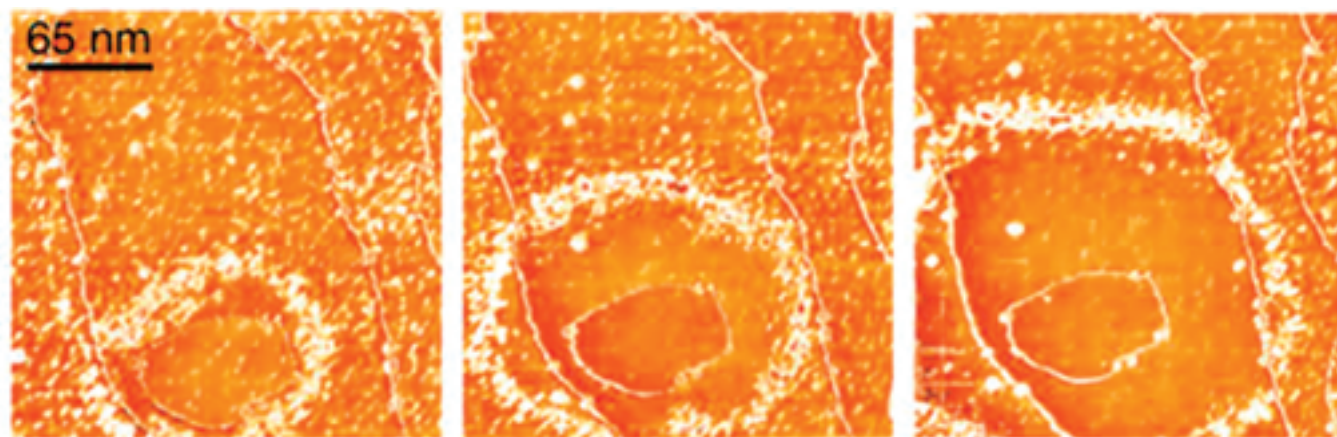




Latest RESEARCH



PHYSICAL CHEMISTRY

Reaction Fronts on the Atomic Scale

Scientists from the Fritz Haber Institute of the Max Planck Society, Berlin have revealed the atomic processes leading to so-called chemical reaction fronts on the surface of a catalyst (SCIENCE, 31 August 2001). This success has been achieved by the research team of Christian Sachs and Joost Wintterlin from the department of "Physical Chemistry" led by Prof. Gerhard Ertl.

Chemical reactions usually proceed in a uniform manner, i.e., in the entire reaction volume the processes end more or less at the same moment. Some reactions, however, behave differently, they "ignite" at some location and propagate in a front-like manner. The field of chemistry has for a long time been aware of these phenomena, which can also be effectively explained using theoretical models. However, up until now it was unknown if the assumptions underlying these simple models, so-called reaction-diffusion models, provided

a correct description of the processes on the atomic scale. For the first time, scientists at the Fritz Haber Institute have now directly revealed the molecular processes in a reaction front using a scanning tunneling microscope. It was shown that the concepts of simple reaction-diffusion models cannot be applied to the small scale of atoms and molecules. In particular, interactions between the reacting particles have to be taken into account to accurately predict the characteristics of the fronts such as their velocity.

Front-like propagation is not restricted to chemistry, but can be observed in other areas of nature and even in social processes. Forest fires, for instance, exhibit a similar behaviour; further examples include the plague epidemics in the Middle Ages or the introduction of farming in Europe in the neolithic age. All of these processes begin in a small area, after which they spread in a front-like manner, and their mathematical description is al-

ways quite similar. For chemical reactions, which only involve uniform, relatively simple molecules, the underlying processes seem particularly easy to understand. The reaction starts at some location, forming a small quantity of the reaction product. For certain chemical reactions the product then enters the reaction again, causing the process to accelerate. Once started, the reaction therefore becomes faster and faster, leading to a strong increase of the product concentration in this area. At the same time the highly concentrated product begins to spread by diffusion and expands into the surrounding area. Here it starts the reaction again. This sequence constantly repeats itself, corresponding to the propagation of a front. The velocity at which the front travels can be much greater than the diffusion rate. This behaviour can be understood in principle using simple theoretical models which only take the reaction and the diffusion into account (hence the name reac-

Scanning tunneling microscope images of a reaction front occurring during oxidation of hydrogen on a platinum surface. The front appears as a bright ring that propagates at a velocity of 15 nanometres (= a millionth of a millimetre) per minute. The bright spots in the front are islands consisting of a few OH molecules.

PHOTOS: FRITZ-HABER-INSTITUTE

tion-diffusion model). Nevertheless, there are indications that this description is too simple.

Scientists from the Fritz Haber Institute working with Christian Sachs and Joost Wintterlin from the department led by Gerhard Ertl have discovered fronts in the catalytic oxidation of hydrogen at low temperatures. Hydrogen and oxygen react on the platinum surface, which acts as a catalyst, to form water. Measurements were carried out under ultra-high vacuum conditions using a scanning tunneling microscope that can provide images of atoms and molecules on surfaces. In this way chemical reaction fronts could be visualized which, for this reaction, are between 10 and 100 nanometres (= a millionth of a millimetre) wide.

The Berlin scientists have observed the formation of OH molecules on the platinum surface as an intermediate product. The OH molecules combine with hydrogen atoms to form water (H₂O). However, the water formed in this way enters the reaction again, and reacts with oxygen atoms which are still available, to give OH. The local concentration of OH thereby increases, leading to an accelerating production rate of OH and, in consequence, of H₂O. Water is able to diffuse on the platinum surface and initiate this process in the surrounding area. As a result, a reaction front propagates across the surface; the intermediate product OH becomes enriched in the front. Having achieved the visualization of the atoms and molecules reacting in the fronts, the scientists observed much more

complex processes than those on which reaction-diffusion models are based. As assumed in the models, the particles do actually react and diffuse – but not independently of each other. The OH and H₂O molecules exhibit strong interactions which, for example, lead to the formation of small islands as a result of attractive forces between the particles. This explains why the velocities and profiles of the fronts measured in the experiments do not agree with the theoretically predicted values. The scientists are now hoping that these findings will allow them to develop better theoretical models which can then be applied to other examples of this widespread phenomenon. ●



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STRUCTURAL BIOLOGY

Molecular Combat

Certain antibiotics hinder the formation of proteins in ribosomes – the "protein factories" of bacteria. Scientists from the research group for ribosomal structure at the Max Planck Society at DESY in Hamburg (group leader: Ada Yonath) and the ribosome research group at the Max Planck Institute for Molecular Genetics, Berlin (group leader: François Franceschi) have succeeded in explaining the action of these antibiotics right down to their atomic details (NATURE, 25 October 2001). They were able to determine the interaction between a ribosomal subunit of the bacterium *Deinococcus radiodurans* respectively with five different clinically relevant antibiotics. This provides new starting points for inhibiting the degree of resistance to antibiotics and also for simplifying the development of new antibiotics, a process which has so far remained both lengthy and expensive.

