100 YEARS AGO

In our issue for June 24 we briefly described the run of the *Turbinia* from the Tyne to the Solent. We understand that during the three weeks the *Turbinia* was in the Solent she made frequent runs of many miles at a time, at speeds of from 30 to 35 knots .... On Tuesday, June 29, with a distinguished company on board, she was run up to nearly full power, and maintained the unprecedented speed of 35 knots, or over 40 miles per hour, for the length of the line of battle-ships, or about 5 miles. During this run there was an absence of strain, and from this fact it seems that the limit of speed in this little vessel has not yet been reached, and that after further improvements, at present in progress (having returned to the Tyne last week), she will be capable of not only maintaining her position as much the fastest vessel afloat, but will be able to give many knots to any competitor engined with reciprocating engines.

From *Nature* 15 July 1897.

50 YEARS AGO

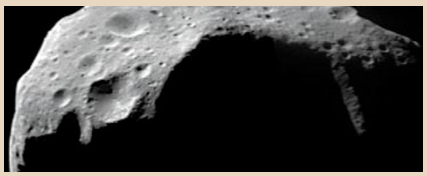
A description of developments [in television] was given in a lecture on May 29 before the Television Society by Dr. D. Starkie, of the Plastics Division of Imperial Chemical Industries, Ltd. Dr. Starkie demonstrated two prototype Schmidt television projection systems for home receivers, using cathode ray tubes of $2^{1}/_{4}$ or $3^{1}/_{2}$ in. diameter, respectively. The picture size given by both systems is 16 in. × 13 in., the chromatic aberration is small, and the resolution is claimed to be far better than is required for the present B.B.C. television transmissions using 405-line scanning. Although the smaller of the two systems requires a 'throw distance' of 40 in. between the cathode ray tube and the viewing screen, it was shown how this could conveniently be incorporated in a receiver console of normal dimensions. A third Schmidt system suitable for television projection in small cinemas was also demonstrated: this contained a mirror of 18 in. diameter and gave a picture with a length of diagonal of $12^{1}/_{2}$ ft.

From *Nature* 19 July 1947.

Many more abstracts like these can be found in *A Bedside Nature: Genius and Eccentricity in Science, 1869–1953*, a 266-page book edited by Walter Gratzer. Contact David Plant. e-mail: subscriptions@nature.com

Asteroids

Made of craters



Mathilde is a very odd asteroid, for its surface turns out to be covered in giant craters. It is also exceptionally dark, reflecting just 4% of the light that falls on it, and exceptionally light, just 1.3 to 1.5 times the density of water.

The picture includes one of the largest craters, more than 30 km across (half the diameter of Mathilde). The image is from the NEAR (Near Earth Asteroid Rendezvous) spacecraft, which flew within 1,200 km of Mathilde on 27 June, *en route* to its main destination, an orbit around the near-Earth asteroid Eros. During the brief flyby, NEAR measured Mathilde's mass from its gravity. Its density is roughly half that of the meteorites that come from this class of asteroid, so presumably Mathilde is full of cavities.

Those huge craters must have been made by the impacts of asteroids several kilometres across, which should have broken Mathilde up. How has it survived? The density measurement may be a clue: if Mathilde is half rock, half void, its structure might dampen the impact shock waves.

Another puzzle is the asteroid's slow rotation-period of once in 17.4 days. Those same impacts, mostly being off-centre, would have made it spin rapidly. It must have lost angular momentum somehow, perhaps by outgassing like a comet (but why so violently?), or perhaps by tidal dissipation from a large satellite (but where is that satellite now?).

Some questions are easier to answer. One of the principal investigators, Joe Veverka, was asked at a press conference whether the shadowed craters might be holes that go all the way through. "No," he said, "we don't see any stars."

