

Suspended by sound

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Ultrasound waves can levitate heavy balls of tungsten. This contact-free method of keeping items suspended in the air can be applied to the investigation and processing of new materials.

It is well known that radiation can exert a force. The solar wind, for example, is caused by sunlight blowing away microscopic dust particles, and its force on a sunbather is equal to the weight of a fly. It is probably less well known that sound waves also exert a force. The radiation force on a tiny sphere from a travelling sound wave is weak, proportional to the sixth power of the ratio of the sphere radius to the wavelength of the sound. But it can become more substantial — proportional to the third power of this ratio — in a standing sound wave, of the sort that occurs near reflecting walls. It has previously been shown that a siren operating at 3,260 Hz and an appropriate reflector can freely levitate drops of liquid and bubbles¹, or even a steel ball 1 cm in diameter². As Xie and Wei³ show in *Applied Physics Letters*, the levitating force of ultrasound (which has a frequency too high for humans to hear) can be enhanced even further by carefully designing the shape of the reflector. This allows them to levitate balls of high-density tungsten.

The strongest acoustic forces are exerted by the standing sound waves formed inside an almost closed box. But the 'single-axis geometry', in which a concave circular reflector faces a vibrating cylinder that emits ultrasound at a frequency of 16.7 kHz (Fig. 1), is more convenient and provides easy access to the levitating samples. Such levitators can be used to simulate the microgravity conditions of space in a terrestrial laboratory. Conversely, they are used to position samples

in space experiments, where there is no gravity. They have also been used to process materials where it is important to avoid the contamination of samples by the container wall — for example, for growing ice particles⁴, undercooling liquids far below their freezing point⁵, and heating liquid crystals⁶ and ceramics⁵ to high temperatures.

Xie and Wei³ have managed to increase the force and stability of single-axis acoustic levitation, and so were able to levitate balls of tungsten, which has a density of 18.9 g cm⁻³. They achieved this by optimizing the diameter of the vibrating cylinder and the distance, radius and curvature of the concave reflector. To understand the relationship between these geometric parameters and the observed enhancement, the authors developed a detailed model.

They began by computing the sound wave generated in their levitator from hydrodynamic theory to give the time-averaged mean square pressure and mean square velocity of the vibrating air at each point in space. They inserted these values into a general expression for the time-averaged potential of the acoustic radiation force acting on a small rigid sphere. This expression was first derived by Lev Gor'kov in an ingenious paper⁷ in 1962 (see also the discussion and application of this formula in ref. 8). It says that the sphere is attracted to regions with large air velocities and repelled by regions with high pressures. This seems intuitive — the sphere avoids places at high pressure and prefers places with large nega-

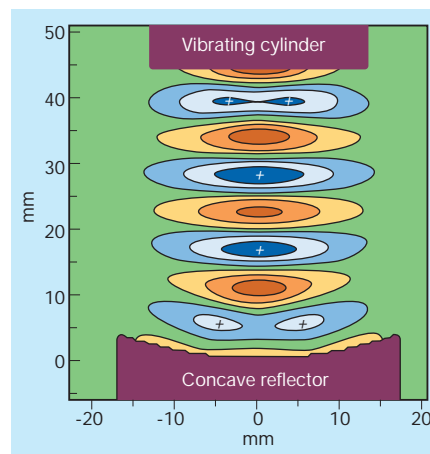


Figure 2 Contour lines of the acoustic potential computed by Xie and Wei³. Tiny objects can be levitated in the four potential wells (or minima) denoted by crosses. The middle two wells are located on the central symmetry axis, and the top and bottom wells are ring shaped. The separation of the cylinder (top) and concave reflector (bottom) in the resonance mode is approximately two wavelengths, which is 20.3 mm for sound with a frequency of 16.7 kHz.

tive Bernoulli pressure, which is proportional to the velocity squared. (Negative Bernoulli pressure provides the lifting force on an airplane wing.) But the acoustic force is a nonlinear effect; with a linear approximation of the model, any sound wave oscillates symmetrically over time, so all time averages would be zero and there would be no radiation force.

The acoustic potential calculated by Xie and Wei³ is shown as a contour plot in Fig. 2. This configuration corresponds to the resonant state in which the distance between emitter and reflector is approximately two sound wavelengths, which at 16.7 kHz is 20.3 mm for air at room temperature. The minima of the acoustic potential are marked by six crosses. As expected, these minima occur at four heights, close to the maxima of the velocity amplitudes, and their vertical spacing is approximately half a wavelength. If the sound intensity is large enough, each of these minima (or potential wells) can trap and levitate a small sample when the maximum vertical gradient of the potential (slope of the potential well) exceeds the gravitational force.

Xie and Wei³ show that the resonance frequencies and positions of stable levitation given by their model are in good agreement with the observed locations of the levitated spheres. The contours of the potential in Fig. 2 show that the two middle potential wells sit on the vertical axis of symmetry, but the wells next to the emitter and reflector form larger rings around the symmetry axis. This theoretical finding explains why the two samples at the top and bottom in Fig. 1b are located slightly off the central axis.



Figure 1 Acoustic levitation by ultrasound. In Xie and Wei's latest experiment³ the force produced by a standing wave of 16.7-kHz ultrasound, which forms between a vibrating cylinder (top) and a concave reflector (bottom), is enough to levitate small objects. The freely floating objects are: a, three polymer spheres; b, four liquid crystal samples; c, a water drop deformed to a pancake shape by the uneven acoustic pressure; and d, a heavy tungsten sphere levitated in the lowest resonance mode, which has one potential minimum.

