

Ingo Titze, Associate Editor

Hyaluronic Acid—The Multigrade Motor Oil of the Human Body

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MUCH IS WRITTEN AND ADVERTISED these days about products that alleviate joint pain, like glucosamine, chondroitin, and hyaluronic acid. When tissues rub against each other during motion, molecular changes can occur that can compromise gliding and rotating in our limbs and other body parts. Arthritis is an example of this.

The most amazing of the biological lubricants is hyaluronic acid (HA), also known as hyaluronan. In a water solution, it forms a clear viscous liquid, odorless and tasteless. It can be harvested from the vitreous humor of the eyeball, a rooster comb, an umbilical cord, or from bacteria. It has been around for thousands of years, in primitive as well as advanced forms of life. It seems to serve as a multigrade lubricant whenever friction takes place.

Why multigrade? It's not a term used in biology or medicine, but it's useful for establishing an analogy between friction in an automobile engine and friction in body parts. When you put oil into your car engine, it is forced (by an oil pressure pump) between the pistons and the cylinders of the engine. Expandable and contractible rings around the pistons make a tight fit between the pistons and cylinders so that no "piston-slapping" occurs when the up-and-down movement of pistons occurs at a rate of around 10–100 times a second. The quality of the oil is based on its ability to adjust its viscosity (the multigrade) to accommodate engine temperature and speed of piston movement. Viscosity is a measure of resistance to flow (or more accurately, shear rate between adjacent fluid layers). A high viscosity fluid absorbs the rubbing between hard surfaces (like pistons against cylinders), whereas a low viscosity fluid allows more rapid movement.

So, let's get back to the biological oil—hyaluronic acid. Its molecule is a long strand, known as a polysaccharide. The fundamental unit is a disaccharide, but this unit is repeated end to end on the order of 10,000 times, making a "string" of an astounding 10 m (30 feet) in length if it were completely uncoiled. We think of molecules as being submicroscopic, never to be seen with any normal optical instrument. The HA molecule would stretch from one side of a large room to the other, but its diameter would be so small that we still couldn't see it. Furthermore, it would be translucent.

In the body, and specifically in the vocal folds, the HA molecule is never stretched out. It forms a ball, overlapping and interleaving with itself many

times. Its viscosity is determined by four main factors: 1) molecular size, which can vary over a range of about 5:1; 2) concentration (or the opposite measure, dilution) in water; 3) temperature; and 4) the rate at which it is sheared (deformed). Viscosity goes up with molecular size, with concentration, with lower temperature, and with slower deformation. In the vocal folds, temperature change is not a major issue because the body regulates temperature. We don't know how much molecular size can be regulated in the vocal folds. Concentration is a major factor, however. As water enters the vocal folds from the bloodstream, it attaches to the HA molecules (by weak hydrogen bonds) and dilutes the HA fluid as a whole. The viscosity then decreases, which allows the vocal folds to vibrate more easily. In addition, the vibration itself lowers the viscosity, more so at high frequencies than low frequencies.

This all seems good, so what's the problem? What is yet to be determined is how fluid in the vocal folds redistributes itself under the forces of vibration. If it migrates to the boundaries and does not stay in the central vibrating region, the effective viscosity could go up with prolonged phonation. This would then trigger a rise in phonation threshold pressure, which would make phonation more effortful. Vocal fatigue would set in. As anxious as some of us are to get an answer to this, we must give voice scientists some time to solve this puzzle.

In summary, HA is a fascinating substance fabricated by cells within our vocal folds. Once we understand its role more thoroughly, perhaps some way of managing its abundance and mechanical properties will become part of a vocal health regimen for singers.

Ingo R. Titze is Distinguished Professor of Speech Science and Voice at the University of Iowa and Executive Director of the National Center for Voice and Speech at the University of Utah. His formal education is in physics and electrical engineering, but he has devoted much of his studies to vocal music and speech. Dr. Titze has published more than 400 articles in scientific and educational journals, coedited two books titled *Vocal Fold Physiology*, and now has three books in print: *Principles of Voice Production*, *The Myoelastic Aerodynamic Theory of Phonation*, and *Fascinations with the Human Voice*. He has lectured throughout the world and has appeared on such educational television series as *Innovation*, *Quantum*, and *Beyond 2000*. He is a recipient of the William and Harriott Gould Award for laryngeal physiology, the Jacob Javits Neuroscience Investigation Award, the Claude Pepper Award, the Quintana Award, and the American Laryngological Association Award. He is a Fellow and a Silver Medalist of the Acoustical Society of America, and a Fellow of the American Speech-Language-Hearing Association. Dr. Titze has served on a number of national advisory boards and scientific review groups, including the Scientific Advisory Board of the Voice Foundation and the Division of Research Grants of the National Institutes of Health. In addition to his scientific endeavors, Dr. Titze continues to be active as a singer. He is married to Kathy Titze and has four children and eight grandchildren. Mail should be addressed to Ingo R. Titze, National Center for Voice and Speech, 330 WJSHC, Iowa City, IA 52242. Telephone (319) 335-6600.



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