Stephen Battersby

Familial Parkinson's disease

The awakening of α-synuclein

Michel Goedert

Parkinson's disease is characterized by a progressive neuronal degeneration which predominantly affects the dopaminergic nerve cells of the substantia nigra in the brain; the surviving cells contain characteristic cytoplasmic inclusions known as Lewy bodies, which are not normally present. Like many neurodegenerative disorders, Parkinson's disease either occurs in a common sporadic form or it can be inherited in a much rarer, familial form. But unlike other disorders, the nature of the mutations associated with familial Parkinson's were unknown. This has now changed with the discovery of a mutation in α-synuclein, a presynaptic protein, in four kindreds with early-onset, autosomal-dominantly inherited Parkinson's disease, reported last month in *Science* by Polymeropoulos *et al.*[1].

Last year, Polymeropoulos and colleagues established linkage of familial Parkinson's disease (FPD) in a large, well-characterized Italian–American kindred to a region on the long arm of chromosome 4 (ref. 2). Their latest work has pinpointed the gene within this region that is mutated in FPD, namely that encoding α-synuclein. Moreover, the mutation has been identified as an alanine-to-threonine amino-acid substitution at position 53 (denoted as A53T) of this protein[1]. This same mutation was found not only in the Italian–American kindred but also in three apparently unrelated Greek families with FPD. The A53T substitution in α-synuclein segregated with the disease in all four pedigrees, with the exception of one individual from the Italian– American kindred, who had Parkinson's but had apparently inherited a different mutation from his father. None of 157 control individuals had the A53T change.

Synucleins are highly conserved, with rodent and zebrafinch α-synucleins being respectively 95 and 86% identical to the human protein[3–5]. One surprising feature is that the mouse, the rat and the zebrafinch all have a threonine at position 53 of α-synuclein, like the mutant human protein. This raises the possibility that the A53T change could represent a rare polymorphism, although its presence in four unrelated kindreds with FPD makes this unlikely.

Human α-synuclein is an abundant 140-amino-acid protein of unknown function whose major site of expression is the nervous system, where it is concentrated in presynaptic nerve terminals[5–7]. It was first identified in electric fish, and named synuclein in recognition of its apparent localization in presynaptic nerve terminals and portions of the nuclear envelope[3]. This nuclear localization was never confirmed,

Figure 1 **Repeats in human α-synuclein. Residues 7–87 of the 140-amino-acid protein are shown. Amino-acid identities between at least five of the seven repeats are indicated by black bars. The alanine → threonine mutation at residue 53 that is associated with familial Parkinson's disease is shown in the sequence between repeats four and five (A → T).**

however, and all subsequent studies reported staining of only presynaptic nerve terminals.

Three different synuclein genes are known. Human α-synuclein has also been called NACP (for precursor of the non-β-amyloid component of Alzheimer's disease), because of the apparent association of one of its fragments with some of the extracellular β-amyloid deposits that constitute the neuropathology of Alzheimer's[5]. Human β-synuclein is 61% identical to α-synuclein and its gene maps to the long arm of chromosome 5 (refs 6, 8). Like α-synuclein, it is expressed at high levels in brain, where it localizes to presynaptic nerve terminals[6]. It also carries an alanine at position 53, suggesting that it might be worthwhile to look for mutations in β-synuclein in familial forms of Parkinson's disease. Unlike rodent and zebrafinch α-synucleins, mouse, rat and bovine β-synucleins all have an alanine at position 53 (refs 9, 10). A third synuclein (synuclein-like protein) is mainly expressed in the peripheral nervous system[11].

Synucleins have a highly conserved amino-terminal repeat region, a hydrophobic middle section, and a less well-conserved, negatively charged carboxy-terminal region. They are modified post-translationally, but the exact modifications are not known[6]. Over half of the α-synuclein molecule is taken up by seven imperfect repeats of eleven amino acids, each having a conserved six-amino-acid core with the consensus sequence KTKEGV (in single-letter amino-acid code; see Fig. 1)[3–5]. Core sequences of individual repeats are separated by five amino acids, with the exception of repeats four and five, which are separated by nine amino acids. The A53T change associated with FPD lies in this nine-amino-acid sequence (Fig. 1).

