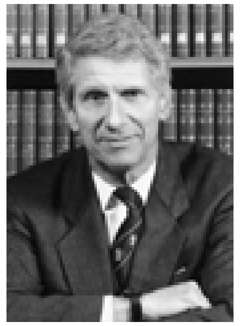
Medical Research, he was able to test his idea of synchrotron radiation as a source for X-ray scattering experiments on a specially built optical bench at DESY in Hamburg. The initial experiments that Holmes carried out with Gerd Rosenbaum in 1970 already provided promising results. The X-ray structural analysis of an insect muscle, which the two scientists started in 1971 using this method, was a real breakthrough. "However, the significance that synchrotron radiation has for molecular structural biology goes far beyond the expectations we had at the time," says Holmes.

ACTIN IN THREE DIMENSIONS

Although the "swinging cross bridge hypothesis" has been quoted in every textbook since 1972, it remained difficult to observe the cross bridge in flagranti delicto. Moreover, in the following years it appeared that it was not the entire cross bridge that moved during the power stroke but merely a small part that points away from the actin, which did not make the task any easier. The largest part of the cross bridge mass appears to tack itself onto the actin and not to carry out any major movements. For the following twenty years there was only limited progress. In order to understand in detail the way in which proteins function, and to set up or test hypotheses about their reaction mechanisms, it is necessary to be able to manipulate them by means of molecular biological techniques and to know their three-dimensional structure at an atomic level. This did not happen until the 90's.



Kenneth Holmes (born 1934) received the Gabor Medal of the Royal Society of London in 1997, then the European Latsis Prize 2000 and in March this year the Aminoff Prize awarded by the Royal Swedish Academy of Sciences.

At the beginning of the 90's Kenneth Holmes' work group was able to resolve the atomic structures of G (globular)-actin and F (fibrous)-actin. F-actin is the main component of the thin filaments and is made up of individual G-actin building blocks. The resultant helix resembles two chains of actin molecules that wind around each other (see Fig. 3). One actin molecule consists of 375 amino acids with a total of around 3,000 atoms. The way towards a three-dimensional view of this molecule was no easy undertaking; the only method of determining the atomic structure of large molecules is X-ray structural analysis that presupposes it is possible to manufacture well-ordered crystals. However, the individual building blocks of actin aggregate spontaneously to thin filaments that cannot be crystallised. Nevertheless, together with the enzyme deoxyribonuclease I actin forms a very stable 1:1 complex that can be crystallised. However, the structural analysis of these crystals turned out to be difficult. Only new developments in both recording and evaluation of the X-ray diffraction data and in the structural analysis method itself, all of which were advanced by Holmes' collaborator Wolfgang Kabsch, rendered a three-dimensional high-resolution image possible. This shows that actin is a flat molecule that can be divided into a total of two main domains or four subdomains. Subdomain 1 contains the main binding sites for the myosin cross bridge. The group of Ivan Rayment, Madison (USA), solved the structure of the cross bridge in 1993.

The atomic model of the myosin molecule has provided much new information. Thus it is not the entire head of the myosin molecule that rotates but rather there is a hinge in the middle so that the outer part of the head acts as a lever, as was suspected earlier. Moreover, X-ray crystallographic examinations of the myosin head have shown that the lever arm occurs in two conformations (they are represented in light and dark blue respectively in Fig. 1 on page 50). These are the end stages of the lever arm movement. Now it remains for physiologists to work out the details of the lever arm movement – using the modern methods of molecular physiology. Results up to now support the molecular model of the cross bridge cycle, the "swinging lever arm hypothesis", very well.

Incidentally, whilst an Englishman, Kenneth Holmes, is studying the "molecular power stroke" in Heidelberg, and last year received the European Latsis Prize endowed with 65,000 Euros for his work, it was a German, Tim Wooge, who this year stroked the Cambridge eight to victory.

