ing reversible? If bacteriorhodopsin is not completely extracted from the membrane and the AFM tip is brought back to the membrane surface, will the unfolded helices resume their folded states within the membrane, and, if so, under what conditions? Can one conduct repeated cycles of partial unfolding and refolding?

Theoretical considerations (*10*) indicate that force-induced unfolding of "two-state folders" (proteins that fold in one step) should occur cooperatively, whereas the unfolding of "non–two-state folders" (proteins that fold in two or more steps) should proceed by the formation of intermediates. Other considerations (*11*) predict that the force needed to rupture weak interactions will depend on how quickly the force is applied. This dependence on speed has been observed for the unfolding of spectrin (*7*). It remains to be seen if it also applies to the unfolding of the individual elements of bacteriorhodopsin.

Perhaps there are also lessons here for future AFM studies of force-induced unfolding and folding of soluble proteins. First, investigating the purple membrane in which the bacteriorhodopsin molecules of the two-dimensional lattice all point in the same direction offers clear advantages because only a limited portion of the protein is accessible to the AFM tip. For some soluble proteins (such as the bacterial heat shock protein GroEL) this is also the case (*12*). Second, a biophysically rigorous interpretation of the information that is available in the force curves requires the specific attachment of the AFM tip to a unique site on the protein. As Oesterhelt *et al.* demonstrate, this too can now be accomplished with genetic engineering.

All-in-all, the results reported by Oesterhelt and co-workers offer an exciting new approach to tackling a long-standing and difficult problem—how proteins fold and become inserted into membranes.

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PERSPECTIVES: ASTRONOMY

New Stars on the Block

Ray Jayawardhana

Much glory in astronomy comes from probing the farthest reaches of the universe for the most exotic beasts. But poking around closer to home for more prosaic objects has its own rewards—such as finding small groups of relatively isolated young stars destined for the limelight. Over the past few years, one such group, known as the TW Hydrae Association, has attracted quite a following, as evidenced by the high attendance of a special session during the recent American Astronomical Society meeting.

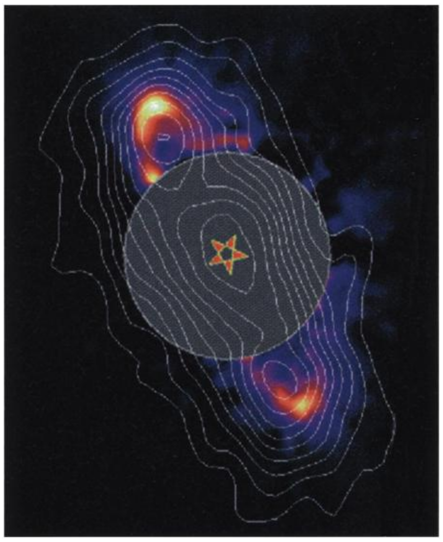
The reason for this widespread interest is that the TW Hydrae group, and others like it in the solar neighborhood, may tell us a lot about the birth of stars and planetary systems. The TW Hydrae Association, in particular, appears to be at the age at which planet formation is believed to occur. It may even be possible to take a picture of a newborn planet around one of these stars.

The star TW Hydrae first caught astronomers' attention back in 1978 (*1*). George Herbig noted that it had the earmarks of a young low-mass star, or so-called T Tauri star, including variability in brightness, a strong $H\alpha$ emission line in its spectrum, and a high abundance of lithium (an element that is easily fused in nuclear reactions and thus does not survive in older stars). Most T Tauri stars are found in clouds of gas and dust, the presumed sites of their birth, such as the Orion nebula. Curiously, TW Hydrae is not.

Subsequent work added further evidence for TW Hydrae's youth and indications for the presence of a circumstellar disk and revealed four other stars in the same region of the sky with similar characteristics (*2*, *3*). Three years ago, Kastner *et al.* (*4*) suggested on the basis of strong x-ray emission from all five systems that the group forms a physical association at a distance of roughly 150 light-years. Since then, at least seven more stars have been identified as candidate members of the TW Hydrae Association, on the basis of the same signatures of youth and the same motion across the sky as the original five members (*5*).

The group consists mostly of low-mass stars, typically a few tenths of the mass of the sun, and includes several binary systems as well as one remarkable quadruple system, HD 98800, in which two pairs of stars appear to orbit a common center of gravity. There is only one higher mass star, HR 4796A, which is twice as massive as the sun and about 20 times as luminous. The TW Hydrae stars are estimated to be roughly 10 million years (My) old (*4*, *6*), older than most T Tauri stars in star-forming regions, which are usually only about 1 My old.

The origin of the TW Hydrae Association remains a bit of a mystery. There is no obvious parent cloud (*1*, *2*), and the stars are dispersed across some 20° on the sky and 60 light-years in radial distance, making it difficult to determine their birthplace (*7*). Were they born in a low-mass cloud that has since dispersed? Or could these stars be escapees from known star-forming regions (*8*)? The slow velocities of TW Hydrae stars through space favor in situ formation, suggesting that clouds may disperse more quickly than previously thought (*9*).



Young stars reveal their secrets. This dusky disk around the star HR 4796A, a member of the TW Hydrae Association imaged in the infrared, may be the debris of planet formation.

