The last male heir of an ancient Whitley family that probably originated in Normandy, Maskelyne was educated at Westminster School, where he received a good grounding in the classics. During his vacations, he was initiated in the writing and architecture of the ancient Greeks and Romans. He enjoyed self-taught academic pursuits, including the study of mechanics, which was the subject of his master's thesis. He then went on to study mathematics as the indispensable tool for the proper understanding of these related sciences. Having mastered the art of mechanics, he then turned his attention to the study of natural philosophy, particularly mechanics, pneumatics, and hydrodynamics. He further studied these at Trinity College, Cambridge, graduating in 1754 as seventeenth wrangler. After being ordained in 1755, he accepted a curacy near London, where, rather than seeking a livelihood in the Anglican Church, he devoted many of his leisure hours to assisting the astronomer royal, John Hadley, in comparing tables of refraction. He was elected a fellow of Trinity College, Cambridge, in 1756 and of the Royal Society the following year.

In his biography of Maskelyne, Samuel Johnson wrote that he was a man of great ability and a very great improvement of character. He was highly recommended by his friend Charles Dibdin, who admired his ability to combine scientific and literary skills. Johnson also noted that Maskelyne was a man of great learning, with a wide range of interests, including mathematics, astronomy, and geography. He was a skilled draftsman, and his illustrations were highly regarded. He was also a gifted writer, and his works were widely read and admired. He was a member of the Royal Society, and his papers were published in the Society's Proceedings.

Justin Morgan, in his biography of Maskelyne, wrote that he was a man of great learning, with a wide range of interests, including mathematics, astronomy, and geography. He was a skilled draftsman, and his illustrations were highly regarded. He was also a gifted writer, and his works were widely read and admired. He was a member of the Royal Society, and his papers were published in the Society's Proceedings.

Among Maskelyne's many duties at the Royal Observatory was to assess the performances of a considerable number of chronometers submitted for an official trial by two principal watchmakers, John Harrison and Thomas Mudge. Maskelyne, who had just been appointed astronomer royal, arranged for four naval officers to be in attendance to testify to the general utility of the lunar-distance method for finding longitude at sea to within 1° or 2° of error. He also presented a memorial in which he proposed that the practical application of the method could be facilitated by the preparation of a nautical ephemeris with auxiliary tables and explanations. These plans crystallized the foundation of the system that lay behind the most accurate method of determining longitude, and the Admiralty appointed Maskelyne the government astronomer royal to supervise the work of the astronomers and the preparation of the nautical ephemeris. In 1765, Maskelyne, as a result of the exceptionally high degree of reliability of chronometers, had the desirable effect of establishing a consistent system.

This periodical is undoubtedly Maskelyne's greatest monument to astronomical science. It is still a useful navigational aid even though the linear distances mentioned in the tables themselves became obsolete by the beginning of the nineteenth century, mainly as a result of the exceptionally high degree of reliability of chronometers.