CHRISTINA BECK

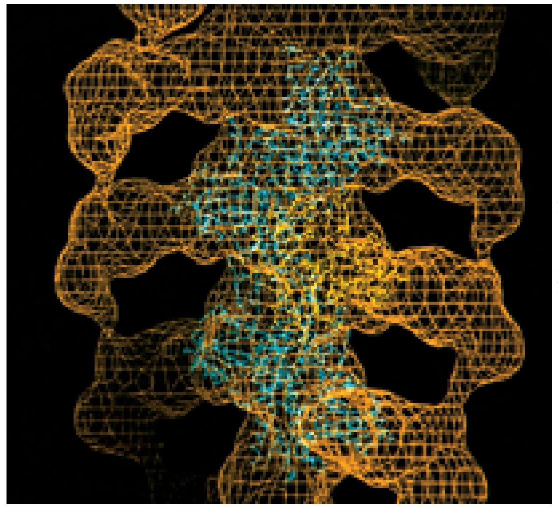


Fig. 3: The atomic models of the individual molecules (four in blue, one in yellow) can be fitted into a three-dimensional grid model (orange) of the F-actin draped with myosin-S1 (the myosin head). This portrays the interaction of the actin and myosin on an atomic level.

PHOTOS: MPI FOR MEDICAL RESEARCH (1) / ARCHIVE (1)

New Supercomputer for Observing the Earth and Black Holes

In a joint operation, radio astronomers and geodesists are analysing digital data streams from networks of telescopes around the world. A new high-performance computer, which can not only supply razor-sharp images from the energy outflows of quasars at the edge of the observable universe but also allow tiny changes in the rotational speed of our Earth or minimal variations in its axis to be seen, has recently officially gone into service at the Max Planck Institute for Radio Astronomy (MPIfR) in Bonn. As **HUBERT MARKL**, *President of the Max Planck Society, wrote in his welcoming address, "This will herald the dawn of a new era for high-resolution radio astronomy in Bonn and for geodetic research".*

At the launch of the new high-performance computer (from left) Markus Rothacher, Munich, Dietmar Grünreich, Frankfurt, Hayo Hase, Wettzell, Hermann Seeger, Bad Neuenahr, Richard Wielebinski, Bonn, Anton Zensus, Bonn and Peter Brosche, Bonn.

The new machine, a so-called correlator, is a "hardwired" digital computer. It is 4000 times more powerful than its predecessor and the final upgrade boasts a computing power of 25 thousand billion instructions per second.

Radio astronomers and geodesists employ Bonn's "Mark IV correlator" to analyse digital data gathered using Very Long Baseline Interferometry (VLBI). In this process numerous radio telescopes scattered around the world observe an astronomical object simultaneously. Typically such joint projects involve between eight and 20 individual antennae which may be located between 100 and 10,000 kilometres apart.

These large distances mean that antennae and correlator cannot connect with each other "coherently" (broadband) in "real time" during the observation. This forces the VLBI measuring process to be carried out in three separate main stages:

Each VLBI station receives the cosmic radio signals completely independently of the other stations and stores them at a high data rate. Extremely stable atomic clocks (hydrogen masers) on each antenna ensure distortion-free reception (an extreme form of hi-fi) and also precise time tagging of the data recorded digitally on magnetic tape. On completion of the observations, which generally take several hours, the magnetic tapes with the primary data from all the stations are transferred to the location of the processing centre. There, the data streams from all antennae are 'reconstituted' in play-back drives and fed into the correlator via high-speed links where they are 'superimposed' in pairs, i.e. made to interfere.

The final stage comprises calibration and further analysis of the data produced by the correlator using general purpose, programmable computers with astronomical or geodetic software. At this point, all the observables of interest to astronomers and geodesists can be determined from the interferometer data; these include in particular the in-

Astronomy's sharpest images are obtained by a correlator analysing simultaneous observations from radio telescopes scattered around the world.

tensity distribution, i.e. the radio image of the observed cosmic object, its position and the Earth rotation parameters.

The first two steps require an overall "VLBI system" consisting of units for recording, storing, reproducing and correlating streams of signals at high data rates, that is to say, large bandwidths. This is an important requirement for the sensitivity and accuracy of the measurements.

The new high-performance computer can correlate in pairs data streams of up to 256 million bits per second. In future, recording rates will even reach one billion bits per second and higher. By way of comparison: four million bits are required to encode 250 typewritten pages.

The correlator processes the data received from the individual antennae within the global VLBI network as if they were received from one single giant telescope the size of the Earth. It uses them to synthesise the sharpest images possible in astronomy.

With the help of VLBI technology, details of distant cosmic radio sources, such as quasars, can be distinguished with angular resolutions of less than one thousandth of an arcsecond – that is like looking at an object the size of a coin in the USA from Germany. This offers radio astronomers the opportunity, for example, of directly observing the area immediately surrounding the black hole suspected in the centre of our Galaxy.

