genetic drift. Although drift could cause one mutant allele to increase to a high frequency, it seems improbable that drift would cause at least two, and probably four, distinct mutant chromosomes all to increase in frequency. Moreover, the multiple distinct mutants at high frequency argue against a simple hitch-hiking hypothesis in which selection at a nearby locus elevates the frequency of a new mutant. Might there be or have been some selective advantage to individuals heterozygous for a PKU allele? It is already well known that heterozygotes for the hereditary anaemias are resistant to malaria and this accounts for the high incidence of these mutations in areas where malaria is endemic. What might such an advantage be for heterozygotes for PKU? There are no clear answers; but some type of selection for PKU alleles seems possible. The possibility that selection operates at this locus, even among normal PAH alleles, is suggested by the very nature of the two different haplotypes (1 and 4). These two haplotypes occur at almost exactly equal frequencies. For the five RFLPs in the 30 kilobases at the 3′ end of the PAH locus, these haplotypes are complementary — where one has a restriction site present the other does not[4]. This observation suggests that, at least for this part of the gene, these two haplotypes have been evolving separately for a long time. Although random genetic drift could cause almost any distribution, the equal frequencies of these ancient haplotypes is very suggestive of balancing selection.

Information on the frequencies, in other populations, of RFLP haplotypes for both normal and PKU chromosomes may help resolve these and other questions, such as the origin of PKU in the Yemenite Jews[8]: was the PKU allele brought in from Europe or did it arise independently? In the past few weeks S. Avigad, B.E. Cohen and Y. Shiloh at the Sackler School of Medicine, Tel Aviv University, have characterized the PKU mutant in the Yemenite Jews (personal communication). These unpublished data indicate that in five different families all the PKU alleles have a deletion of an entire exon. Shiloh and colleagues have fully characterized the two PKU chromosomes in one patient and find that both are deletion alleles and have the same RFLP haplotype, one that has not been observed in European caucasians. Based on their preliminary and still partial characterizations, the haplotypes in the remaining families seem to be the same. Again, a single mutation (deletion) seems to have occurred and to have increased in frequency along with the haplotype in which it occurred. This PKU allele is not of European origin, but either drift or selection could explain the high frequency of PKU alleles in Yemenite Jews.

The studies I have discussed here are changing the way medical geneticists must deal with counselling for PKU; they offer all interested individuals the ability to have much more certain information on their carrier status. The studies also illustrate both the complexity of the evolutionary history of a major genetic disease and the great power of molecular-genetic techniques to illuminate the evolutionary facts, if not yet the evolutionary forces. □

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Louis de Broglie (1892–1987)

Louis de Broglie, who died on 19 March, was the last surviving, great founder of quantum physics. His theoretical discovery, in 1923, of the existence of matter-waves was the starting point of all the developments based on the notion of the wavefunction, from which Schrödinger derived the equation bearing his name. Louis de Broglie's ideas were thus the direct source of the new mechanics that now pervades the whole of physics and that came to be known as quantum mechanics after it was formally identified with the mechanics independently developed in 1925–26 in Copenhagen and Göttingen. In 1929, de Broglie was awarded the Nobel prize for this work.

The circumstances that led Louis de Broglie to his basic idea are interesting. Maurice de Broglie, his elder brother, was a physicist himself, and had a private laboratory in which he performed significant experiments on X-rays. Louis first studied history for a short time, but when Maurice showed him the texts of the 1911 1st Solvay Conference (of which he had been a scientific secretary) Louis, then aged 19, was so interested by the new problems discussed there that he turned to theoretical physics and particularly to analytical mechanics. After World War I he resumed his studies in the field and in 1923 he published three notes in the *Comptes Rendus de l'Académie des Sciences*.

These three notes are basic. In the first, Louis de Broglie proposed to associate a wave with any free particle and, making use of relativistic arguments, he derived the value of the wavelength (this is the famous Louis de Broglie formula). In the third, he demonstrated the equivalence of the principle of least action applied to a particle and Fermat's principle applied to the associated matter-wave.

By the end of 1923 Louis de Broglie had already mastered some of the main concepts of what was to become quantum physics and during 1924 he developed his ideas in his PhD thesis. This was sent by Paul Langevin to Einstein, who immediately understood its fundamental importance, drew the attention of the scientific community to it and used the ideas in it in his development of Bose–Einstein statistics.

In the course of his life, Louis de Broglie made a number of other successful investigations. He was, for example, the first to write down the relativistic equations for a massive, spin-1, free particle in 1934, and during the Second World War he constructed the equations describing the motion of spin-*n*/2 particles, *n* being any positive integer. Throughout his life, however, Louis de Broglie remained puzzled, at a deep level, by the discovery that he himself had started in 1923.

Although quantum mechanics worked so beautifully, he felt, as did Einstein, that neither he nor anyone else understood what it meant as a description of nature. This belief soon prompted him to try to interpret the quantum-mechanical formalism by considering a particle as a singularity in a wave (the 'double solution' theory). He presented the simplified 'pilot-wave' variant of this theory at the 5th Solvay Conference in 1927. It is the ancestor of all the so-called 'hidden-variables' interpretations of quantum physics. In fact the main ideas and formulas of David Bohm's hidden-variable theory, published in 1952, were essentially rediscoveries of this 25-year-old pilot-wave theory (although Bohm's work did go much further). During his last years of study Louis de Broglie returned again to the problem of a proper understanding of quantum physics.

Louis de Broglie was a polite and unaffected man. He belonged to a very aristocratic family (he inherited the title of Duke from his brother) but his interests were almost exclusively directed towards scientific knowledge. Despite all his illustrious charges (Académie des Sciences, Académie Française) he led a very simple, almost ascetic life. He was a professor at the Sorbonne and he also wrote excellent, popular works describing to a large audience the conceptual problems raised by twentieth century physics. Bernard d'Espagnat

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