COSI SIMILI, COSI DIVERSE

2. LEFT FOOT IN RIGHT SHOE

There exist molecules that have all the same atoms in them, and the atoms are all connected up to each other in the same way, and yet… they are not identical. Like hands, they are nonsuperimposable mirror images. Look in the mirror please, in case you haven't done that lately. That dismal looking character staring back at you has a ring on his or her left hand, when you had it on your right. And a left hand is not a right hand.

Such mirror image molecules (they're called chiral, from the Greek word for hand; the two forms are said to be enantiomers of each other) have the same color, they melt or boil at the same temperature. But… they often have different biological properties.

Take morphine, to which all of us who have ever had an operation are grateful (and which is strongly addictive), is a chiral molecule. One of its mirror-image forms makes us love and fear the molecule; the other enantiomer is a much less effective painkiller and is also less addictive. Aspartame is a modified amino acid that is 200 times sweeter than sugar. Its enantiomer tastes bitter. There is a patent for another sweetener made from a left-handed sugar which is sweet but indigestible (because our bodies only digest well right-handed sugars), therefore nonfattening. One form of limonene smells like oranges, its enantiomer like turpentine. A bark beetle, *Ips pini,* is attracted to the eponymic chemical ipsdienol; the mirror image form of the molecule has no effect on the bug.

Enantiomers are truly the same and not the same.

Why the difference in the properties of left- and right-handed molecules? It takes a hand to know one—the molecules in our bodies, simple and complex as they are, the molecules that recognize what we eat or what is injected into us, are often handed. In fact, all the proteins, those wonderful chemical factories that disassemble food into molecular pieces, only to reassemble the fragments elsewhere in the body into hair, skin, heart tissue, and sperm, the proteins that also do all the work of transport and defense, are built up of amino acids of one specific handedness—they're all lefties. They curl up, these proteins, into globular equivalents of a glove, a messy-looking tailoring job of a glove that is most certainly not identical to its mirror image, and that either fits very well, or doesn't fit one enantiomer of morphine or limonene or aspartame.

The left foot in the right shoe is coming, just wait.

In the laboratory, when one makes a molecule that could exist in mirror image forms, one usually winds up making an equal mixture of the two enantiomers. How to separate them (for instance to test the biological activity of the two forms)? On rare, rare occasions, the molecule crystallizes in macroscopic crystals that are mirror images of each other. This rare event happened in 1848 for the young Louis Pasteur with the potassium salt of tartaric acid, a naturally occurring molecule, sometimes crystallizing on the corks of bottles of white wine. He could then physically separate the crystals with a pair of tweezers. He was very lucky, but as Pasteur said "Chance favors the prepared mind."

Pasteur came upon another way to separate enantiomers. This was based on the ability of microbes to digest a molecule that was left-handed, while its enantiomer passed unperturbed through the digestive system. This works, but half the material is wasted. And though, through the workings of evolution, there is a bug for nearly every food, some laboratory-made products have not been here long enough for microorganisms to evolve to use them..

The way the "resolution of enantiomers" is often done is based on a simple idea, which I can illustrate by telling you an outtake from an unmade Fellini film. You know that armies are occupied most of the time with pretty silly things. So there is this huge pile of left and right handed shoes, and an officer at the Military Academy in Modena has been given the task of separating them. He is left-right challenged, but he has a couple of hundred men with nothing to do. So he takes the pile of shoes and the men to a parade ground. He measures off a 100 meter course, and has each man put on one of the shoes (left or right) on his right foot. The men are then instructed to hop down the course, on just the right foot.

It is pretty obvious what will happen – the guys with a right foot in a right shoe will get ahead of the ones who had the misfortune to put on a left shoe on their right foot. The men are then instructed to take off their shoes, and the proud officer has two piles of shoes, neatly separated.

That's the way the army is, and for sure not just the Italian army. Anyway, this is how a mixture of enantiomers is often resolved! The mixture is reacted with a handed molecule, often derived from nature (that's the right foot of the soldiers). The molecules react, and then can be separated – a right foot in a right shoe is not the mirror image of a right foot in a left shoe – it's a physically distinct object, with its own properties. Once separated, the reaction is reversed. Pretty neat.

I know you're going to ask me: "So how come all the molecules of nature have one handedness and not the other? Well, that's for another day.