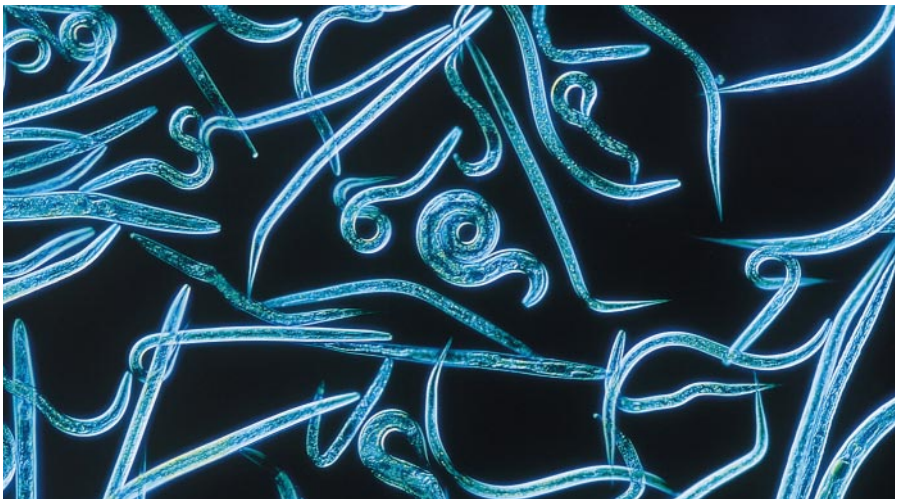

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Figure 1 **Worming out its secrets — the genome of the nematode *Caenorhabditis elegans* is now "essentially complete".**

gate *C. elegans* genes. Comparison with predicted human proteins shows that whereas 32% of worm proteins are similar to human sequences, 70% of human proteins identify similar sequences in *C. elegans*[1] — presumably this difference reflects the relative lack of information about human proteins. Those of us with established 'worm' labs are approached monthly, if not weekly, by people who have discovered that *C. elegans* contains a gene similar to one that they are studying. Indeed, although the worm lacks genes for some proteins, such as sodium channels, trk receptors and connexins, it has something for almost everyone. Genes have been identified for most known signalling proteins and transcription factors (see, for example, refs 6 and 7), as well as many genes that are similar to human disease-related genes.

But the benefits of the sequencing project go beyond merely identifying genes and working out the sequence. First, the *C. elegans* groups have shown that complex genomes can be sequenced. A strong argument can be made that the work of the *C. elegans* Genome Sequencing Consortium changed the course of the Human Genome Project, pushing it from a mapping mode to a sequencing mode. Second, the *C. elegans* project has been a model for how an efficient genome effort can be run. As far as I know, the consortium was the first to show the efficiency and cost-effectiveness of using an assembly-line approach rather than a researcher-orientated strategy. Third, the *C. elegans* Genome Project has stimulated the creation of powerful software needed to manipulate the genomic data. For example, the development of ACeDB (standing for 'a *C. elegans* database') by Richard Durbin and Jean Thierry-Mieg showed that infinite-record databases could be constructed. This database has been applied to other genome projects such as *S. cerevisiae* and the plant *Arabidopsis thaliana*. Another example is GENEFINDER, constructed by Philip Green and LaDeana Hillier, which shows how coding sequences can be identified despite the complications of intron–exon structure and alternative splicing.

Fourth, and to me most important, the *C. elegans* Genome Project is a superb model of how sequencing can best serve the scientific community. When he first described the project, John Sulston remarked that one of his main goals was to promote an open and free exchange of materials. From the start, all data, clones and sequence were freely available, leading to the involvement of the entire *C. elegans* community. This cooperation accelerated the mapping phase of the genome project by connecting the physical and genetic maps, and the openness was increased as the genome was sequenced. In a sense the *Science* paper, although a welcome benchmark, is somewhat anticlimactic because sequence data (even unfinished sequences) were made available as they were produced[3,4].

Obtaining the sequence — in itself an extraordinary achievement — sets the stage for the much larger project of analysing and understanding the genome. About 15% of the predicted genes have been confirmed by cDNA analysis. Confirmation, correction and annotation of the sequence will take many years, and will depend on our understanding of *C. elegans* biology. Even more important will be analysis of the regulatory pathways that link the genes, their products and their biological functions. Those studying *C. elegans* have always taken pride in the fact that they try to look at the whole animal. So, although publication of the sequence is an occasion for celebration and congratulation, it is also a call to get back to work. □

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**Biomechanics**

# The quirks of jerks

**M. A. R. Koehl**

The back-and-forth motion of ocean waves can rip off plants and animals that are attached to the shore, and therefore affect the structure of bottom-dwelling communities in shallow coastal habitats[1,2]. By analysing the forces on organisms in waves, we can try to understand why some body designs are resistant to being washed away, whereas others are more vulnerable. Flexible organisms such as kelp, for example (Fig. 1, page 623), can avoid large hydrodynamic forces by moving with the water as it sloshes shoreward and seaward. But, reporting in *Limnology and Oceanography*, Denny and colleagues[3] point out the danger of going with the flow. A flexible organism that moves with the surrounding water gains momentum, which can impose an inertial force on the structure that attaches it when the tether yanks the organism to a halt. Through a series of simple mathematical models, the authors show that the inertial force on a flexible organism that has reached the end of its rope can sometimes be larger than the hydrodynamic forces it experiences.

