filaments. The rates in question have been determined[5]; ADP-bearing subunits dissociate five times as fast from filament ends as ATP-subunits. A depolymerizing filament with terminal ADP-subunits loses monomers at five time the rate of a lengthening one with an ATP cap. In other words, the composition of a shortening filament end favours depolymerization and that of a lengthening filament end disfavours it. It follows that the preferred direction of filament growth depends on the concentration of actin monomers. At high monomer concentration, attachment of monomers prevails over dissociation, leading to lengthening filaments with ATP caps. At low monomer concentration, association is slower than dissociation.

Filaments thus shorten and possess terminal ADP-subunits. Near the so-called critical concentration, at which the transition from shortening filaments into lengthening filaments occurs, relatively small changes in the monomer concentration lead to a major change in the polymerization mechanism of actin. Just below the critical monomer concentration, ADP-subunits dissociate rapidly from filament ends; just above it, filaments develop ATP caps and dissociation of the terminal ATP-subunits is slow. The lesson is that small changes in monomer concentration, under the right circumstances, can exert a greatly amplified effect on the composition of filament ends, very probably on their reactivity towards 'capping' proteins, and certainly on the growth rate of filaments[4].

Despite this considerable advance in our understanding of actin assembly, important questions remain to be answered. For example, do ATP-monomers bind to an ATP cap at the same rate as to filament ends with ADP-bearing subunits? A recent theoretical discussion analyses the consequences that the answer might have[6]. If the ATP-monomers prefer ATP caps, lengthening filaments with their ATP caps will continue to grow because they can incorporate monomers rapidly, whereas shortening filaments, with terminal ADP-subunits, will go on depolymerizing because they bind monomers only slowly. Thus both lengthening and shortening filaments will coexist in the solution, and will interconvert only slowly. No experimental evidence for this phenomenon yet exists, but the theoretical treatment shows what ramifications of the ATP-hydrolysing system may come to light.

Another open question is whether or not the two ends of the filaments behave differently in the above respects. Under physiological conditions, the barbed end binds and releases actin molecules about ten times faster than the pointed end. In most types of experiment, the sum of the growth rates at the two ends is measured. Because of the much higher activity at the barbed end, the information that emerges reflects mainly the events at that end, for they swamp the slower reactions occurring at the pointed ends. Many proteins are known to bind to the barbed ends and there modulate the polymerization and disassembly of actin[7]. Indeed, only one cytoskeletal protein has so far been found to associate with the pointed ends of filaments[8]. Perhaps, in general, the barbed filament ends in cells are occupied by proteins which regulate their dynamics, whereas the pointed ends are most often free. This makes it all the more important to develop methods for investigating what goes on at the pointed ends of the filaments. □

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Albrecht Wegner is in the Institut für Physiologische Chemie, Ruhr Universität Bochum, Postfach 10 21 48, 4630 Bochum 1, FRG.

100 years ago

ACCORDING to the *North China Herald* there died a few months ago at Pekin, the greatest Chinese mathematician of the present century. His name was Li Shan-lan, and he was Professor of Mathematics at the Foreign College in the Chinese Capital. He differed from the mathematicians of Europe in this respect, that he denied the non-existence of a point. "A point," said Prof. Li, "is an infinitesimally small cube," and in saying this he only reproduced the theories of Chinese sophists 2000 years ago. A great writer of that age said: Subtlety is the occult part of the minute. Be a thing subtle or gross, it seems to me that it must have a form. But I take it that what is neither gross nor subtle can neither be talked of nor imagined.

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Drosophila development

Abdominal gene organization

from Phil Ingham

OVER the past few months, the growing interest in the developmental genetics of the fruitfly, *Drosophila melanogaster*, has received an added stimulus from the discovery of a 'homoeo box' sequence that characterizes some of the genes underlying development[1,2]. One focus has been on the bithorax complex — a cluster of genes that control the development of all segments of the *Drosophila* body posterior to the second thoracic segment. Yet, while the discovery of several homoeo box sequences in the bithorax complex has facilitated identification and analysis of a transcript deriving from its distal or 'abdominal' region [1], understanding of this region at the developmental and genetic level has remained less than comprehensive. An extensive analysis by Morata and co-workers, published on page 108 of this issue[3], goes a long way towards redressing the balance. Intriguingly, the genetic organization of the bithorax complex that emerges corresponds well with the distribution of homoeo box sequences (see ref. 4) within the complex.

The induction and identification of mutant alleles of genes has had an important impact on the study of the bithorax complex. Mutations mapping to the proximal region of the complex have dramatic effects on the development of the adult fly; *bithorax* (*bx*) and *postbithorax* (*pbx*), for example, transform the small metathoracic appendage, the haltere, into the much larger mesothoracic wing[5,6]. Equally as striking is the replacement of part of the first abdominal segment by thoracic legs that is caused by *bithoraxoid* (*bxd*) mutations. Using these gross changes in developmental potential as an assay, E.B. Lewis has carried out a detailed dissection of the proximal region of the complex[6,7,8]. The complexity of the genetic organization that is revealed has since been confirmed in almost every particular at the molecular level[9]. Lewis has demonstrated the existence of four genes or functional units, *abx* (*anterobithorax*), *bx*, *pbx* and *bxd*, each of which controls the development of a specific developmental compartment[10] from the posterior compartment of the mesothoracic segment to the anterior compartment of the first abdominal segment. All four genes seem to be subsumed by a fifth gene, named *Ultrabithorax* (*Ubx*), mutations of which fail to complement *abx*, *bx*, *pbx* and *bxd* mutations. The region of the body affected by all these mutations is thus termed the *Ubx* domain[3]. Molecular analysis has revealed that *abx*, *Ubx* and *bx* mutations all fall within a single large transcription unit (termed the *Ubx* unit) whilst *bxd* and *pbx* mutations map in a smaller adjacent transcription unit (the *bxd* unit)[9]. This genetic and structural complexity is still not fully understood, but it seems that transcripts from the *Ubx* unit are required in all four compartments that constitute the *Ubx* domain[11], and that transcription may be potentiated in two of the compartments by the *bxd* unit[4,12].

In contrast to these complexities of control by the proximal region of the bithorax complex, Lewis suggested that the development of each abdominal segment of the fly is simply controlled by one of the *infra-abdominal* (*iab*) genes[6]. Whilst this provides a reasonable working model of the bithorax complex as a whole, it makes no predictions about the nature (if any) of the hierarchical organization of the abdominal region of the complex. The novel and important finding of Morata and collaborators[3] is that the abdominal region