modern database software and the birth of the field of cheminformatics. Originally defined by F.K. Brown in 1998,[80] cheminformatics has been applied in drug discovery to store, index, and search information related to individual compounds or groups of compounds. Specialized software provided by companies such as Chemaxon, Core Informatics, Tripos, and Dotmatics is now common place in drug discovery, and allows scientists to evaluate millions of data points with the click of a mouse (Figure 2.19).

Milestones in Biotechnology

Although there were many remarkable discoveries made in the first 70 years of the twentieth century, such as penicillin antibiotics,[81] benzodiazepine central nervous system (CNS) drugs,[82] and macrolide antibiotics,[83] drug discovery scientists of this age were limited in their ability to identify and interrogate targets of interest. The generation of new animal models was restricted to selective breeding of naturally occurring mutations (e.g., the nude mouse) and protein production was limited by the expression levels of proteins in naturally occurring cells. Similarly, the development of cellular assays was dependent on naturally occurring cell lines. The dawn of the age of biotechnology, however, ushered in a new era of drug discovery and disease understanding. Beginning in the 1970s, the restrictions imposed by natural evolution and selection were lifted as scientists began to develop technologies that allowed them to manipulate the DNA of living organisms. Initial experiments in the early 1970s designed to demonstrate that non-native DNA could be prepared (recombinant DNA) and transferred into living cells (transfection technology) were quickly followed by the application of similar technology to generate animals with non-native DNA (transgenic and knockout animal models). In 1975, monoclonal antibodies were introduced, adding further fuel to the biotech fire, and by 1980 companies such as Genentech and Amgen were founded to harness the new techniques for therapeutic purposes. Continued scientific advances, such as polymerase chain reaction (PCR) technology, successful macromolecular therapeutics (recombinant proteins, monoclonal antibodies, and receptor construct/fusion proteins), and the Human Genome Project, further expanded the reach of biotechnology. By the end of the twentieth century, less than 30 years after the initial experiment that launched the field, biotechnology had transformed the process of drug discovery and created a multi-billion dollar industry of its own. In early 2009, Genentech was purchased by Roche for over $46 billion,[84] and as of the end of 2013, Amgen had grown into a $90 billion company.[85] These examples clearly demonstrate the importance of the biotechnology revolution and the profound impact it had on the pharmaceutical industry.