Ribosomes are complex macromolecules consisting of approximately 60 different proteins and three to four nucleic acid chains (ribosomal RNA). They are responsible in each cell for the formation of essential proteins by translating the genetic code that contains the building instructions for the proteins. Ribosomes consist of two independent subunits of differing sizes, which carry out different functions during protein biosynthesis. The small subunit (30S in the

Erythromycin (red) blocks the tunnel of the 50S subunit of the ribosome. Both RNA strands of the 50S subunit are shown in blue, the ribosomal proteins are shown in golden yellow.

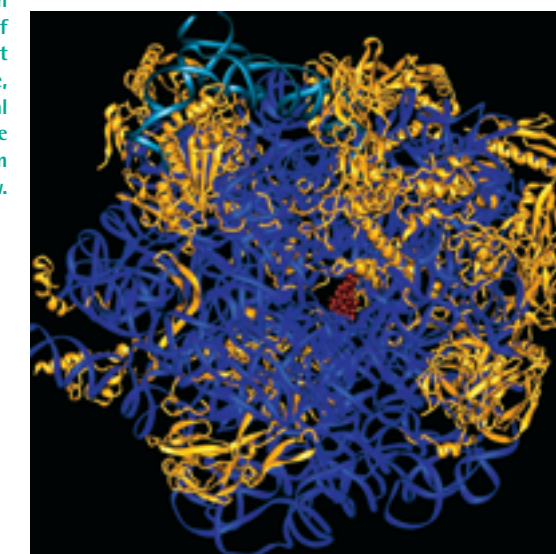
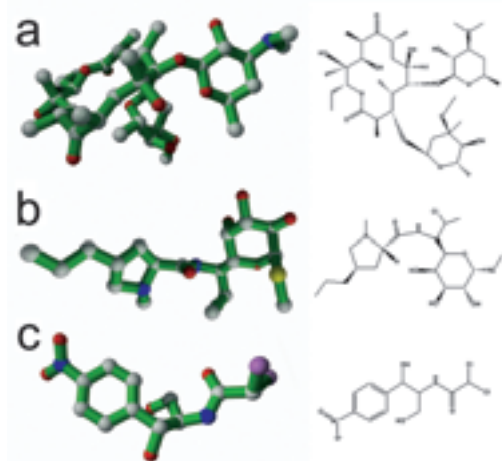


FIG.: RESEARCH GROUP FOR RIBOSOMAL STRUCTURE AT THE MPS AT DESY



Antibiotics are just as small as effective molecules. The diagram shows a three-dimensional structure (left) and the chemical structure (right) for a) erythromycin, b) clindamycin, and c) chloramphenicol.

case of bacterial ribosomes) is essentially responsible for deciphering the genetic code, whilst the large subunit (50S) joins together the individual amino acids in the so-called peptide transferase reaction to form a long amino acid chain which is finally folded into a protein molecule. During its production, the amino acid chain is partially located within the 50S subunit, in a tunnel that is approximately 100 Angström in length and 15 Angström in width, and this protects it from enzymatic attack (1 Angström is equivalent to one ten-millionth of a millimetre). In 1999, for the first time ever – following more than 20 years of intense research – it was possible to explain the complicated structure of ribosomes with atomic resolution.

The central role of the ribosome during protein biosynthesis also makes it a preferred target for many antibiotics (substances that will inhibit or kill bacteria) and cytostatic agents (substances that inhibit tumours). However, up until now the details of the working mechanism had remained unknown. Chloramphenicol, clindamycin and erythromycin are some of the antibiotics that can be used against *Bacillus anthracis* (anthrax), which has hit the headlines over the past months as a result of recent tragic events. Furthermore, the

so-called macrolide antibiotics are used to fight against a multitude of bacterial infections ranging from acne to syphilis.

With the aid of biochemical data scientists had already discovered that erythromycin only stops the peptidyl transferase reaction once a short amino acid chain has been formed. The structure of the 50S subunit complexed with erythromycin and also with the two other macrolides (roxithromycin and clarithromycin) shows that this class of antibiotics blocks the tunnel of the 50S subunit through which all proteins are threaded. This leads to a premature termination of the protein synthesis. Chloramphenicol is extremely effective in the treatment of a broad spectrum of bacterial infections, including serious anaerobic infections and cocci bacteria. It is also used in the treatment of pneumocystis-induced lung infections in AIDS patients. Both antibiotics bind directly in the peptidyl transferase centre of the ribosome. The structures of the ribosomal subunits with clindamycin and chloramphenicol confirm the assumption that these antibiotics interrupt protein synthesis by means of "molecular mimicry". That is to say, they are similar to amino acids and are therefore incorporated into the ribosome instead of an amino acid. As they are inherently unable to enter a peptide binding, they bring the peptidyl transferase reaction to a standstill – and this kills the bacteria. These days the majority of antibiotics are not used in the treatment of bacterial infections, but in the production and preservation of foodstuffs. As a direct consequence of this, many pathogenic organisms are becoming increasingly multi-resistant to a large number of different antibiotics.

In the 1950s this resistance had already encouraged the outbreak of bacterial dysentery in Japan, triggered by multi-resistant strains of *Shigella* dysenteriae, an infection which still kills approximately 600,000 people annually throughout the world. In the meantime the problem of antibiotic resistance has become a matter of such urgency that it is being described as a worldwide health crisis by the World Health Organisation (WHO). Following the introduction of a new antibiotic, it normally takes no longer than two to three years before the first resistant pathogens appear. The development of new antibiotics is therefore barely able to keep pace with the increasing spread of resistant bacteria strains: in the past 30 years only one new class of antibiotic drugs has come onto the market. Elucidation of the structural basis of the large ribosomal subunits in connection with the different antibiotics, and knowledge therefore of the interaction between antibiotics and ribosomes, will now make it possible to significantly speed up the lengthy and cost-intensive development of new medicines. ●



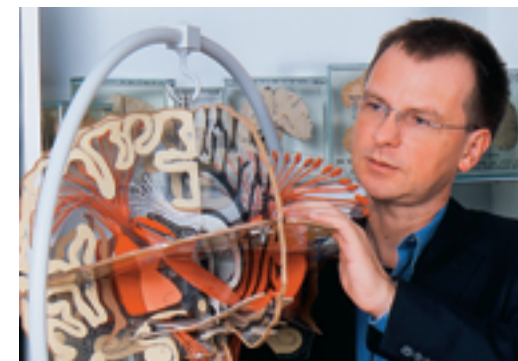
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CELL BIOLOGY

Taking the "Estrogen Route" to Fight Alzheimer's



Christian Behl and his colleagues at the Max Planck Institute for Psychiatry are researching the protective effect of estrogens on nerve cells of the brain.

