Eternal dissymmetry

Magdolna Hargittai*[a] and István Hargittai*[a,b]

[a] *Structural Chemistry Research Group, Hungarian Academy of Sciences, Eötvös University, H-1518, Budapest, Hungary. Fax: +36 1 372 2731; e-mail: hargittaim@ludens.elte.hu*

[b] *Institute of General and Analytical Chemistry, Budapest University of Technology and Economics, H-1521 Budapest, Hungary*

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The teachings of Louis Pasteur about chirality continue to instruct and inspire.[1]

Louis Pasteur was the first to suggest that molecules can be chiral. In his famous experiment 155 years ago, in 1848, he recrystallised a salt of tartaric acid and obtained two kinds of small crystals that were mirror images of each other. Pasteur prepared beautiful cardboard models, which have been preserved and are exhibited in the Pasteur Museum at the Pasteur Institute in Paris. Pasteur may have been motivated to make these models of large scale because Jean Baptiste Biot, the discoverer of optical activity, had very poor vision by the time of Pasteur's discovery.[2]

As a moving moment in the history of science, it was left to Biot, rather old by then, to present Pasteur's findings to the French Academy of Sciences. The ever careful Biot first had Pasteur demonstrate his experiment to him in person. In Pasteur's description:[3]

'When [the solution] had furnished about 30 to 40 grams of crystals, he asked me to call at the Collége de France in order to collect them and isolate before him, by recognition of their crystallographic character, the right and the left crystals, requesting me to state once more whether I really affirmed that the crystals, which I should place at his right, would deviate [polarized light] to the right, and the others to the left. This done, he told me that he would undertake the rest. He prepared the solutions with carefully measured quantities, and when ready to examine them in the polarizing apparatus, he once more invited me to come into his room. He first placed in the apparatus the more interesting solution, that which ought to deviate to the left. Without even making a measurement, he saw by the appearance of the tints of the two images, ordinary and extraordinary, in the analyzer, that there was a strong deviation to the left. Then, very visibly affected, the illustrious old man took me by the arm and said, 'My dear child, I have loved science so much throughout my life that this makes my heart throb.''

According to the Nobel laureate George Wald,[4] 'No other chemical characteristic is as distinctive of living organisms as is optical activity.' The roots of Pasteur's discovery reach farther back than Biot's work. According to J. D. Bernal,[5] Pasteur's discovery arose at a meeting place of hitherto distinct disciplines. They were crystallography, physics and chemistry. He also showed that the fruits of the discovery benefited new branches in these sciences.

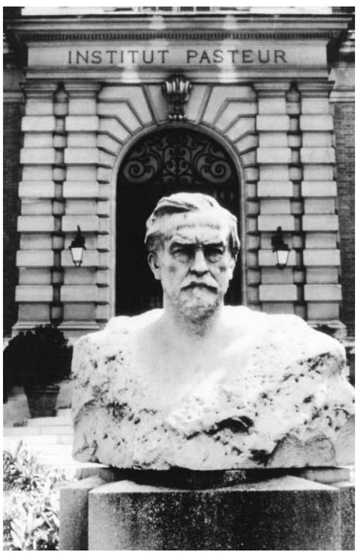

Figure 1 Louis Pasteur's bust in front of the Pasteur Institute, Paris (photograph by the authors, © Hargittai Photo).

Of course, not only material objects can have chirality or handedness. Bach's *The Art of the Fugue* is a beautiful example. Handedness is also an area of symmetry that is charged with philosophical implications. Immanuel Kant[6] wrote about the puzzle of the isometric left and right hands that cannot be made to coincide in space and called the nonsuperposable mirror images 'incongruente Gegenstücke' (incongruent counterparts). Then, of course, Lord Kelvin[7] gave a definition for chirality that has stood the test of time, 'I call any geometrical figure, or group of points, chiral, and say that it has chirality if its image in a plane of mirror, ideally realised, cannot be brought to coincide with itself.'

