MTOCs, but the challenge now is to identify these proteins and find out how their positions are established.

Part of the temporal regulation of microtubule assembly could involve translocation of γ-tubulin to and from centrosomes[4,5,13], but it is clear that, at least in fungi, γ-tubulin is present at MTOCs when no spindle is present[7,8]. The microtubule nucleating ability of the γ-tubulin ring complexes thus appears to be turned on and off by the cell-cycle regulatory machinery. The most obvious model is that the microtubule-nucleating ability might be turned off in interphase and, at the G2 to M transition, a kinase involved in cell-cycle regulation (for instance the $p34^{cdc2}$ kinase) might phosphorylate γ-tubulin, or some other proteins in the nucleating complex, and turn microtubule-nucleating ability on.

The results of Zheng *et al.* point to another possibility, however. Although the γ-tubulin ring complexes are present in the cytoplasm of unfertilized *Xenopus* eggs, they do not nucleate microtubule assembly until they become part of centrosomes, after fertilization. So it is somewhat surprising that ring complexes purified from unfertilized eggs nucleate microtubule assembly. One highly speculative, but intriguing, possibility is that in the egg they are complexed with an inhibitor molecule that blocks microtubule nucleation. This molecule might be removed artificially during the purification process. In a more natural situation, phosphorylation of such an inhibitor molecule at the onset of mitosis might cause it to release from the γ-tubulin ring complex and turn on the nucleating capacity of the complex. □

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OBITUARY

Jeffries Wyman (1901–95)

JEFFRIES Wyman, who died at his home in Paris on 4 November 1995, was a biophysicist who contributed much to our understanding of haemoglobin and its interactions with oxygen and other ligands, as a result of his work at Harvard and later at the University of Rome. His writings show that he was a master of the thermodynamics of these complex interacting systems.

Following in the footsteps of his grandfather, the first Jeffries Wyman, who was one of the founding members of the National Academy of Sciences, Jeffries started his research career at Harvard. He first looked into the dielectric constants of aqueous solutions of amino acids and peptides, which were known to be highly polar molecules. The dielectric constants of their aqueous solutions proved to be much greater than that of water, and the values were systematically related to structure. Jeffries brought his findings and interpretations to Lars Onsager, which stimulated Onsager to produce the first satisfactory theory of highly polar liquids, later improved by John G. Kirkwood.

In 1937 his first haemoglobin paper appeared, with Bernard German as coauthor, on the pH titration curves of oxy- and deoxyhaemoglobin. Measurements on oxyhaemoglobin were now possible because glass electrodes had only recently become available. Jeffries made a key thermodynamic analysis of the data, a forerunner for his later and far more extensive treatments. One such analysis, of linked functions and reciprocal relations, appeared in 1948, in the context of a review of haem proteins, and proved a powerful tool for interpreting experimental data.

It was while visiting fellow scientists in Japan in 1950 that he had a sudden flash of insight. At the time, no three-dimensional data were available on the structure of any protein, but it had long been known that the crystals of oxy- and deoxyhaemoglobin belonged to different classes. Felix Haurowitz had recently demonstrated this by showing the breakup during the transition between the two states. Jeffries realized that the rearrangement of the crystal structures implied a change, on ligand binding or release, in the conformation of the molecules themselves. As he was to put it in the published paper "...the reason why certain acid groups are affected by oxygenation is simply the alteration in their position and environment which results from the change of configuration of the hemoglobin molecule as a whole accompanying oxygenation".

This was a clear statement of the concept that Jacques Monod was later to christen allosterism. Jeffries developed the idea at Harvard with his student David Allen, and the paper was eventually published in 1951. Today, in the wake of overwhelming and detailed confirmation by the work of Max Perutz, the idea seems so obvious that we take it for granted.

Jeffries resigned from Harvard a year later to become the first Science Attaché of the American Embassy in Paris. After three years he went on to serve as Director of the UNESCO Science Cooperation Office for the Middle East, with headquarters in Cairo, with responsibilities extending from Morocco to Pakistan.

When that assignment came to an end in 1960, he was for a time uncertain what to do. His doubts were resolved by a visit from a brilliant and enthusiastic young Italian, Eraldo Antonini, who urged Jeffries to join his group at the University of Rome, working on haemoglobin on problems closely related to those studied by Jeffries at Harvard. He agreed to come for one year and stayed for twenty-four, in what proved to be the most productive years of his research life.

A visit to Paris in 1964 to discuss allosterism with Monod, whom he knew from his years at the American Embassy, and J.-P. Changeux, led to the paper by Monod, Wyman and Changeux published in 1965 on a model for allosteric enzymes, including haemoglobin as an "honorary enzyme". This was one of the most influential of the many models proposed to account for such phenomena. Jeffries followed this by a large and rather formidable paper on "allosteric linkage" in 1967, and continued to work on allosterism for the rest of his life.

He was coauthor of two books: *Biophysical Chemistry* (1958), which he and I wrote together, dealing with topics we had presented at Harvard; and *Binding and Linkage: Functional Chemistry of Biological Macromolecules* (1990) with Stanley J. Gill. The latter was the product of some twelve years of thought and rewriting, in constant consultation with critical friends. It represents a final legacy of the two authors, both of whom have now died, and a powerful tool for investigators in this important and difficult field.

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