Is there a chemical structure hiding in estrogens, in female sex hormones, that can be used as a "lead structure" for an active substance against Alzheimer's disease? Can estrogens themselves influence the illness process behind this dementia? New experimental findings of a research group at the Max Planck Institute of Psychiatry, Munich clearly confirm these facts.

The female sex hormones estradiol, estrone, and estriol, which are described as estrogens, do not only serve the purposes of reproduction. They also exert all kinds of beneficial "side effects", for instance on the heart and circulatory system, on the metabolism of the bones, and not least on the brain: here estrogens – as neurohormones and protective factors – play a varied role in the structure, function, and preservation of nerve cells.

An independent junior research group at the Max Planck Institute of Psychiatry in Munich, headed by Christian Behl, is investigating the neuroprotective activity of estrogens, i.e. their protective influence on nerve cells. This research group made a surprising discovery about estrogen some years ago.

By means of biochemical proof it was established for the very first time that estrogens act as

neuroprotective antioxidants as a result of their chemical structure: they capture chemically aggressive molecules – "free radicals" –, thereby preventing their destructive oxidizing influence on the molecular tools or structural elements of the nerve cells, so-called oxidative stress. In this function, the scientists also talk of "free radical scavengers", estrogens that resemble vitamin E and form a type of molecular protective shield for the nerve cells.

In addition to this purely structural and chemical effect, estrogens also intervene directly in numerous biochemical processes within the nerve cells. In the meantime, Behl and his colleagues focused their attention on one of these activities in particular: the processing and "biochemical cleavage" of the protein amyloid precursor protein, or APP for short, in nerve cells. During the course of this APP processing, an error can occur which has fatal results. A toxic protein is then formed from the APP, the beta amyloid, which is deposited as aggregates, in the so-called amyloid plaques, in the brain of Alzheimer's patients. The formation of these beta amyloid units is therefore regarded as being one core process and trigger for Alzheimer dementia. Earlier studies had already shown that estrogens clearly influence APP processing and suppress the formation of toxic forms of beta amyloid. Up until this point, the precise molecular mechanism involved in this estrogen activity had remained unknown, and this was the area on which Christian Behl and his colleagues concentrated. It has now been possible to present two fundamental results. On the one hand, it was shown that the influence of the estrogens on APP processing does not exclusively take place via

estrogen receptors and therefore does not take place via the "classic" hormonal mechanism of the estrogen effect. On the other hand, it was discovered that the effect of the estrogens on APP processing in the nerve cells takes place at great speed and is carried out via specific intracellular signal factors, so-called mitogen-activated protein kinases (Manthey et al., *European Journal of Biochemistry*, 267; 5687-5692, 2001). A fundamental discovery that could be concluded from this is that estrogens also clearly influence APP processing in these types of nerve cells in the brain, which do not possess any functional estrogen receptors whatsoever.

These new findings on the estrogen effect in the brain provide new starting points that have already been intensively pursued by Christian Behl and his colleagues, including Sharon Goodenough, Dieter Manthey, Jürgen Zschocke, and Bernd Moosmann: in terms of the effect being a protective antioxidant, it is necessary to identify those particular structural elements of the estrogen molecules which are responsible for these non-hormonal protective "side effects". It will then be possible to use these chemical components as pharmaceutical "lead structures" to develop new antioxidative neuroprotective medicines. These would then be used due to the non-existence of feminizing effects on both men and women. Behl sums up the route towards achieving this goal as follows: "On the one hand, we can improve the chemical structure of the estrogen so that the structural antioxidative activity is intensified and neuroprotective designer antioxidants are created. We have already made decisive steps in the development of this type of estrogen-related

antioxidative structures and have identified the first highly active molecular structures that are already being tested in animal models. However, as receptors for estrogens exist in various regions of the brain, an additional research approach is the identification of genes that are switched on or off in the nerve cells by the estrogens and influence the survival of the nerve cell. Using so-called DNA-arrays/DNA-chips, genetic programmes can be discovered that make nerve cells in women and men resistant to

THE BOOK ON THE SUBJECT

Those wishing to find out more about known neuro-protective activities triggered by estrogens in the brain should take a look at the book "Estrogen – Mystery Drug for the Brain?" which has recently been published: in this book Christian Behl provides an overview of the current state of knowledge on the subject, with reference to both pure research and clinical experiences. The book, published in 2001 by Springer Verlag, Vienna/New York, has been written in English and is a valuable and informative work not only for specialists, but also many other interested and informed readers such as doctors or medical journalists.

the neurodegenerative process. On the basis of this data, medicines can be developed which specifically activate these protection programmes – and then estrogens themselves, at least as a whole, would no longer be needed to create neuroprotective effects." For the time being, the Munich researchers will of course require substantial amounts of estrogen to investigate the traces of neuroprotection shown by these hormones and this will perhaps ultimately lead to a medication that can fight Alzheimer's disease and other neurodegenerative disorders such as strokes. ●