The mechanical flexibility of organisms attached to the substratum can reduce the fluid-dynamic forces that they must withstand by several mechanisms. Flexible organisms — such as trees in the wind and sea anemones in tidal currents — experience a considerable reduction in the drag force that pushes them downstream as they are reconfigured by the moving fluid into more streamlined shapes[4,5]. Flexibility can also sometimes protect the attachment organs of bottom-dwelling creatures from bearing large forces if the creatures are subjected to the back-and-forth water motion of ocean waves. Wave-swept organisms are subjected to forces that depend on the instantaneous velocity (drag and lift) and acceleration (added mass force and virtual buoyancy) of the water relative to them[4,6,7]. The sum of these forces on a rigid organism in waves varies with time as the water flows back and forth. In contrast, a

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Figure 1 **Flexible organisms like these kelp attached to wave-swept shores can avoid bearing hydrodynamic forces by moving with the water. But, according to Denny *et al.*[3], they may experience large inertial forces if they are suddenly stopped short at the end of their leash.**

flexible organism that can move with the water in waves can avoid being pulled by these hydrodynamic forces until it is strung out in the direction of flow and the water moves past it. The longer the organism relative to the distance the water moves before it flows back the other way, the more likely the organism is to avoid flow forces at times when accelerations and velocities are high[8].

Denny *et al.*[3] now point out that such a reduction in hydrodynamic force may not protect the structure that attaches the organism to the shore from potentially damaging loads if the inertial force on the organism is high when it reaches the end of its tether and suddenly stops moving with the flow. They used mathematical models to illustrate how the mass and size of an organism, the stiffness of its tether, and the period and peak velocity of the waves affect the inertial force on the organism when it reaches the end of its rope.

The authors propose that a dimensionless index, the 'jerk number', can be used to predict when inertial forces are important for a wave-swept organism. They used this approach to model the forces on kelp with upright, bending stipes, kelp with rope-like stipes, and mussels attached by stretchy, visco-elastic byssal threads. The jerk number is the ratio of the maximum inertial force that could act on an organism under particular wave conditions to the maximum hydrodynamic force that it would encounter if it were stationary and did not go with the flow. High jerk numbers (and, thus, large inertial forces) occur when the frequency of the back-and-forth motion of the waves is low relative to the resonant frequency of the organism. In such cases, flexibility is not a force-reducing mechanism. In contrast, if the period of the waves is short relative to the time it takes the organism to get strung out, the inertial force is low or zero because the mass never reaches the end of its tether. So, the tether is not pulled and flexibility can reduce the forces experienced in waves.

The mechanical properties of the tissues that attach organisms to the substratum can have a big effect on their likelihood of experiencing large forces. For example, extensible kelp stipes act as shock absorbers, allowing the plants to withstand transient high forces[9]. The visco-elastic properties of an organism's tissues cause different mechanical responses to environmental flows that vary on different timescales[10]. Denny and colleagues also explored tuning of an organism's material properties in time-varying flow environments. Their models revealed that the inertial loading of wave-swept organisms peaks at specific frequencies. So, the authors suggest that the structure and material properties of organisms might be altered — either by physiological response or during evolution — such that potentially damaging loads are avoided. An area for exploration might be how such tuning is maintained as these organisms grow and as flow conditions change with the seasons. □

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**Structural biology**

# The ABC of a versatile engine

**Michael J. Welsh, Andrew D. Robertson and Lynda S. Ostedgaard**

Early in evolution an engine called a nucleotide-binding domain (NBD) was created. As evolution progressed, this engine proved quite adaptable — it now powers an amazing variety of machines. On page 703 of this issue, Hung and colleagues[1] describe the structure of the histidine permease NBD domain from *Salmonella typhimurium*, giving us a first look at this remarkable molecular engine. And, like any engine seen for the first time, we are eager to find out how it works.

Members of a large family of proteins called the ATP-binding cassette (ABC) transporters[2] contain two NBDs together with two membrane-spanning domains (MSDs). These proteins are found in archaea, eubacteria and eukaryotes, and are increasingly recognized as the cause of human genetic diseases. The NBDs of different ABC transporters have considerable sequence similarity, and they all bind and hydrolyse ATP. In contrast, the transmembrane helices in the MSDs show little sequence similarity.

The organization of the NBDs and MSDs into a polypeptide chain varies between different ABC transporters. In many prokaryotic transporters, such as the *S. typhimurium*

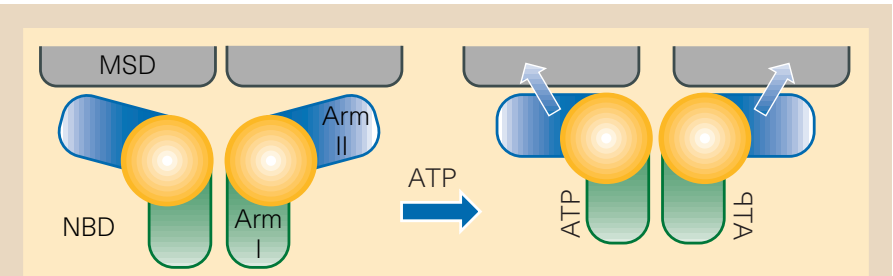


Figure 1 **The nucleotide-binding domain (NBD) of *Salmonella typhimurium*. ATP-dependent conformational changes in the NBD are transduced into conformational changes in the membrane-spanning domains (MSD).**