Portraits in medical genetics

Journal of Medical Genetics 1988, **25**, 561–564

Pierre Louis Moreau de Maupertuis (1698–1759)

ALAN E H EMERY

From the Medical School, University of Edinburgh, Edinburgh EH8 9AG.

SUMMARY Maupertuis was one of the most important scientists and original thinkers of the 18th century. He refuted the preformationist theories of the time, and from his study of the inheritance of genetic traits proposed various ideas which forecast the genetic theory of inheritance. He applied the concept of probability to genetic problems and introduced experimental breeding as a means of studying the inheritance of genetic traits in animals. However, he considered his greatest contribution to science to be the 'Principle of Least Action'. Yet paradoxically it was this, through the vitriolic attacks by Voltaire which it engendered, which resulted in his work being largely ignored until recent times.

Pierre Louis Moreau de Maupertuis was among the greatest scientists and original thinkers of the 18th century (fig 1). His contributions to mathematics (the Principle of Least Action), and his refutation of preformationist theories alone would have justified his pre-eminence. However, of particular interest was his study and interpretation of pedigrees of genetic traits, the application of the concept of probability to genetic problems, the introducing of experimental breeding as a means of studying the transmission of inherited traits in animals, and his proposed theories of inheritance, all ideas which were far ahead of their time. But his originality and contemporary reputation were almost entirely overshadowed by Voltaire's attacks on his work. In fact, apart from a passing reference by Sir Walter Scott in his *Letters on demonology and witchcraft* published in 1830 to an apparition of him which appeared to a professor in the Berlin Academy where Maupertuis had been President(!), he remained largely unknown until recent years.

Maupertuis and preformationist theories

By the 18th century it was generally believed that embryonic development represented no more than the expansion of a miniature, already in existence in the sperm or egg. Pre-existence theories held that

FIG 1 Pierre Louis Moreau de Maupertuis reproduced from his *Oeuvres* (1756).

such miniatures had been in existence since the creation of the universe. On the other hand, preformationist theories believed that the miniature which grew into the full organism was actually formed within the body of the parent,¹ either in the sperm (animalculists) or the egg (ovists). These various ideas, to which nearly all naturalists were firmly committed at the time, were carefully explored by Maupertuis and shown to have no validity.²⁻⁴

His interest in such matters was originally kindled by the exhibition in Paris of an albino Negro. In his *Venus physique (Deux dissertations. L'une sur l'origine des hommes et des animaux, et l'autre sur l'origine des noirs)*,⁵ at first published anonymously in 1744-45, he marshalled various reasons for rejecting the pre-existence and preformationist theories (*Oeuvres*, vol 2, pp 1-133; 137-68; 267-82)⁶: firstly, because they were not supported by careful anatomical studies; secondly, because from considerations of the transmission of hereditary traits the embryo is contributed to by both parents and can resemble either; and thirdly, none of the theories explained the occurrence of congenital defects, including an albino born of normal dark skinned Negro parents, or hybrids between different species which resemble both parents.

Maupertuis and genetics

Maupertuis has been considered a precursor of Mendel by some^{2,3,7} and for good reasons. In his attempts to refute the preformationists, he searched for a genealogy which would support his beliefs. Around the time he moved to Berlin he began to study a large family with polydactyly which was transmitted from one generation to the next. This was the family of Jacob Ruhe, a surgeon in Berlin, and was described in detail by Maupertuis in his *Venus physique (Oeuvres*, vol 2, letter XIV, pp 275-6).⁶ The pedigree is shown in fig 2 (the order of

the sibs in each generation is not given by Maupertuis). About this time a similar family had also been described in a book by Réaumur. However, though Maupertuis refers to Réaumur's studies, he makes no mention of the pedigree. It seems possible that this may have been because Maupertuis was only familiar with the first edition of Réaumur's book published in 1749 in which the pedigree is not mentioned² and is only described in the second edition published later. Huxley detailed Réaumur's family, named Kelleia from Malta, in an essay on 'The origin of species' in 1860 and subsequently published in his *Darwiniana*.⁸

From the Ruhe pedigree, Maupertuis concluded that the disorder could be transmitted by either males or females. That is, there are contributions to the fetus from both parents ("... *que le fœtus participe également du père et de la mère*"). He then estimated the probability of such a pedigree occurring by chance rather than through some hereditary mechanism. Taking into account the estimated incidence of the disorder at the time, he calculated that the occurrence of all the affecteds in three generations by chance alone would be only once in 8×10^{12} . His approach thus presages the application of probability theory to genetic problems. He also had a great love of animals, keeping many as pets and detailed his success in following the transmission of polydactyly through the offspring of an affected bitch which he bred from, thus establishing experimental breeding as a means of studying the inheritance of genetic traits.

He then proceeded to develop a theory of heredity to explain his observations which in many ways forecast the genetic theory of inheritance and the role of genes. He proposed that heredity was due to particles present in the germ cells which were derived from, and were responsible for the formation of, the various different organs and structures of the body. He even suggested that this idea might be tested by mutilating animals generation after generation when certain structures might then be expected gradually to diminish in size, an idea held for many years by Lamarckians and the subject of Arthur Koestler's *The case of the midwife toad*.