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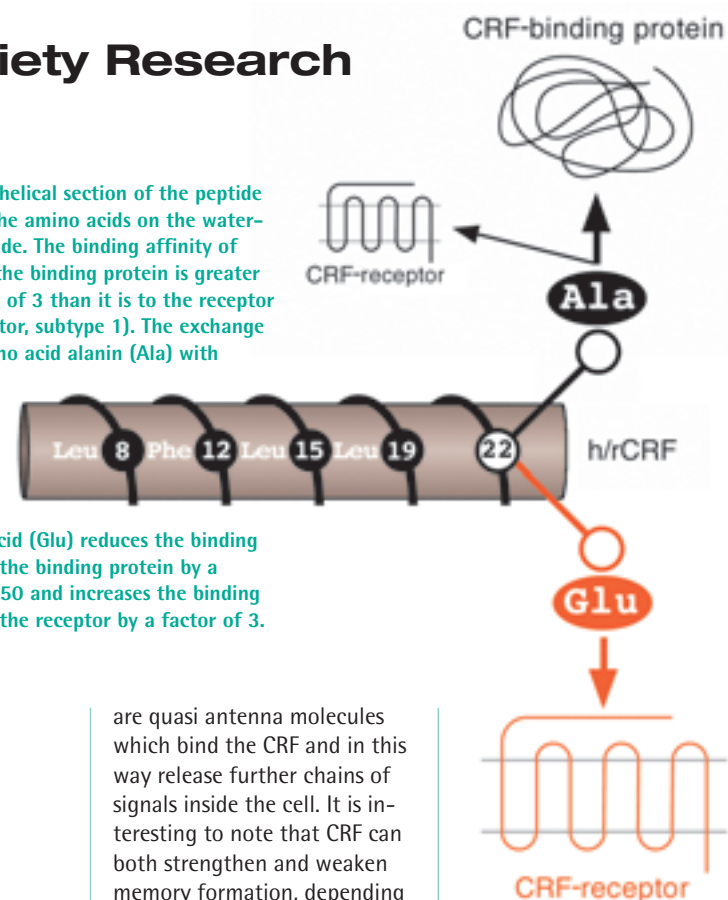
EXPERIMENTAL MEDICINE

Amino Acid Switch for Tools in Anxiety Research

In the journal PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (25 September 2001, Vol. 98) scientists from the department headed by Joachim Spiess at the Max Planck Institute for Experimental Medicine, Goettingen reported on the discovery of an amino acid switch in the stress hormone CRF: through the exchange of a single amino acid they have succeeded in selectively modifying the binding characteristics of the molecule. On the basis of this observation it should be possible in the future to develop selective CRF-like peptides (short protein sections) which act as specific agonists or antagonists, and this would enable significant progress to be made in the systemic and cellular research of CRF actions.

Stress is an experience known to everyone. There are many types of stress or anxiety-inducing stimuli. Yet whilst external stressful stimuli may differ considerably, the chemical reactions which are released in our body follow one basic pattern: in response to a stressful stimulus, a chemical signal molecule is released in the brain of humans and other mammals – the corticotropin-releasing hormone (corticotropin-releasing factor CRF), consisting of a 41 amino acid building block. It firstly travels via the nerve fibres to a portal vessel system above the pituitary gland and then moves along in the blood stream of this vessel system into the front section of the pituitary gland where it stimulates the secretion of the hormone corticotropin, which triggers the release of so-called glucocorticoids from the adrenal gland. The scientists call this complex chain of activities the hypothalamus-pituitary-adrenal axis or simply the stress axis. This axis plays an extremely important role in the specific adaptation of the body to stress situations. Under pathological conditions, such as depression and anxiety disorders, the normal functioning of this stress axis can be considerably disrupted. In addition to the role it plays in the activation of the stress axis, the CRF signal molecule is also involved in memory consolidation, anxiety, and food intake by actions in the brain. These CRF effects are transmitted by means of various receptor subtypes embedded in the cell walls. These

The alpha-helical section of the peptide CRF with the amino acids on the water-repellent side. The binding affinity of h/rCRF to the binding protein is greater by a factor of 3 than it is to the receptor (CRF receptor, subtype 1). The exchange of the amino acid alanin (Ala) with




glutamic acid (Glu) reduces the binding affinity to the binding protein by a factor of 150 and increases the binding affinity to the receptor by a factor of 3.

are quasi antenna molecules which bind the CRF and in this way release further chains of signals inside the cell. It is interesting to note that CRF can both strengthen and weaken memory formation, depending on which CRF receptor subtype of a brain region it has bound. Furthermore, CRF is not only bound to various receptors of the brain cells but also to a so-called CRF binding protein. In the human brain this protein binds around 50 percent of the available signal molecule and does so with greater strength, or affinity, than the aforementioned receptors. The scientists still do not fully understand the biological function of this binding protein, but there is no doubt that it provides an important pharmacological reservoir of CRF that could be used, for example, to improve memory formation. To achieve better understanding of the brain functions produced via the CRF receptors, the scientists are attempting to create CRF-analogs which are selectively bound by either one of the receptor subtypes or by the binding protein. In 1995 Andreas Ruehmann, Ines Bonk, and Joachim Spiess from the

Department of Molecular Neuroendocrinology at the Max Planck Institute for Experimental Medicine in Goettingen, together with Chijen Lin and Michael Rosenfeld from the Howard Hughes Institute in San Diego had already produced a selectively binding antagonist of this type, known as the peptide anti-sauvagine-30. In their latest publication in the PNAS, scientists from the same department – Klaus Eckart, Olaf Jahn, Jelena Radulovic, Hossein Tezval, Lars van Werven and Joachim Spiess – have now demonstrated that the exchange of a single amino acid in the CRF molecule decides whether or not CRF is bound to its binding protein. If the amino acid alanin is exchanged for the amino acid glutamic acid, then the molecule will no longer have high affinity to the bind-

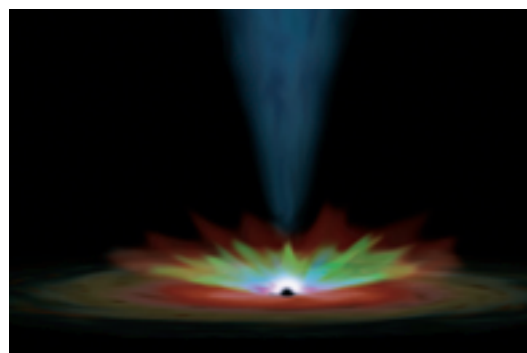
ing protein but merely to the CRF receptor. In this way, the scientists have in their grasp a so-called molecular switch with which they are able to selectively change the binding characteristics of the signal molecule. The amino acid exchange takes place in an alpha-helical region of the CRF molecule which has a high level of water-repellency. The scientists in Goettingen have already succeeded in using this scientific discovery in the development of antagonists: they modified the antagonist, astressin, whose employment in animal experiments has so far been limited due to its low solubility and which has a low affinity to the CRF binding protein. Introduction of the "switch amino acid" glutamic acid reduced the affinity to the CRF binding protein and increased binding to the CRF receptor. At the same time, the water solubility of acidic astressin, brought about by these modifications, was increased to such an extent that it could be effectively used in animal experiments – anxiety reactions in mice can now be easily suppressed using acidic astressin. The scientists at the Max Planck Institute in Goettingen are currently working on antagonists with greater selectivity for subtypes of the CRF receptors. ●

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GRAPHICS: MPI FOR EXPERIMENTAL MEDICINE

ASTROPHYSICS

Flashing Light from Black Hole



Artist's impression of the black hole X-ray transient XTE J1118+480, based on simultaneous X-ray and optical observations. Mass drawn from a secondary star (left) forms an accretion disk which feeds mass to the hole (dark reddish and brown colours). During the infall X-rays (white region) as well as plasma outflows in the form of jets are emitted. An additional slow outflow produces, after typically half a second time-of-flight delay, strong ultraviolet (purple), optical (green), and infrared (red) emissions. The blue fuzz indicates the base of the much faster jet that produces radio emissions but at distances well outside the scale of this image.