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Being the nearest group of young stars (and three times closer than the nearest previously known star-forming region), the TW Hydrae Association offers a unique opportunity to study the evolution of cir-

The author is at the Harvard-Smithsonian Center for Astrophysics, 60 Garden Street, Cambridge, MA 02138. E-mail: rayjay@cfa.harvard.edu

cumstellar disks and planet formation. Furthermore, its estimated age of 10 million years provides a strong constraint on disk evolution time scales and fills a substantial gap in the age sequence between previously known 1-My-old T Tauri stars and 50-My-old nearby open clusters. It has been suggested that circumstellar disks evolve from dense, actively accreting structures to sparse, passive remnants within about 10 My (*10*). During this transition, grains may assemble into planetesimals, or the disk may be cleared by planets. The circumstellar disks of the TW Hydrae stars exhibit a wide variety, from classical T Tauri accreting disks, to planetary debris systems, to systems without measureable disk emission at near-infrared wavelengths implying cleared-out inner disks (*11*). A spectacular debris disk with a central cavity has been directly imaged around HR 4796A (*12*, *13*). The diverse disk properties suggest that the TW Hydrae stars are at an age when disks are rapidly evolving through coagulation of dust and dissipation of gas.

If planets have indeed formed around these stars, it may be possible to detect them with large ground-based telescopes. Adaptive optics, a technique that corrects for the blurring of the atmosphere, allows one to search within several astronomical units (AU) of the TW Hydrae stars (an AU is the average distance between Earth and the sun) for planets a few times as massive as Jupiter. Newborn planets are quite warm, and such objects should therefore be sufficiently luminous to be detected at the distance of this stellar group. In other words, we should be able to look for newborn giant planets located at distances from their parent stars similar to those of giant planets in our own solar system. At least one brown dwarf, a "failed star" not massive enough to ignite hydrogen fusion, has already been found in the TW Hydrae Association (*14*), and searches for objects of even lower mass are under way (*15*).

The commotion surrounding the TW Hydrae Association has prompted astronomers to look for other groups like it. The all-sky survey done by the Roentgen Satellite (ROSAT) satellite has been particularly useful in identifying isolated young stars through their x-ray emission. Of the recently discovered stellar groups, MBM12 and Eta Chamaeleontis (Eta Cha) are particularly interesting. At about 200 light-years, MBM12 is the second-nearest group of young stars after the TW Hydrae Association, containing only 30 to 100 solar masses of gas. It does not appear to be gravitationally bound and may be breaking up on a time scale comparable to the sound-crossing time (*16*). Thus, in a few million years, the young stars in MBM12 may appear as isolated objects not associated with any cloud material, very similar to how the TW Hydrae stars appear at present. On the basis of ROSAT detections followed by ground-based optical spectroscopy, Hearty *et al.* (*17*) have identified eight low-mass young stars associated with MBM12. Most of them are classical T Tauri stars and are likely to be a younger population than the TW Hydrae members. Eta Cha is a cluster of a dozen young stars first identified in x-ray measurements (*18*). As with the TW Hydrae group, Eta Cha is far from any substantial cloud. Its members are much less dispersed than the TW Hydrae stars and may represent an epoch intermediate between MBM12 and TW Hydrae Association.

The exploration of these nearby groups of young stars is progressing at a breathtaking pace. In the past few months, telescopes in Arizona, Hawaii, Chile, and Australia were trained on them with a variety of optical, infrared, and radio instruments. Many questions remain, but the prospects they offer for learning about star formation in the solar neighborhood and the origin and diversity of planetary systems ensure that interest in them will not wane quickly.

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PERSPECTIVES: NEUROBIOLOGY

Receptors as Kissing Cousins

Graeme Milligan

Cellular processes as different as growth factor signaling and transcription depend on interactions between proteins. Given this, it may not be surprising that certain receptors bind to related but different receptors as well as to each other. However, the dogma has been that members of the seven-transmembrane helix G protein–coupled receptor (GPCR) family pair up with their own kind but do not bind to other family members (*1*). Several recent studies, including a report by Rocheville *et al.* (*2*) on page 154 of this issue, provide evidence that GPCRs can pair up with even rather distantly related relatives to form heterodimeric receptors with distinct properties. Rocheville and coworkers show that the dopamine D2 receptor and the somatostatin SST5 receptor form heterodimers. Although pharmacologically distinct, these two GPCRs are coexpressed in striatal and pyramidal neurons of the cortex. If the reported interaction between the δ and κ opioid receptors (*3*) (closely related GPCR family members) can be considered as a pairing of brother and sister, then the union of the D2 and SST5 receptors is more akin to a marriage between kissing cousins.

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These findings have caused something of a shock. This is despite earlier experiments in which the coexpression of two mutant (nonfunctional) angiotensin II receptors resulted in formation of a homodimer that once more could activate signal transduction pathways after binding ligand (*4*). Clear evidence emerged last year that formation of heterodimers between GABA (γ-aminobutyric acid) R1 and R2 receptors was necessary for a fully functional $GABA_B$ receptor (*5*).

The usual strategy for studying receptor heterodimerization is to coexpress differentially tagged forms of the receptors and then to immunoprecipitate them (*3*). Although standard for elucidating the interactions between cytoplasmic proteins, the highly hydrophobic nature of GPCRs mandates their extraction from the membrane before immunoprecipitation. This necessity renders

The author is at the Division of Biochemistry and Molecular Biology, University of Glasgow, Davidson Building, University Avenue, Glasgow, Scotland G12 8QQ, UK. E-mail: g.milligan@bio.gla.ac.uk