Science for Singers

A SERIES OF VOICE RESEARCH COLUMNS BY INGO R. TITZE, PHD

Engineering Vocal Fold Tissues

Over the centuries, musical instrument makers have spent countless hours in search of the ideal materials for sound production and resonation. Steel, brass, wood, gut, and various synthetic materials (polymers) have been shaped into vibrating and sound reflecting structures. The reed of an oboe, the top plate of a violin, the bell of a french horn, a piano string, or a xylophone plate all have some commonalities in their material properties. They must be deformable under vibration, absorb some energy, and give back some energy after brief moments of storage. Most important, their properties must be consistent over time. Nobody likes to play an unpredictable instrument, except perhaps as a gig.

Metals can be engineered. Brass, for example, is an alloy of copper and zinc, with the percent composition of each element and its purity being controllable. Plant and animal materials (woods, skin, gut) are less controllable in a laboratory sense, but there are many varieties from which to choose. The density, grain, moisture content, and other factors play an important role. But what about the materials that vibrate in the vocal folds or along our respiratory tract? Do we have any control over them? Can they be engineered with any degree of predictability?

There was a time in my life, early in my research career, when I would have jumped to a quick “no” answer. I would then have qualified this answer with “except, perhaps, with nutrition and exercise, but to a limited degree.” Now it appears that the prospect of systematically engineering vocal fold tissues is within scientific reach.

The process is as follows. Material-making cells (fibroblasts) that are adaptable to their environment are grown (cultured) outside of the body, in an incubator. These cells, which are young in their reproduction stage and young in expressing themselves with extracellular products, are harvested from a donor (human or animal). They are placed in an environment that is relatively friendly to tissue growth---usually a porous, sponge-like “scaffold” made of natural or synthetic fibers. The scaffold is filled with fluids that carry the appropriate nutrients to the cells. The cells can then be subjected to forces (e.g., gravitational, vibrational, or stretching) that define how they are going to reproduce and how they will make their own materials for deposition outside of the cell wall. The idea is a bit like gardening. The growth of a plant is defined by the following:

1. The seed
2. The soil
3. The irrigation
4. The wind, snow, and other forces (trampling, pruning, etc.)

Quite analogously, the biological engineering of protein is dependent on the same factors. The DNA of the cell is like the seed. It determines the basic genetic structure of the plant. But the soil (the equivalent of the scaffold of fibers), the irrigation (the equivalent of soluble fluids between the fibers), and the forces determine how this plant is going to grow once it is seeded. The extracellular material that the fibroblasts produce also depends on these factors. Thus, by stretching or vibrating the fibrous scaffold, we can influence the kind of additional protein fibers that the fibroblast cells produce. Ultimately, they may replace the original synthetic scaffold with an entirely new one, perhaps more able to handle the forces imposed on it.

The vocal folds are subjected to unusual vibrational and collisional forces. It is conceivable that repair of injured vocal folds will in the future be undertaken with engineered tissue, that which has already been exposed to the appropriate forces and other environmental factors. A wilder speculation may allow us to believe that we can improve on nature by growing "super vocal folds," those that have all the properties ideal to vocal fold vibration.

However this turns out, probably much less dramatic than presented here in a "wild dream," it is important to understand that, in biology, function determines structure and growth, as structure and growth determine function. We can influence the growth and regeneration of our tissues by what we do to them, certainly by exercise and nutrition. In that sense, we are our own tissue engineers.

This column originally appeared in the September/October 1999 issue of The NATS Journal.