Gas in the vicinity of a black hole is heated by the hole's enormous gravity forces and starts radiating X-rays. According to popular theory, these flares will illuminate the gas at larger distances from the hole, heating it up and causing it to radiate visible light. This "light echo" should be measurable by simultaneous measurements of the X-rays and the visible light from the object. The best observations of this kind have now been made by astronomers from the Max Planck Institutes for Extraterrestrial Physics and Astrophysics at Garching (NATURE, 8 November 2001).

Surprisingly, the results seem to contradict the light echo theory. The team of Gottfried Kanbach and Henk Spruit suspects that, instead, the visible light has its origin in a flow of gas emitted from the vicinity of the black hole. The researchers in Garching chose the so-called "X-ray transient" XTE J1118+480 (now officially known as KV Ursa Majoris) for their investigations – a celestial body located more than 6000 light years away. From earlier observations it is known that this X-ray source probably has a black hole of more than six solar masses at its centre. A stream of gas fed to the hole from a companion star first forms an accretion disk around

it. The gas gradually falls into the hole from this disk. Fluctuations in this cause the X-rays to flare up.

Kanach and his colleagues observed XTE J1118+480 in July last year simultaneously with NASA's X-ray telescope Rossi XTE and at visible wavelengths with the Skinakas observatory on Crete. These observations were made with the OPTIMA photometer developed at the Max Planck Institute for Extraterrestrial Physics; it allows detection of very fast light variations, accurately timed with a GPS based clock. With these simultaneous observations, the rapid fluctuations in X-rays and visible light could be correlated with each other. "To our surprise, the optical light reacted much quicker to the X-rays than predicted by the light echo model", says Henk Spruit. In fact, a rapid increase in the visible light starts in less than a tenth of a second after an increase in X-rays.

The researchers interpret this observation as indicating the presence of a strong outflow of mass originating from the vicinity of the hole. According to this view, a strong magnetic field redirects part of the mass flow onto the hole into a flow away from the disk. Whenever a lump of gas falls into the hole, this outflow also becomes denser. This disturbance propagates outward with the flow and causes an increase in the visible light. This happens at some distance, about 20,000 km from the hole, where the emission of visible light is at its most effective. Simple estimates then show that the flow has to move at less than a tenth of the speed of light. The delay of the visible light compared with the X-rays is therefore explained as being due to the time it takes the flow to

travel this distance. The light itself would be cyclotron radiation emitted by electrons spiralling in the strong magnetic field.

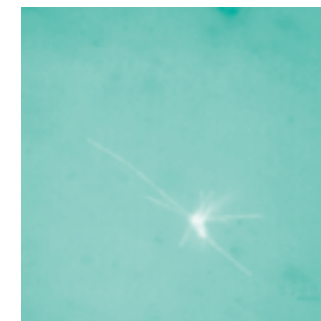
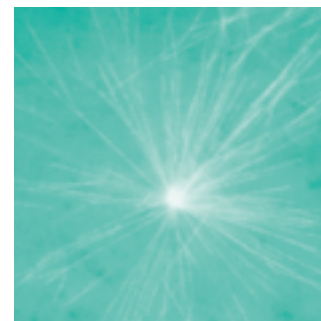
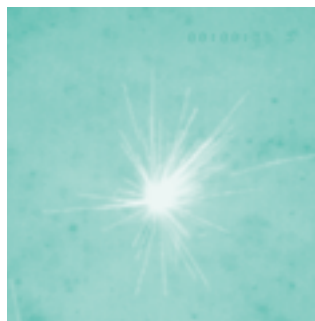
This relatively slow flow would be a new phenomenon associated with black holes in our galaxy, but it may be related to outflows seen in Active Galactic Nuclei. Up until now, only the fast but tenuous so-called radio jets are known, travelling at some 90% of the speed of light and best observed with radiotelescopes. To test the slow-flow model, the researchers are planning further observations on other similar objects. K V Uma itself has disappeared as an X-ray source following its 7-month outburst. ●



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The pictures show the extension and contraction of various microtubule fibres emanating from the microtubule organisation centre.



PHOTOS: MPI OF MOLECULAR CELL BIOLOGY AND GENETICS

ILLUSTRATION: MPI FOR ASTROPHYSICS / SPRUIT

CELL BIOLOGY

The Random Fate of Polymers

Even cells have a "skeleton" – a frame made from filamentary protein molecules which not only carries out support functions but also allows movements of the cell to take place and is involved in the transport processes within the cell body. An important role for this cell skeleton is played by the so-called microtubules which undergo constant assembly and disassembly: a dynamically unstable process that researchers at the Max Planck Institute of Molecular Cell Biology and Genetics have "reproduced" in model form for the very first time (SCIENCE, 9 November 2001).

"Dynamic instability" – is not a reference to the current fluctuations in share prices on the stock market but a description of the characteristics of microtubules, tiny polymers constructed from the protein tubulin which are an essential component of the cytoskeleton. At the same time, share prices certainly have something in common with microtubules – they also alternate between optimistic growth and catastrophic decline. Microtubules also transit from a catastrophic situation to a more profitable status, and scientists refer to this as depolymerization and polymerization: the shortening or lengthening of microtubules through the loss or addition of tubulin

building blocks. The entire population of microtubules in the cell at any one time consists of a mixture of both slowly growing and quickly contracting polymers. The interconversion between these two different states takes place in a purely stochastic manner. The dynamic behaviour of microtubules had already been discovered in 1984. It represents the fundamental organisational principle for a whole series of important cellular procedures. In contrast to bone skeletons, which carry out the support function exclusively, this dynamic basic state enables the cytoskeleton to also carry out cellular movements: in this way microtubules organise the transportation of cell organelles, the growth of nerve cell fibres, or the segregation of chromosome pairs during cell division. So how does this happen? The microtubules occur in greatest density around the cell nucleus and radiate outwards from here in fine filigree fibres to the cell periphery. As a result of its dynamic instability, a newly formed microtubule will only survive if both its ends are protected against depolymerization. In cells the so-called minus ends of the microtubules are usually protected by the microtubule organisation centres from which these fibres grow. The organisation centres continuously produce new microtubules which have a purely random distribution. A micro-

