What does it mean for a molecule to generate force? A good way to think about the force generated by a molecular machine is that force is one of the products of the cyclic, fuel-consuming chemical reaction. If the chemical reaction is favorable it will go forward even against a moderate load force. But if the force is too high, then it will inhibit the reaction, just like a high concentration of a chemical product would.

Force generation or force sensation? Rather than being a force-generating enzyme, it might be better to think of a protein machine as being a force-sensitive enzyme. Indeed, suppose that the different chemical states in Figure 1A correspond to different signaling states: the red state could be the closed state of an ion channel or the inactive state of a kinase and the green could be the open or active state. Then a rightward-directed force will tend to bias the channel into its open or active state. In this case a transition between two states can be used for sensing force rather than generating it.

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Q & A

R. McNeill Alexander

Neill Alexander is a Research Professor in the Institute for Integrative and Comparative Biology, University of Leeds. He has worked on the biomechanics of animals ranging from jellyfish to elephants and dinosaurs, and also on humans. Much of his research has been on running and jumping, especially on the roles of tendon elasticity. He has been Secretary of the Zoological Society of London, responsible for supervising the management of its operations including London and Whipsnade Zoos. He has also served as Editor of Proceedings of the Royal Society B. He is the author of seventeen books, including Animal Mechanics *(1968, 1983) and* Principles of Animal Locomotion *(2003).*

What attracted you to biomechanics in the first place? It seemed a possible way to save my PhD. I was working in the Cambridge University Zoology Department, on the gas-filled swimbladders that serve as buoyancy organs in fishes. We thought they might have a secondary function as pressure sensors. Expansion and compression of the gas, as the fish swam up and down in the water, might be detected by sense organs in the swimbladder wall. I was subjecting fish to small pressure changes, and trying to record responses in the brain. Sixteen months' work had yielded no useable results. But I was sharing a laboratory with Ken Machin, who had trained as a physicist. He suggested I should shift my interest from the neurophysiology of the swimbladder to its mechanics, and I completed my PhD successfully in a further 19 months.

Have you ever looked back? I wavered badly after an expedition to the Guyana rain forest in 1960. I was carried away by the amazing diversity of the fish fauna, and especially by the adaptive radiation of the jaws and teeth of characins and catfishes. I wrote a couple of papers on them, and almost settled down to be a descriptive functional morphologist. Fortunately (I think) I soon decided that biomechanics was a more promising field, both for scientific progress and for a career. I became interested in relating the mechanical properties of bone and muscle to the performance required of them in strenuous activities. For example, most teleost fish feed by sucking food into their mouths. I recorded pressures inside their mouths, calculated the stresses in the muscles involved, and found that they were close to the maximum stresses recorded in experiments with isolated muscles.

And you soon abandoned fish, didn't you? I realised that fish are difficult material, for that kind of research. The hydrodynamic forces on them are distributed over their bodies, and there is some awkwardly complex anatomy, notably in the structure of the head and the arrangement of fibres in the swimming muscles. Legs are much easier. Forces on the feet can be recorded by means of a force plate set into the floor, and the skeleton is a simple system of levers. A move from Bangor to Leeds in 1969 seemed a good opportunity for a new start.

In my early days at Leeds I investigated the mechanics of jumping by a dog, as another example of a strenuous activity. I found that as the ankle bent and extended again, in the last footfall before take-off, the calf muscles remained almost constant in length: most of the movement was due to stretching and recoil of the Achilles tendon, which had a catapult-like effect. Previously we had thought of tendon as an almost-inextensible link between muscle and bone. Now it appeared that it might have an important function as a spring. I went on with colleagues to show that tendons are important as energy-saving springs in kangaroo hopping and human running. Much of my later work stemmed from that.

Have you a scientific hero? Ken Machin, not just because he saved my PhD but mainly because of his contributions to biology. After graduating in physics, he did a PhD in radio-astronomy. Then, remarkably, he was appointed to a post in the Cambridge University Zoology Department, helping zoologist colleagues with the physical implications of their research. He and John Pringle showed how occasional electrical stimuli could keep the fibrillar flight muscles of insects in a state of oscillatory contraction, at the natural frequency of any mechanical system to which they were connected. They attached the muscle to a device whose electronically simulated stiffness and mass could be varied, and performed the first-ever work loop experiments. Then Machin went on to work with Hans Lissmann, on the electric sense of some fish that live in turbid water, or are active at night. He worked out the physics, showing how the sense could locate objects of different electrical conductivity in the surrounding water.

Have you any worries about the future of biomechanics? I am worried that so many students are scared by quite simple mathematics, such as elementary calculus and trigonometry. Many university teachers are probably making things worse, by keeping equations out of their lectures. I was disheartened by a review of my book *Principles of Animal Locomotion*, which argued that I should not expect students to tolerate an average of 0.36 equations per page. Mathematics is the language of mechanics, and biomechanics will decline without mathematically competent recruits.

