinase and ribonuclease activities, PERK stands as a kind of missing link in the evolution of stress-response proteins. The physiological roles of the mammalian stress-response proteins, and possible cross talk among them provide an exciting area for future study. □

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100 YEARS AGO

The performances of the submarine vessel, *Gustave Zédé*, appear to have given much satisfaction to naval experts on the other side of the Channel, though our own engineering papers are by no means impressed by the experiments. We learn from the *Times* that the semi-official *Moniteur de la Flotte*, commenting upon the trials of the *Gustave Zédé*, says that at length, after twelve years of continued efforts, the problem has been solved. The *Gustave Zédé*, unassisted, has steamed from Toulon to the Salins d'Hyéres and to Marseilles ... and has successfully discharged her missiles at the mark. On the surface she is almost invisible, and presents a target scarcely capable of being hit; below water her presence is revealed neither by the noise of her engine nor any movement of the surface. The objection raised against the submarine boat that she is blind loses force, since the *Gustave Zédé* makes momentary appearances on the surface to redirect her course, while she has a telescopic tube, with an arrangement of prisms and mirrors, utilising the principle of the *camera obscura*, which permits the surroundings to be surveyed, though imperfectly, in case of emergency. The *Gustave Zédé* has restricted range, owing to the great weight of the electric accumulators; but the new boats of the Naval class will have auxiliary steam for surface navigation.

From Nature 19 January 1899.

50 YEARS AGO

Under the title "The Value of the Individual", Mr. F. I. G. Rawlins, in Occasional Paper No. 5 of the British Social Hygiene Council, asks physicists to look beyond their immediate pre-occupations. Physical science, he argues, arrives at a point where it can go further; but this does not justify the assumption that there is nowhere further to go. Modern physical theory cannot (with Laplace) postulate a universe which is a self-maintaining system, about the origins or destiny of which it is superfluous to inquire. The step from physics to theology is not compulsory; but there is nothing to prevent it and a good deal to encourage it. Only when that step is taken can the universe be seen as an environment with a meaning, where human personality is able to realize itself.

From *Nature* 22 January 1949.

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Animal behaviour

Monkey business in the aquarium

Rory Howlett

Occasionally, long-lost works come to light to the delight of scholars and laypersons alike — a sketch by Rembrandt, a Shakespeare sonnet or an early recording by the Beatles. So it is with the publication in *Evolution and Cognition* of a paper based on a manuscript drafted in February 1979 by Konrad Lorenz. The paper (K. Lorenz, K. Okawa & K. Kotrschal *Evol. Cogn.* **4,** 108–135; 1998) has been completed by translator Kurt Kotrschal and Keiko Okawa, a former student of Lorenz who has also provided additional results.

Along with Karl von Frisch and Nikolaas Tinbergen, Lorenz was a co-recipient of the 1973 Nobel Prize in Physiology or Medicine for their discoveries concerning "organization and elicitation of individual and social behaviour patterns". At the time of his death in 1989, Lorenz had plans to write a book about "the biology, notably ethology of perciform fish", on the basis of long-term observations of coral-reef fish. Observations on the competitive interactions within reef fish species had featured large in Lorenz's classic text *On Aggression* (Harcourt Brace, 1963).

Many marine fish, including those that inhabit coral reefs, have larvae that are essentially planktonic, living at the mercy of ocean currents. A crucial stage is when they come out of the planktonic phase and settle on the reef. This recruitment phase is characterized by profound changes in morphology, behaviour and colouring. Lorenz was most struck by the vivid coloration of reef fish, and proposed that these colour patterns act as signalling 'posters' in the acquisition and defence of a territory. Others argued that the patterns might be involved in species recognition and mate choice, or defence against predators, either by way of camouflage or as warning signals.

Perhaps more than any other ethologist of his time, Lorenz recognized that to distinguish between these competing hypotheses, and to understand fully the social development of reef fish, detailed behavioural observation as well as experiment was required. In 1967, he spent some time in Hawaii making further notes on the behaviour of reef fish, but evidently realized that what was needed was a large marine aquarium where the fish could be observed at leisure, and in which interactions between the fish could be experimentally manipulated.

The opportunity came in the mid-1970s, when Lorenz used money from his Nobel prize to construct a large reef tank at his home in Altenberg, Austria. This was no typical living-room tropical aquarium, but a giant $4 \times 4 \times 2$-metre observation tank containing 32,000 litres of circulating sea water. The tank was stocked with the young of the Indo-Pacific coral-reef fish *Zanclus cornutus*, shown in the picture here, known as the Moorish idol or the *kihikihi* in Hawaiian. The first batch of fish did not prosper, but a second attempt to stock the tank was successful and between April 1976 and July 1978 Lorenz spent at least 1,000 hours observing the fish.

In the wild, newly recruited Moorish idols are territorial, defending their patch of reef. Later, individual territoriality breaks down and schools of more mature fish will often roam a common territory. Similar changes in behaviour occurred in the aquarium. When first introduced to the tank, the fish partitioned the available space into individual territories at the bottom and walls of the tank. During the following months, neighbouring fish fused their territories and defended them against outsiders, and with time further fusing of territories occurred. By 1978, two cohort groups, composed of fish aged five and six years respectively, roamed the entire tank keeping out of each other's way. Subsequent introductions were attacked, often fatally, but sometimes they managed to integrate into a new group; such interlopers occasionally sparked aggressive interactions between existing group members. Under natural conditions, such mechanisms might modulate group size to provide an optimal balance between warding off predators and competition for food, mates and so on.

The initial breakdown of individual territoriality fascinated Lorenz. During this period individuals seem to change the way in which they respond to 'poster colour' stimuli, depending on the ecological context and the motivational state of the fish. In the aquarium, at least, the character of the 'dyadic' relationships between pairs of fish provided evidence of individual recognition. Initially the interactions between fiercely territorial fish were aggressive. During the transition from strict territoriality to sociality, however, the dyadic relationships were characterized by a suite of ritualized behaviours apparently aimed at appeasement. These included parallel 'side-by-side' grazing along territorial borders, pseudospawning at the bottom of the tank, and eel-like swimming.

Complex appeasement behaviours are usually associated with highly social animals with well-developed cognitive abilities, such as primates. Lorenz's findings demonstrated the potential for complex sociality in the Moorish idol, and similar behaviours are now known to occur in other coral fish, butterfly fish, for instance. In their commentary, Kotrschal and Okawa liken the dynamic social structure of the Moorish idol to the 'fission–fusion' social behaviour of chimpanzees, which is characterized by dominance hierarchies and shifting coalitions of individuals. But whether the Moorish idols similarly ape primate social organization in the wild remains to be established. □

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