tubule that grows out from this type of centre can be stabilized if its "plus end" is trapped by specific proteins. If this happens, then the microtubule will form a fairly stable binding element between this structure and the organisation centre. For this reason, microtubules only spread in specific areas of the cell and create a mechanism for the spatial organisation of cells and for directional movements of organelles. Compared with microtubules assembled from purified tubulin, microtubules in a physiological environment polymerize four times as fast and transit more frequently between polymerization and depolymerization. The Max Planck scientists Anthony Hyman, Kazuhisa Kinoshita, and their colleagues set out to discover the factors controlling the dynamic properties of microtubules. In the case of the African clawed toad, *Xenopus laevis*, they came across a microtubule-related protein, XMAP215 for short, which significantly increases the polymerization rate of the microtubules: without XMAP215, no microtubule growth takes place in the African clawed toad. Furthermore, the researchers were able to identify the dominant "catastrophe trigger": the protein XKCM1, a member of the kinesin family, destabilizes the microtubules and therefore gets the shortening process underway. Both factors therefore have an opposing effect on

micro-tubule stability. Using in vitro tests, the scientists were able to demonstrate that the interaction of these two proteins clearly determines the stability of the microtubule network: XMAP215 alone provides a quicker polymerization rate, comparable with those observed in vitro. When XKCM1 is added, the polymerization rate is not affected. However, XMAP215 reduces the destruction rate triggered by XKCM1, i.e. the transition into the depolymerization process. "The similarity between dynamic instability in vivo and our in vitro system consisting of tubulin, XMAP215, and XKCM1 is obvious", says Anthony Hyman. "We possibly hold the key in our hands that will allow us in the future to also perform complex cellular processes such as the organisation of cell division spindles in vitro." Not only would the scientists be one step closer to understanding the basic principles of cellular organisation, but these findings could also become relevant for the medical world. It has already been known for a long time that defects in microtubule dynamics influence cancer disease. Microtubules are therefore a target for chemotherapy: taxol, for example, stabilizes microtubules and prevents dynamic instability. In certain types of cancer, such as breast cancer, it triggers the death of the cancer cells. ●



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ASTRONOMY

X-ray View of Venus

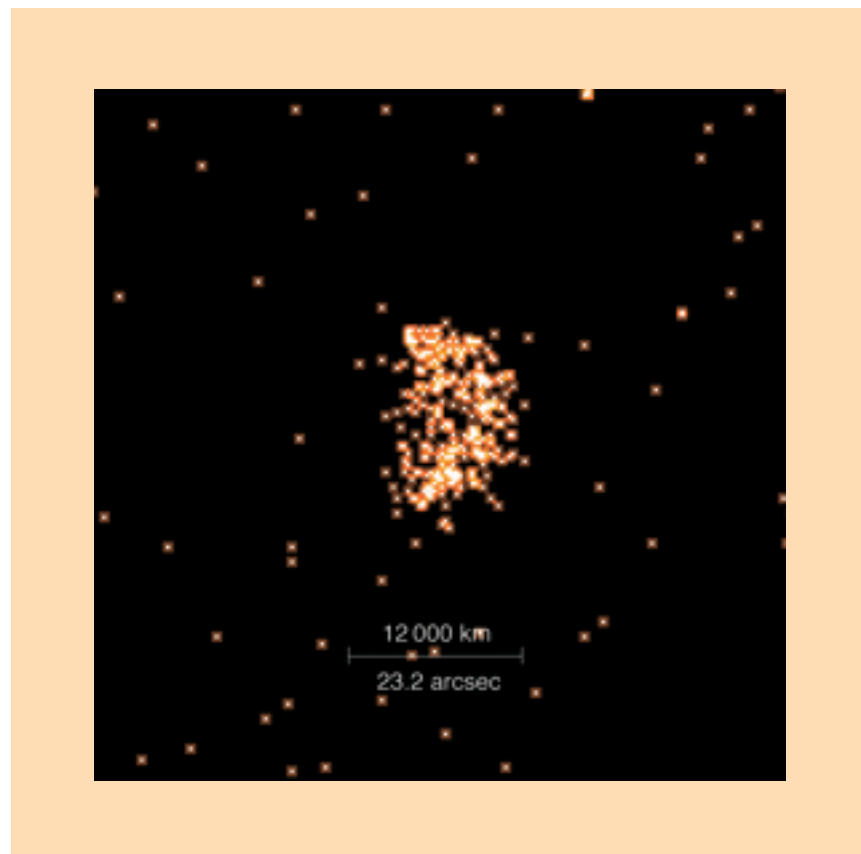
A German-American team led by Konrad Dennerl from the Max Planck Institute for Extraterrestrial Physics (MPE) in Garching near Munich has captured the first ever view of Venus using an X-ray telescope; the instrument is orbiting the Earth on board the Chandra satellite. The "X-ray fluorescence" occurs in the upper layers of Venus' atmosphere. It is caused by X-rays from the sun. A Low Energy Transmission Grating developed at the Max Planck Institute in Garching played a major role in these observations as it allowed high resolution spectroscopy to be carried out using the Chandra telescope. The scientists will report on their findings in the next editions of the renowned technical journal *Astronomy & Astrophysics*.

Venus circles the Sun at an average distance of 108 million kilometres, therefore within the Earth's orbit: the angular separation of Venus from the Sun, as seen from the Earth, consequently never exceeds 48 degrees. For this reason, we observe it as a bright morning or evening star in the Eastern or Western skies at dawn/dusk, but never at midnight in the far South. The small angular distance to the Sun presents a problem for most X-ray satellites: they are only capable of viewing objects at an angular distance of approximately 90 degrees from the sun, otherwise scattered solar light interferes with the observation, the satellite heats up or – in the case of fixed solar cells – the power supply is disturbed.