The VLBI method also enables the position of compact radio sources in the sky to be determined with unequalled precision. Geodesists use these objects as cosmic reference points to measure to the exact millimetre, for example, the distance between the continents on Earth or the orientation of the Earth's axis. Movements of parts of the Earth's crust, such as shifting continental plates, can be tracked in this way, as can changes in the Earth's axis or rotational speed and thus in day length - variations which occur over the course of days, weeks, months and longer periods.

PHOTOS: MPI FOR RADIO ASTRONOMY

FOUR MACHINES OPERATING AROUND THE WORLD.

Germany's Federal Agency for Cartography and Geodesy (BKG) in Frankfurt/Main helped finance the "Mark IV correlator" now operating at Bonn's MPI for Radio Astronomy to the tune of some five million Marks. The new supercomputer is to be used for astronomical and geophysical measurement and shared roughly equally between the MPI for Radio Astronomy and the University of Bonn's Geodetic Institute. Bonn's VLBI correlator was developed by the Massachusetts Institute of Technology. NASA, USNO (United States Naval Observatory) and the Smithsonian Institute in the USA and also BKG, JIVE (Joint Institute for VLBI in Europe) and NFRA (Netherlands Foundation for Research in Astronomy) in Europe were involved. So far, a total of four of these machines are in operation around the world, two in the USA and two in Europe.

A new high-performance computer, used to analyse data gathered with Very Long Baseline Interferometry (VLBI) both for astronomy and surveying the Earth, has officially begun operation at the MPI for Radio Astronomy in Bonn. In the photo below right (from left) Wolfgang Zinz, Kuchenheim, Richard Wielebinski, Bonn, Hermann Seeger, Bad Neuenahr and Dietmar Grünreich, Frankfurt.

Since 1973, Bonn's astronomers and geodesists, together with international research institutes, have used the large 100 metre diameter radio telescope near Bad Münstereifel-Effelsberg for astronomical and geodetic VLBI measurements. Meanwhile the astronomical VLBI group at Bonn's MPIfR has been working with Dr. Anton Zensus, director at

the institute, on opening up, not just the centimetre, but also the shortwave millimetre range to VLBI measurement. However, a number of technical challenges need to be overcome first. Yet millimetre wave VLBI does allow detailed observations which are breathtakingly accurate with angular resolutions of just a few millionths of an arcsecond: so that, in theory, a stone, 10 centimetres across, on the moon could be seen from the Earth.

Meanwhile, radio astronomers have extended their observations based on VLBI into space with an antenna orbiting the Earth. By combining this with ground-based VLBI networks, they can synthesise a virtual supertelescope with a diameter many times that of the Earth. Like a zoom lens, these VLBI measurements of cosmic objects at the edge of the universe, such as black holes, make details visible which are all the finer the shorter the wavelength examined. A first major step in this direction was been taken in

in 1997 when Japan launched HALCA, a radio antenna eight metres in diameter, into orbit around the Earth. Together with ground-based VLBI networks, this "syntheses" a 30,000-kilometre supertelescope. That is three or four times bigger than the largest virtual antenna attainable with a VLBI network on Earth.

The MPI for Radio Astronomy was also involved in this project from the outset and will play an even larger part in further development of space VLBI. The institute's 100-metre radio telescope is an important player in international VLBI. Its unusually accurate and large collecting surface makes it one of the most sensitive interferometry instruments in any VLBI network, both for observations in the centimetre- and also in the millimetre wavelength range. The same goes for the 30-metre radio telescope near Granada in southern Spain: here the MPI for Radio Astronomy, together with Spanish and French partners, is involved in the world's largest single telescope for millimetre waves operated by the "Institute for Millimetre Radio Astronomy" (IRAM).

MONITORING THE EARTH'S ROTATION AND CRUSTAL MOTION

The University of Bonn's geodetic VLBI group, led by Prof. James Campbell, is concentrating its research on regularly measuring and monitoring variations in the Earth's rotation. These activities form part of the German Satellite Geodesy research group (FGS) and the International VLBI Service (IVS) acting as suppliers to the International Earth's Rotation Service (IERS).

The majority of geodetic VLBI observations are performed by the 20-metre radio telescope at the Wettzell 'Fundamentalstation' in the Bavarian Forest. The 100 metre radio telescope at Effelsberg is also occasionally involved for measuring tiny movements in the Earth's crust, particularly in the area between the Upper Rhine valley and the Lower Rhine bay. This region is known as western Europe's seismic 'weak zone' making itself felt through occasional earthquakes. ●