was sufficient for recognition of HLA-E by NK cells. So, besides the presence of anchor residues for binding to HLA-E, unique features in HLA class I signal sequences must determine proper cleavage, transport and trimming for loading onto HLA-E. The capacity of HLA class I signal sequences to hold this amount of information sets a fascinating precedent for a similar regulation of cellular functions by signal sequences of other proteins. □

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Chemical dynamics

Noisy waves

Frank Moss

Random fluctuation, or noise, is familiar from communication, where a single parameter such as voltage varies with time. Usually it is a nuisance, but sometimes, because of the peculiar phenomenon known as stochastic resonance, it is a boon. Noise is also present in many extended natural phenomena: a number of interacting elements might be spread over a two-dimensional surface, each subject to local noise. Certainly we expect the noise to affect the dynamics of such a system — perhaps to a large degree — but are there systems in which the noise can increase some collective, or coherent, dynamical property? If a certain degree of noise were to maximally increase such a property, the process would be called spatiotemporal stochastic resonance (STSR). As Sándor Kádár, Jichang Wang and Ken Showalter report on page 770 of this issue[1], STSR has now been achieved experimentally for the first time — an achievement that may have implications for the workings of the brain.

The Belousov–Zhabotinsky reaction is a self-sustaining reaction–diffusion system, in which straight or spiral waves of activity can propagate in a thin film. Using a photosensitive version of the reaction, Showalter and colleagues applied spatiotemporal noise as part of a two-dimensional optical image. The image is of a rectangular region, divided into a large number of square subregions or cells, and the intensity of the light falling on a given cell determines its state of excitability by controlling the rate of photoproduction of Br^- ions (which are inhibitors of autocatalysis in this reaction). A high light intensity keeps the region below the threshold of excitability, with the result that disturbances are rapidly quenched. Conversely, with little or no light, disturbances grow into waves that propagate indefinitely[2].

The average light intensity for all cells was adjusted to maintain the entire region in the subexcitable state, so that indefinitely sustained waves were impossible. To this average, time-dependent noise was added. Waves propagating into the region from an external source lived longer, and so propagated further, in the presence of this spatially distributed, time varying noise. An optimal noise intensity resulted in sustained waves. Adding still more noise worsened wave propagation and broke up the waves into segments of random lengths. Spiral waves could also be induced (Fig. 1a).

The authors define a signal strength for the propagating waves: the ratio of the length of coherent wave segments as they pass a certain point in space relative to their lengths on entering the subexcitable region. The signal strength passed through a maximum as the noise intensity passed through the optimum value — the signature of stochastic resonance[3,4].

These results are successfully simulated using a modified 'Oregonator' model[5], so

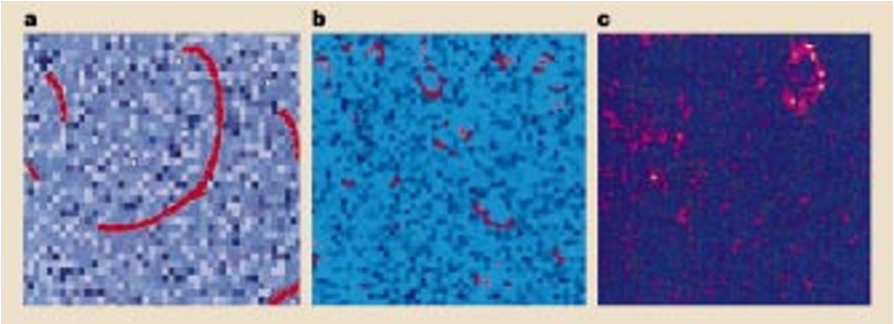

Figure 1 **Noise-mediated spiral waves. Waves excited by noise;** a, **in the Belousov–Zhabotinsky chemical reaction;** b, **the 'Oregonator' numerical model; and** c, **a cultured network of brain tissue (astrocyte syncytia).**