The American X-ray satellite Chandra can approach the Sun to a minimum angular distance of 45 degrees. This is just enough for Venus, though it must be located at a maximum distance from the Sun and this occurs around every 19 months on two successive occasions. In January 2001, the timing was right: Venus shone as a bright evening star and was visible through the telescope as a "half-moon". Venus shines very brightly as its dense atmosphere reflects a large proportion of solar light into space. This presented a particular challenge for the scientists, as the planet's bright optical light could degrade the X-ray measurements. At the same time, attenuating filters must not be too dense, otherwise they will weaken not only the visible light but also the X-

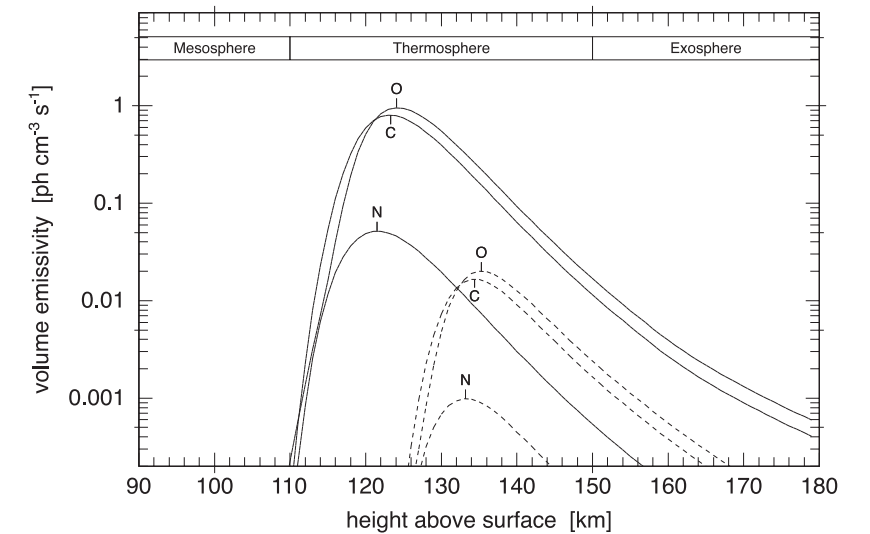
rays under investigation. The filters on board Chandra are designed to suppress the optical light with an intensity adequate for most X-ray sources. However, in the case of Venus, the densest filter still allows some light to penetrate. Whilst this does not have a significant effect on the X-rays images, it does degrade spectral investigations where radiation is analysed in terms of wavelength. To overcome this problem, the scientists used special observation technology. The transmission grating developed at the Max Planck Institute for Extraterrestrial Physics disperses the radiation captured by the telescope so that the optical light is deflected onto areas outside the X-ray detector and can no longer cause any interference. At the same time, the

The first X-ray image of Venus, captured on 13 January 2001 using the X-ray telescope on board the Chandra satellite.



grating also enables a precise analysis of the X-ray spectrum to be carried out. This showed that X-ray radiation is essentially concentrated on only 2 wavelengths which correspond exactly with the X-ray fluorescence lines of oxygen and carbon, the main components in the carbon dioxide atmosphere of Venus. How does this fluorescence occur? X-ray photons from the Sun catapult an electron from both the oxygen and carbon atoms, and advancing electrons immediately re-occupy the positions that have just become free. During this process, radiation is released and this is the X-ray fluorescence observed. Unlike the optical photos, the X-ray image clearly detects Venus as a half-lit crescent with considerable brightening on the sunward limb. Researchers at the Max Planck Institute for Extraterrestrial Physics have simulated this effect in detail on the computer. "The fluorescence X-rays are most powerful at heights of 120 to 140 km. In the X-ray range, Venus' Sun-lit hemisphere appears surrounded by an almost transparent luminous shell which looks brightest at the limb, as we can see most of the luminous material here", says Konrad Dennerl. The properties of these upper atmospheric layers, of the thermosphere and the exosphere, can therefore be effectively investigated using X-ray observation. An additional interesting discovery: in contrast to the X-ray radiation of comets, the interaction between the heavy, highly ionized atoms of the so-

ILLUSTRATION: MPI FOR EXTRATERRESTRIAL PHYSICS



The intensity of the X-ray fluorescence radiation in the atmosphere of Venus in relation to the height above the surface. The continuous lines represent the vertical incidence of sunlight ("subsolar"), whilst the dotted lines refer to oblique incidence ("terminator"). In all cases the fluorescence radiation is most powerful at heights of 120 to 140 km. The letters C, N, O correspond to carbon, nitrogen and oxygen; these elements emit the fluorescence radiation.

lar wind and the atmosphere plays a secondary role with Venus. "This is mainly due to the fact that the gas in the atmosphere is significantly denser and more concentrated than that in the coma of a comet", says Dennerl. The complexity of the measurements is reflected in the statistics: the intensity of the registered X-ray radiation was one ten billionth of the optical radiation – the detector only captured an X-ray photon approximately every 40 seconds. For this reason, Chandra had to observe Venus for three hours and "collect" the photons. During this time, Venus and the Earth travelled in their orbits around the Sun and Chandra moved around the Earth. This "choreography" caused the X-ray image of Venus to move over a range of twenty times its diameter. To achieve a sharp image, the photons had to be individually corrected in line with this movement, and the CCD detector had to be read every three seconds. The X-ray photons on the image appear as individual dots.

At the time of the observation, the visible diameter of Venus was only around an eightieth of the angular diameter of the Moon; Chandra has now made it possible for objects on such a small scale to be resolved in X-rays. ●



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PSYCHOLOGICAL RESEARCH

Why are we particularly good at performing symmetrical movements

Max Planck Researchers disprove a twenty year old doctrine: movements are coordinated by way of perception and perceptual imagery, and not in the motoric system. In bimanual movements there is a tendency towards mirror symmetry which has often been explained by the co-activation of homologous muscles. Researchers at the Max Planck Institute for Psychological Research have now discovered that the symmetry tendency is actually towards perceptual mirror-symmetry, regardless of the muscles involved. Movements which are easily perceived seem to be easily controlled. People are able to perform highly complex, even "impossible" movements, when the perceptual effect of the movement is simple (NATURE, 1 November 2001).

Humans tend to synchronize their hand movements in a mirror-like fashion. Even involuntary slips from asymmetrical movement patterns into symmetry occur, especially with higher movement velocities. How can this spontaneous tendency towards symmetry in bimanual movements be explained? Most researchers have favoured the explanation that the tendency to move in symmetry is closely related to the symmetric structure of the body and the nervous system.