Have you any hints for newcomers to the field? Use simple mathematical models for clarifying arguments and generating hypotheses. Don't try to make your model as complex as the animal it represents: you will never succeed, and the effort may be counterproductive because it is often not apparent which features of a complex model are responsible for the effects it shows. On the other hand, if a model is simple enough, you can tell what caused the effect. I have found optimization models particularly useful — models that seek the best possible structure or behaviour. For example, if a model tells me that a particular pattern of behaviour is the best possible in given circumstances, and if real animals do something quite different, that suggests that I may have failed to understand the issues at stake.

But haven't optimization models been discredited? There are pitfalls to be avoided. We must remember that, though evolution is directed by natural selection, it is constrained by ancestry: a state that a model suggests as optimal may be inaccessible because it could only be reached via disadvantageous intermediates. It is also important to remember that the incentive to use optimization theory is not to prove that natural selection or learning by trial and error work, but to check our understanding.

Have technical developments brought new opportunities? Emphatically yes. We have seen an extraordinary proliferation of equipment and techniques in the past few years. For example, sonomicrography enables us to record the length changes of muscle fibres within a living animal. Digital particle image velocimetry enables us to record the patterns of flow in the eddies behind a flying bird or a swimming fish, which tell us about energy costs and forces. There are many other examples, offering wonderful opportunities in biomechanics.

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Book review

Hats Off, Gentlemen!

Walter Gratzer

Francis Crick — Discoverer of the Genetic Code
Matt Ridley
(Atlas Books, HarperCollins, New York, 2006) ISBN 006082333X

Jacob Bronowski defined a genius as someone who has had two great ideas. By this reckoning Francis Crick was a genius several times over. Crick towered over 20th-century biology, and yet his name is not, like that of Darwin, or Einstein, or indeed Stephen Hawking, part of the common currency outside the academic groves. Part of the reason perhaps was his indifference to public recognition, and to the opportunities that the Nobel Prize affords for self-exposure. After the award in 1963 he composed the famous reply cards, that read:

Dr F.H.C. Crick thanks you for your letter but regrets that he is unable to accept your kind invitation to:

Send an autograph
Provide a photograph
Cure your disease
Be interviewed
Talk on the radio
Appear on TV
Speak after dinner
Give a testimonial
Help you in your project
Read your manuscript
Deliver a lecture
Attend a conference
Act as chairman
Become an editor
Contribute an article
Write a book
Accept a degree

An affronted recipient purportedly returned such a card with the pencilled addition, "go to stud". Crick wanted in fact little more than to pursue his science unmolested. He declined, as Matt Ridley reveals in this excellent short biography, to sit for his portrait, and his patience ran only to permitting a pencil sketch for

Borrowed from Latin Alexander, from Ancient Greek á¼ˆÎ»ÎÎ¾Î±Î½Î´ÏÎ¿Ï‚ (AlÃ©xandros), from á¼€Î»ÎÎ¾Ï‰ (alÃ©xÅ, â€œI defendâ€) + á¼€Î½Î´Ï- (andr-), the stem of á¼€Î½Î®Ï (anáº—r, â€œmanâ€). Doublet of Alejandro. (General American) IPA(key): /ËŒÃ¦.lÉ¨É¡ËˆzÃ¦n.dÉš/. (Received Pronunciation) IPA(key): /ËŒÃ¦.lÉ¨É¡ËˆzÉ‘Ën.dÉ™/. (Ã¦-tensing, rhotic) IPA(key): [ËŒÃ¦.lÉ¨É¡ËˆzeÉ™n.dÉš]. (Ã¦-tensing, non-rhotic) IPA(key): [ËŒÃ¦.lÉ¨É¡ËˆzeÉ™n.dÉ™]. Hyphenation: Alâ€§exâ€§anâ€§der. Rhymes: -É‘ËndÉ™(É¹), -Ã¦ndÉ™(É¹). Alexander (plural Alexanders). Alexander I, emperor of Russia (1801â€“25), who alternately fought and befriended Napoleon I during the Napoleonic Wars but who ultimately helped form the coalition that defeated the emperor of the French.Â Get a Britannica Premium subscription and gain access to exclusive content. Subscribe Now. Alexanderâ€™s education was not continued after he was 16, when his grandmother married him to Princess Louise of Baden-Durlach, who was 14, in 1793. Alexander is a male given name. The most prominent bearer of the name is Alexander the Great, the king of the Ancient Greek kingdom of Macedonia who created one of the largest empires in ancient history. The name Alexander is derived from the Greek: á¼ˆÎ»ÎÎ¾Î±Î½Î´ÏÎ¿Ï‚ (AlÃ©xandros; 'Defender of the people', 'Defending men', or 'Protector of men'). It is a compound of the verb á¼€Î»ÎÎ¾ÎµÎ¹Î½ (alÃ©xein; 'to ward off, avert, defend') and the noun á¼€Î½Î®Ï (anáº—r, genitive: á¼€Î½Î´ÏÏŒÏ‚, andrÃ³s; meaning 'man'). It is an example of