100 YEARS AGO

We have received further correspondence relating to the two Societies in Lincolnshire, to which reference was made in our issues of December 30 and February 3. It appears that the older Society, the Lincolnshire Naturalists' Union, does not regard with unmixed friendliness the newer and possibly more vigorous Science Society. Into this unfortunate conflict of interests it is not our province to enter, and we can only repeat with renewed emphasis that it is a serious mistake to allow the spirit of rivalry to enter into the matter at all. The welfare of both Societies can only suffer, and the progress of science in the county can only be retarded by friction. The Lincolnshire Science Society explains its origin by accusing the Union of failing to carry out the objects for which it was founded. There may or may not be truth in the accusation, but we are bound to admit that evidence of scientific activity on the part of the Union has not been obtainable. We cannot find the latter body among the corresponding societies of the British Association; neither can we learn that any publication has been issued under its auspices.... We can only hope that Lincolnshire will not present to the scientific world a divided front on a question in which both parties are really striving for the same end.

From *Nature* 17 February 1898.

50 YEARS AGO

On November 12, 1947, it came my way to spend, alone, a couple of hours in the evening with the late Prof. [Alfred North] Whitehead, and Mrs. Whitehead, in their apartment within a stone's throw of the centre of Harvard. It seems likely, therefore, that I was the last person from Britain to see the great man before he died. We talked of Trinity ("Such a good place", he whispered) and its 'characters', of whom he spoke affectionately, coupled with an occasional sly dig, as entrancing as it was kindly. He was devoted to the country of his adoption: a remark stands out in my memory – "The Americans have a streak of tenderness, yes, how valuable that is these days". Many people have used gracious words about our trans-Atlantic cousins, but it was left to him to state their noblest trait, and the one holding out hope for the world.

From *Nature* 21 February 1948.

named after the place of its invention in Eugene, Oregon. The model is a set of three partial differential equations that describe the reaction–diffusion process. Showalter and colleagues added a term to account for the photosensitive generation of bromide ions, and predict wave propagation patterns remarkably similar to those observed in the experiment. Before this experiment, STSR had been studied only theoretically or by numerical or electronic simulation in one-dimensional sets of coupled[6,7] and uncoupled[8] elements, and in two-dimensional arrays of threshold elements[9]. But those 2D simulations, in spite of their simplicity, mimic all the features of the present experiment.

The implications of the present experiment extend far beyond chemical dynamics. Spiral waves, spontaneously generated by noise, have also been simulated with the Oregonator (Fig. 1b). They are strikingly similar to recent observations of noise-initiated and sustained long-range coherent waves of calcium ions in cultured brain tissue[10] (Fig. 1c) indicating a similar underlying dynamical process. The possibility that calcium waves transmit or coordinate information over centimetre distances in glial cell networks (that is, in the brain) has already been suggested, but the role of noise remained obscure. Now that noise-sustained spiral waves have been observed in a well characterized chemical system, we can speculate that spatiotemporal noise may be an important feature of the brain's working. □

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Functional genomics

Double-stranded RNA poses puzzle

Richard W. Wagner and Lin Sun

The human genome is predicted to contain between 50,000 and 100,000 genes[1]. To work out what these genes do, an array of techniques is needed to evaluate the protein–protein interactions and biochemical pathways of any gene product. The nematode worm *Caenorhabditis elegans* is an excellent system for such studies because of its well-understood genetics and development, evolutionary conservation to human genes, small genome size and relatively short life cycle. The 100-megabase-pair genome will be completely sequenced this year, and a total of 17,000 genes have been predicted, many with human counterparts. Approaches used to manipulate gene expression in *C. elegans* include transposon-mediated deletion[2], antisense inhibition[3] and direct isolation of deletions after mutagenesis[4,5]. Although these methods have proved useful, limitations still exist.