In accordance with this traditional belief, the symmetry tendency can be explained by a tendency to co-activate anatomically homologous muscle groups. At first glance, such an explanation appears quite plausible: Homologous muscles, as well as bilaterally situated areas in the two brain hemispheres and in the spinal cord, can easily be activated together. Furthermore, they are interconnected through neuronal pathways, which provide for an intensive and effective "express communication". However, there is obviously an alternative possible explanation. Maybe there is no tendency to simultaneously activate homologous muscle groups, but instead a tendency towards spatially symmetric movements, i.e. movements which look and feel symmetric. Maybe we are able to control easily perceived movements particularly well. In a series of simple movement experiments, Franz Mechsner, Dirk Kerzel, Günther Knoblich, and Wolfgang Prinz at the Max Planck Institute for Psychological Research demonstrated that the symmetry tendency is actually towards perceptual symmetry, without regard to homologous muscles or motoric neuronal commands (NATURE, November 01, 2001). In one of their experiments, the researchers examined bimanual finger oscillation, the

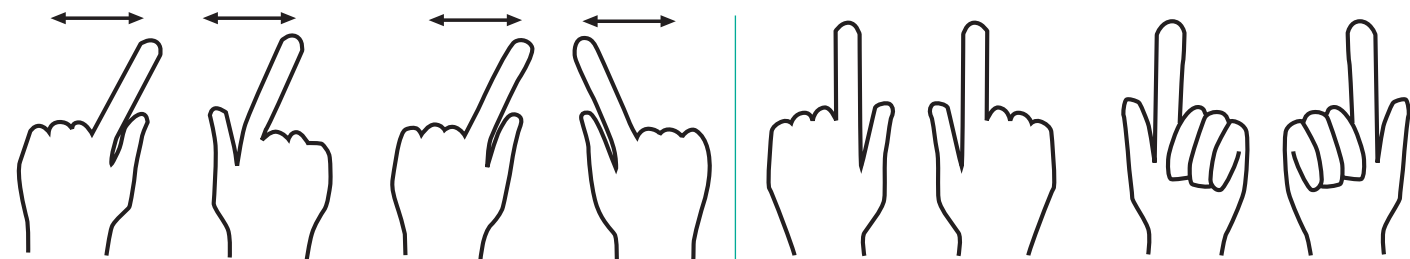
classical model to demonstrate the symmetry tendency (see Figure below). In this model, the participant moves both index fingers synchronously to the left and to the right following a metronome beat. Beyond a critical frequency, it can be observed that most participants switch from this "parallel" movement mode into a symmetric mode, where the two index fingers move towards and away from each other. The symmetric mode, on the other hand, is always stable up to the highest frequencies. The researchers at the Max Planck Institute extended this model in a particular way. Similar to the classical model, participants were instructed to move their index fingers in parallel as well as in symmetry. As an additional and newly introduced condition, one hand was placed palm-up while the other hand was placed palm-down (see Figure below). As for a definition, positions in which both hands are either palm-up or palm-down are called "congruent". Positions where one hand is palm-up and the other palm-down are called "incongruent". Interesting for the experiment are the "incongruent" hand positions, because here the parallel mode of finger oscillation goes together with periodic co-activation of homologous muscle groups. If there actually was a tendency to simultane-

ously co-activate homologous muscle groups, then here the parallel mode of movement should be more stable than the symmetric mode. On the other hand, if there was a tendency towards perceptual symmetry, then the symmetric mode should still be more stable than the parallel mode, even though non-homologous muscle groups are co-activated. The findings were straightforward. In the congruent as well as in the incongruent hand position, the symmetric finger oscillation pattern is more stable than the parallel one, independent of the muscles involved. Spontaneous switches from a parallel movement mode into a symmetric mode can be observed at higher velocities, but not in the other direction. Conclusion. The spontaneous symmetry tendency in finger oscillation is a tendency towards spatial symmetry, without regard to the muscles or motoric neuronal commands involved. Further experiments by the Max Planck Institute researchers suggest that these findings can be generalized: the symmetry tendency in bimanual movements is generally a tendency towards perceptual spatial symmetry. Franz Mechsner and his colleagues suggest that voluntary movements are organized by way of a representation of the intended perceptual goals, whereas the corresponding motor activity is

rather spontaneously and flexibly tuned in. But what is the final explanation for the symmetry tendency? The researchers believe that people tend to perform movements which can be easily controlled via perception and mental imagery. This notion is contrary to traditional theories which have argued that movements are coordinated in motoric neuronal structures. According to these theories, coherent motoric representations, i.e. muscle-oriented neuronal activation patterns, are organized in the motoric system. The Max-Planck researchers argue that we do not control our movements indirectly by way of such motor activation plans, but rather directly by way of perceptions and mental imagery. The researchers' proposal was corroborated in a further experiment: subjects bimanually rotated two non-visible cranks under a table, each of which controlled the circular movements of a visible flag. The left flag circled directly above the left crank and hand, whereas the right flag circled in a 4:3 frequency ratio to the right crank and hand, owing to a gear system. The subject was instructed to circle the visible flags in isofrequency, either in symmetry or in an asymmetrical mode called antiphase. In both cases, the hands have to circle in a 4:3 frequency ratio. This is a highly complex move-

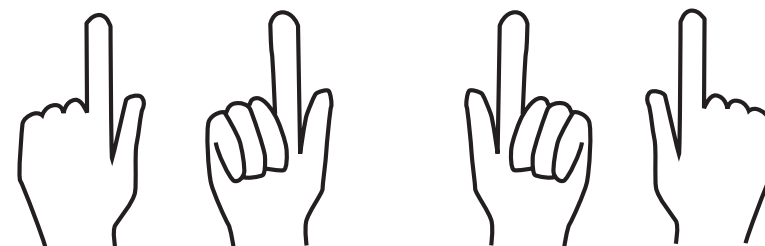
ment, which is impossible for naive subjects. The different movement patterns of the flags are not discernible from the hand movement pattern. Thus, symmetry and antiphase in the flags cannot be produced by coordinating muscular activation patterns. Despite this, subjects were successful in controlling the instructed patterns, solely by way of visual strategies and "forgetting" their hands. This means: In order to perform the instructed simple flag movements, participants easily perform otherwise impossible body movements. Conclusion: Through targeting simple effects, we can perform highly complex movements as long as we attend to the intended effect rather than the exact bodily movements. Apparently we directly control movements through perception and imagery rather than indirectly through coordination processes in the motor system. The corresponding motor activity of sometimes high formal complexity is rather spontaneously and automatically tuned in without having to be organized as an integrated whole. ●

Sample of movement: symmetric movement (right), parallel movement (left).



Congruent positions: both palm-up, or both palm-down.

Incongruent positions: one palm-up and the other palm-down.



ILLUSTRATIONS: MPI FOR PSYCHOLOGICAL RESEARCH



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