Apart from acoustic levitation, there are several other types of contact-free levitation⁹: aerodynamic levitation (by a fluid jet), optical levitation (by a laser beam), electrical levitation (in a quadrupolar alternating electric field), radio-frequency levitation (by the eddy currents induced in a conducting sample by a conical coil), magnetic levitation (in the strong field of an electromagnet, which famously levitated a young frog^{10,11}), and superconducting levitation (by combining superconductors and permanent magnets). In all these types of free flotation, the main aim is to achieve good vertical and horizontal stability, otherwise a small perturbation may cause the levitating sample to fall.

Acoustic levitation has the advantage that it is simple and can levitate both non-magnetic and non-conducting materials. Experiments in microgravity in which metals and alloys are heated and cooled, without touching any container walls, have produced

new materials that cannot be formed by normal cooling, such as metallic glass and new superconductors. The improvements of the single-axis acoustic levitator achieved by Xie and Wei³ — increasing the levitation force with greater stability and predictability — may offer researchers the same opportunities as experiments in microgravity, but at a fraction of the cost. ■

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Human genetics

To clot or not

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In multicellular animals, there has to be a balance between the free flow and clotting of blood. One molecule involved is von Willebrand factor, and the enzyme that cuts it down to size is now unveiled.

Thrombotic thrombocytopenic purpura is a potentially fatal human disease. It results from the widespread, abnormal aggregation of platelets and a protein, called von Willebrand factor, in the small blood vessels of many organs, including the brain and kidneys. The accumulated clots of platelets and proteins obstruct blood flow and cause red blood cells to fragment, leading to serious neurological and renal malfunctioning as well as anaemia, fever and a low platelet count (thrombocytopenia). On page 488 of this issue, Levy and colleagues¹ describe how they tracked down the gene that is mutated in patients with the hereditary form of this disorder. Their work adds significantly to our understanding of the molecules involved in blood clotting.

Von Willebrand factor (VWF) is a large protein that circulates in the blood as multimers of varying sizes. One of its main functions is to mediate interactions between platelets, and between platelets and the walls of blood vessels. Both types of interaction are vital in maintaining the balance between bleeding and clotting.

Thrombotic thrombocytopenic purpura (TTP) was first described² in 1924. But it was only recently linked to an increase in the number of unusually large multimers of VWF in the blood, which suggests that these abnormal forms might contribute to

the development of TTP. Then came the discovery that the activity of an enzyme that cleaves these large multimers into smaller fragments is markedly reduced in the blood of patients with TTP³. In some forms of the disease, patients produce an antibody that blocks the enzyme⁴; in others, the activity is missing altogether³. These observations pointed to the malfunctioning of a VWF-cleaving 'proteinase' as the underlying cause of the disease. Levy *et al.*¹ have now identified the gene, *ADAMTS13*, that encodes this proteinase, and show that mutations in this gene lead to an inactive enzyme and to TTP.

The first clues to the identity of the VWF-cleaving proteinase came about five years ago when the enzyme was partially purified, revealing that it requires zinc ions for full activity and is inhibited by metal-ion chelators^{5,6}. This partially purified enzyme could cleave VWF between the amino acids tyrosine at position 842 and methionine at position 843, generating characteristic fragments. Levy *et al.*¹ followed this proteinase activity to track down the affected gene in families with TTP. They developed an assay to measure how much of the cleavage product was present in patients' blood plasma.

This assay was critical to the authors' success. It allowed them to distinguish between

unaffected people (100% enzyme activity), unaffected individuals who were carriers of the mutant gene (50–60% activity) and TTP patients (2–7% activity). It also gave them the opportunity to undertake a 'linkage' study to pinpoint the chromosomal location of the defective gene, and at the same time to identify mutations that cause TTP. Linkage analysis needs families (pedigrees) with several generations of affected and unaffected people for study, as well as a phenotypic marker — in this case the proteinase activity. Armed with good pedigrees and a good marker, Levy *et al.* embarked on a search for patterns of inherited genes in families with TTP, matching these patterns with enzyme levels until they homed in on a single gene, *ADAMTS13*, on chromosome 9. In a single, elegant study they identified the enzyme, the gene, and the mutations in that gene that cause TTP. Other investigators, using protein-purification methods, have confirmed that *ADAMTS13* is the enzyme that processes VWF^{7,8}.

ADAMTS13 is a newly discovered member of a relatively new family of enzymes — the first *ADAMTS* protein was found only four years ago⁹. The name (which stands for 'a disintegrin-like and metalloproteinase with thrombospondin motifs') reflects the various modules, or motifs, that are found in these proteins (Fig. 1, overleaf). Each module is thought to contribute in some way to the protein's overall function. This must be true of *ADAMTS13* too, as the TTP-causing mutations found by Levy *et al.* are not clustered in one region, but are spread along more or less the entire length of the gene.

It is likely that one or more of the thrombospondin motifs in *ADAMTS13* helps it to dock onto VWF, while the metalloproteinase domain, which contains the active site, does the business of cleaving VWF. The role of the disintegrin-like domain is unknown. Disintegrins are molecules that bind integrin proteins on the surface of cells. Many snake venoms contain disintegrin domains that bind to integrins on platelets, leading to either haemorrhaging or clotting, depending on the venom. The disintegrin-like domain of the *ADAMTS* enzymes is about 40% identical to those of snake venoms. So far, no *ADAMTS* protein has been found to have a disintegrin-like function. But, given the relationship between platelets and VWF, it will be interesting to determine whether this region of *ADAMTS13* interacts with platelets.

We still have much to learn about the *ADAMTS* family. For example, deregulated expression of several *ADAMTS* proteins is implicated in disease (Fig. 1), but *ADAMTS2* and *ADAMTS13* are the only members of the family for which there is a clear association between an inherited disorder and a disturbed enzymatic process. Decreased levels of *ADAMTS2* prevent