Maupertuis believed that each particle had an affinity for a like particle and each of a corresponding pair was transmitted by a parent to its offspring. By their combination they were responsible for the resultant embryo. Furthermore, he postulated that the particle either from the mother or from the father may dominate and if there were too few particles (or they were too weakly attracted to each other), then a defect resulting from a deficiency of particles could occur (*monstre par défaut*). Alternatively, if there were too many particles (or attraction

FIG 2 The Ruhe family with polydactyly studied by Maupertuis.

occurred more than usual) then a defect resulting from an excess of particles could occur (*monstre par excès*). Finally he indicated that a sudden complete alteration of particles (what we would now refer to as a new mutation), if favoured, could account for the origin of a new species.⁹ Thus, as Glass³ has emphasised "... Maupertuis anticipated virtually every idea of the Mendelian mechanism of heredity, the Darwinian process of evolution and the DeVriesian theory of mutations as the origin of species". However, as Sandler⁷ has pointed out, there are several fundamental differences between Maupertuis' ideas and those of Mendel. For example, Maupertuis associated dominance with the organisation of particles whereas Mendel associated it with the expression of one of the alternative forms of a trait. Also Maupertuis' concept of the transmission of inherited traits is seen as resulting from the attraction of maternal and paternal particles for each other, whereas Mendel saw this as involving the separation or segregation of maternal and paternal factors during gamete formation. Nevertheless, there is no questioning the originality of Maupertuis' views, more than a century before Mendel, and it is not surprising that few contemporaries appear to have fully appreciated his work.

Maupertuis the man

Some more recent accounts of the life and work of Maupertuis can be found in Hoefer,¹⁰ Velluz,¹¹ and Glass.¹²

Pierre Louis Moreau de Maupertuis was born on 28 September 1698 in the small town of St Malo on the Brittany coast of northern France. He came from a family of wealth and position. His father was a successful businessman and his mother, who idolised her son, was creative and tender and devoted to her son's education and success in life. At first he was educated privately but at the age of 16 he went to study at the Collège de la Marche, an old and revered institution in Paris. Later he served for a time as an officer in the army of Louis XV, rising to the rank of captain. By now he had developed a particular interest in mathematics and at 25 he was elected to the Paris Academy of Science, largely as a result of his original work in this subject. He visited London in 1728, the year after Isaac Newton died, and was elected a Fellow of the Royal Society in June of that year. He became an ardent supporter of the Newtonian theory of gravitation and its foremost proponent in France. In fact, in May 1736, the French government sent an expedition to Peru and another, under the leadership of Maupertuis, to Lapland in order to measure precisely the length of a degree of longitude which,

if as Newton had predicted the earth is flattened toward the poles, should be longer in the far north than near the equator. On the return journey Maupertuis' ship was wrecked in the Baltic Sea, but fortunately there was no loss of life and his records were saved. The results of both expeditions confirmed Newton's predictions. Maupertuis, who was now famous for his scientific reasearches, was elected to the French Academy in 1743, and later recommended by Voltaire to become President of Frederick the Great's Academy of Sciences in Berlin. He finally accepted Frederick's invitation in 1745, took up residence in Berlin, and married Mlle de Borck.

It was just around this time that he proposed the Principle of Least Action (*Principe de la moindre quantité d'action*) which he considered to be his most important contribution to science. He enunciated the Principle in the Proceedings of the French Academy on 15 April 1744,¹⁰ and further elaborated it in subsequent publications. The Principle, one of the most fundamental generalisations in science, states that the product of the mass of a body by the distance it moves and by the velocity with which it moves, tends toward the least possible, a Principle which indicates a certain economy of nature: "... dans la Nature, la quantité d'action employée pour ce changement est toujours la plus petite qu'il fait possible" (*Oeuvres*, vol 1, pp 42-3).⁶ However, it was this concept which led to the bitter and destructive controversy with Voltaire. How the situation arose is described by Maupertuis himself (*Oeuvres*, vol 2, pp 243-51)⁶ and commented upon in detail by Fee.¹³

The essentials are that one Samuel Koenig, a former friend and fellow student of Maupertuis, charged that the theory was erroneous but, most damning of all, that in any event Leibniz had developed the idea many years previously and had in fact communicated this in a letter to a colleague, a copy of which Koenig claimed to have in his possession. This slur on the integrity of the President of the Academy was a serious one. At Maupertuis' request the Academy demanded that Koenig provide proof of his allegations and the original of the Leibniz letter. This he was unable to do. Meanwhile Voltaire, who until then had been a close friend and staunch supporter of Maupertuis for 20 years, for reasons which are far from clear, unleashed a series of vicious attacks upon Maupertuis. Indeed Voltaire's ridicule did not entirely cease even after Maupertuis' death. There is no doubt that this unsavoury episode seriously undermined Maupertuis' health. He decided to leave Berlin and recuperate in his home town of St Malo. However, on reaching Basel he was too ill to travel further and

he died there on 27 July 1759 before his wife could reach him.

Professor Bentley Glass¹² has provided a very succinct and clear picture of the man himself.

“Maupertuis was a man of singular aspect. He was very short. His body was always in motion; he had numerous tics. He was careless of his apparel. Perhaps he was always endeavouring to attract attention. Perhaps he shared the Napoleonic complex of little men. Certainly he was both highly original and possessed of qualities that attracted friends, especially among the ladies; the Marquise du Châtelet and many other Frenchwomen corresponded regularly with him. He could be gay as well as fiery and violent. Above all he was proud, both of his intelligence and of his accomplishments, and to attack either was to wound him deeply. Above all, he could not understand the character of Koenig, whom he had sponsored and who then gratuitously attacked him, or of Voltaire, whose adulation and friendship so quickly turned to malice and vituperation.”

Maupertuis was without doubt one of the greatest scientists of the 18th century. It is sad that his reputation at the time should have been so completely eclipsed by Voltaire's satirical attacks, and it is only in the last few years that the originality of his contributions to mathematics and genetics has begun to be recognised and appreciated.

I am most grateful to Ms Marcia Lavine for her help

in tracing various references and to Mrs Isobel Black for secretarial assistance.

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Correspondence and requests for reprints to Professor Alan E H Emery, University of Edinburgh, Medical School, Teviot Place, Edinburgh EH8 9AG.