On page 806 of this issue, Fire and colleagues[6] describe a remarkable and surprising technique for inhibiting gene function in *C. elegans*. They turned off a specific gene in progeny worms by microinjecting double-stranded RNA (dsRNA) complementary to the coding region of the gene into the gonads of adult animals. Using a well-characterized gene, *unc-22*, which encodes a non-essential myofilament protein, they showed that injection of dsRNA produced a phenotype characteristic of *unc-22* inhibition — twitching.

In a series of well-controlled studies, the authors also found that injection of dsRNA targeted to a reporter gene for green fluorescent protein resulted in a dramatic — and specific — decrease in protein production. Furthermore, when they injected dsRNA targeted to another gene, *mex-3*, the result was a loss of *mex-3* RNA in early-stage embryos. In other words, at the levels of phenotype, RNA and protein, the interference with gene expression was specific and reproducible.

Perhaps most astounding is the phenomenon that the dsRNA causes gene inhibition. Previously[3], Fire and co-workers had been puzzled by the fact that antisense RNA alone — which is often used to inactivate sense messenger RNA — was only marginally effective. Furthermore, results using the antisense RNA were mimicked by injection of sense RNA, a control in their studies. They later found out that these data could be largely explained by an artefact of the transcription process that was used to generate the antisense and sense RNAs; namely, dsRNA fragments.

Additional experiments by Fire *et al.*, designed to shed light on the possible mechanism of the dsRNA-mediated inhibition, painted an even more mystifying picture. For example, even when only a few copies of the dsRNAs are present in each cell, they are active against highly abundant RNAs. This indicates that the interference occurs either by a catalytic mechanism or at the chromosomal level — and not by a conventional antisense mechanism. The authors also found that only dsRNAs that are complementary to coding regions of the gene are active, and not, for example, those targeted to introns or promoter regions. This argues against a generalized mechanism involving chromosomal inactivation, such as chromosomal deletion. Moreover, dsRNA interference seems to cross cellular boundaries with

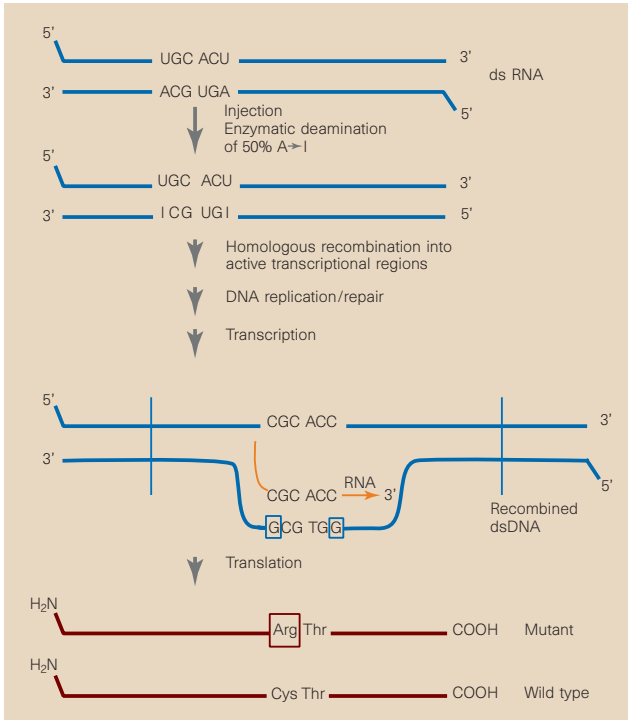

Figure 1 **Possible mechanism for inhibition of gene expression in *C. elegans* by double-stranded RNA. Fire *et al.*[6] have convincingly shown that, at the phenotype, RNA and protein levels, dsRNA-mediated interference with gene expression is specific and reproducible. Perhaps, on injection into worms, dsRNA is modified by dsRNA adenosine deaminase. Transfer of this information back into the chromosome may occur by a recombination event. After replication and mismatch repair, transcription and translation result in mutant proteins that have impaired function.**