Although the function of the repeats is unknown, clusters of basic and acidic amino acids often mediate binding between structural proteins. Biophysical studies have shown that α-synuclein has no significant secondary structure[12]. Such natively unfolded proteins frequently potentiate protein–protein interactions and become structured when bound to other proteins[12]. It will be important to identify binding partners for α-synuclein, as the A53T mutation may disrupt its normal function.

Proteins or fragments of proteins that are mutated in familial neurodegenerative disorders frequently accumulate as deposits that characterize the neuropathology of these disorders. Examples include some familial forms of Alzheimer's disease and some inherited prion diseases. It will no doubt be known soon whether or not α-synuclein is an intrinsic component of the core of the Lewy body.

Neurofilaments and ubiquitin can be detected in Lewy bodies[13,14], but it is unclear whether they are major components of the fibrillar and amorphous material of the core. Human recombinant α-synuclein has been shown to dimerize[15], but it appears to be more soluble than the recombinant protein from the zebrafinch, which aggregates in solution[4,12]. Human α-synuclein with the A53T mutation might thus have an increased tendency to aggregate, especially if the mutation also interferes with the ability of α-synuclein to interact with its binding partner in nerve terminals. Rodent and zebrafinch α-synucleins would not aggregate in nerve cells because they would be bound to other proteins and also because these species have a much shorter lifespan than humans. Lewy bodies are as much a feature of Parkinson's disease as is the dramatic loss of neuronal cells in the substantia nigra.

But Lewy bodies also occur in the brains of patients with other neurodegenerative disorders, especially in the cerebral cortex of patients with a late-life dementia that is clinically similar to Alzheimer's disease. The new work[1] brings α-synuclein to centre-stage, with the promise of new insight into the biology of the Lewy body and the pathogenesis of Parkinson's disease. □

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Daedalus

Guided lightning

Why does lightning go so far? A 100-MV spark will only bridge 20 metres or so; yet a thunder cloud at 100 MV can launch lightning flashes over 1 km long. This is because lightning travels in steps. A 'stepped leader' stroke descends about 20 m from the charged cloud, and pauses. The current ionizes the air along its track; it becomes so conducting that in a few microseconds its sharp end is raised to the 100-MV potential of its cloudy origin. A sharp point at a high potential, of course, is an ideal initiator of electric breakdown. So the stroke proceeds another 20 m, and recreates another sharp conducting point lower down, which breaks down the local air in its turn. Once begun, a stepped flash can travel indefinitely.

So, says Daedalus, with a 100-MV source we could launch our own lightning through any distance of air. But how to aim it? An ultraviolet laser has been used to ionize a path through low-pressure gas, to guide an electron beam; but air would absorb such a beam. These days, however, gyratron valves can generate brief 100-MW pulses at 150 GHz. So DREADCO plasma physicists, with some trepidation, are launching a pulsed gyratron beam from a sharp-ended hollow waveguide which has been charged to 100 MV. The intense narrow beam will energize the air along its track, so that the first 20-m lightning step will follow the beam. The skin effect of the 150-GHz modulation will preferentially ionize the outside of the discharge, forming a hollow waveguide carrying the bulk of the radiation to the end of the step. Here the process will repeat. At the next gyratron pulse, the discharge will step another 20-m step in the beam direction, and so on. Indeed, even a 5-MV source should work; its lightning would advance along the guiding beam in 1-m steps.

As a anti-aircraft weapon, DREADCO's lightning launcher could be quite humane. Most of its power will be dissipated along its track. The target will receive a shock strong enough to wreck its navigation and weapon electronics while causing little structural damage. The lightning launcher could also be useful in rain-making, by triggering potential thunderstorms — ideally from an aircraft above the clouds, to avoid receiving a prompt natural lightning blast back along the ionized channel. Religious zealots would also welcome an airborne lightning launcher. They could direct an apparent thunderbolt at York Minster or Canterbury Cathedral whenever a bishop uttered a heresy.

David Jones