The early success of the chirality concept culminated in Pierre Curie's statement in an 1894 paper,[8] 'c'est la dissymétrie qui crée le phénomène' (dissymmetry creates the phenomenon). This most fundamental symmetry principle means that a phenomenon is expected to exist and can be observed only if certain elements are absent from the system. The forerunner of this principle was Franz Neumann's statement[9] in 1833 that 'the physical properties of crystals always conform to the symmetry of the crystal.'

Pierre Curie did not write much about symmetry and he did not live very long, but Marie Curie and the Russian crystallographer Aleksei Shubnikov did much to convey Pierre Curie's teachings on symmetry to a broader circle of scientists and thereby to help preserving the life of Louis Pasteur's teachings in this area of science.

Returning to Pasteur's story, it is important to stress that his discovery of molecular chirality did not happen out of nowhere. Pasteur himself stated that 'Dans les champs de l'observation, l'hasard ne favorise que les esprits préparés' (In the field of observation, chance only favors those minds that have been prepared). In fact, Pasteur's preparation for his discovery of molecular chirality was so perfect that to the famous biologist Dubos,[10] 'it appeared as if fate had brought together many influences to prepare Pasteur for his scientific adventure.' He was a well-trained chemist with a definite idea about the importance of molecular structure, and he was also a crystallographer, who viewed the crystals as carriers of chemical information. The chemical and physical methods appeared in unison in Pasteur's mind.

It was not only that various areas of science came together in Pasteur's discovery, the discovery gave rise to new branches in science as well. The emergence of stereochemistry was one of the consequences of Pasteur's discovery although it came a quarter of a century later. The discovery also brought about the realization that, in living organisms, biologically important substances occur in one of the two possible versions. This also led to the great question, 'How did it all start? What was the way one of the two was chosen?' This question deeply bothered Pasteur and a century later Vladimir Prelog called this a question of 'molecular theology' in his Nobel lecture. Pasteur is buried in the chapel of the Pasteur Institute and the key phrases of his scientific activities inscribed on the chapel walls include *dissymétrie moléculaire*.

Figure 2 Pasteur's models of enantiomeric crystals in the Museum of the Pasteur Institute, Paris (photograph by the authors, © Hargittai Photo).

Pasteur considered the asymmetric nature of living matter as a fundamental characteristic. Experimentation with molecular asymmetry was always on his mind. Even as late as 1886, he discussed the two asparagines,[10] one of which is sweet while the other insipid. He suggested that the difference might be due to the difference in their actions on the two antipodes of the asymmetric constituents of the gustatory nerve. There are many conspicuous examples of different actions by enantiomeric isomers of various drugs. Suffice it to mention thalidomide, which was known as Contergan in Europe with which many tragedies were connected before it was withdrawn from the market. Since 1992, the U.S. FDA and the European Committee for Proprietary Medicinal Products have required manufacturers to research and characterise each enantiomorf of a potential drug.[11]

In 1960, there was a short note in *Nature*,[12] in which the British physiologist and geneticist John Haldane returned to Pasteur in the wake of the discovery of the violation of parity. The title was 'Pasteur and Cosmic Asymmetry,' and Haldane showed that the roots of Lee and Yang's[13] discovery were in Pasteur's notion 'The universe is dissymmetric.'[14] Parity was, of course, only the first example found to violate symmetry principles in the weak interaction. Next was the so-called CP symmetry violation (C stands for charge conjugation, meaning the change of a particle into an antiparticle, and P stands for parity. The combined CP symmetry means the change from a left-handed particle to a right-handed antiparticle, for example). The discovery of CP violation had conceptually profound implications concerning our ideas about the origin of the universe.[15] As T. D. Lee[16] has noted recently, 'The origin of these symmetry violations is still a mystery.' However, if we consider the combined CPT symmetry (here T stands for time reversal, which is a mirror symmetry with respect to time just as parity is a mirror symmetry with respect to space coordinates) that is not broken; CPT is a very solid symmetry.

The legacy of Louis Paster is rich in scientific achievements that have greatly contributed to the improvement of the quality of life. It is also rich in questions that are the best stimulants for scientific inquiry and they continue to help us in charting our labors in uncovering nature's secrets.

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