Computer Software Review

Molecule Evoluator CIDRUX BV, Park Oosterspaarn 6, 2036 MB Haarlem, The Netherlands. www. cidrux.com. See Web site for pricing information.

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I highly recommend the *Molecule Evoluator* as a unique software program capable of generating libraries of compounds either completely *de novo* with no defined starting point or from a predefined one, e.g., the competitor's lead compound. It should be useful for medicinal chemists in both industry and academia. The library is generated by setting preferences as described below and requesting a library of a specific size. This is followed by an interactive process in which the user looks at the initial results of the projected library, selects one or two molecules of interest, and then uses the program to generate a new library. On average, this new library, after five to nine iterations, will have unique structures that will most likely be patentably distinct from the initial starting point.

Molecule Evoluator is very easy to use. Any medicinal chemist should be able to master it after 30 min using the self-help guide. The program comes with its own easy-to-use drawing tool with features of free-style drawing of the structure and, by holding the mouse over an atom, facile changing of the elemental symbol to N, O, S, P, etc., so that the user can rapidly draw the desired structure. Also, .mol or .sd files can be imported into *Molecule Evoluator* as a starting point. A library can typically be generated within 20−30 min, once a structure is imported.

The program's algorithm utilizes fragments and core scaffolds from the database of the National Cancer Institute, but it can also grow substituents from the core and change the core atoms of the central scaffold. It can modify the ring systems as well in order to create new core scaffolds. The user can control how molecules evolve in the program by setting such preferences as molecular weight, log P, polar surface area (PSA), number of rotatable bonds, number of aromatic rings, allowing cyclophanes, following Bredt's rules, number of hydrogen-bond acceptors, number of hydrogen-bond donors, and other features. In addition, two compounds can be merged or simply modified on an adjustable scale of 0−100%. All the features of the structure, such as molecular weight, log P, PSA, etc. can be displayed with it as new libraries are generated.

I tried the *Molecule Evoluator* by starting with a competitor's lead compound and generating five to eight libraries. In general, when using the program, I was able to obtain distinct, patentable compounds over 90% of the time. In another application, my co-workers and I wanted to obtain molecules that had a higher chance of penetrating the central nervous system and the blood brain barrier. By setting the PSA to below 90, the *Molecule Evoluator* provided structures of sufficient interest that they are going to be synthesized at a later date.

Another interesting trial was starting with the compounds of two competitors and merging them using the *Molecule Evoluator*. This provided a slightly different core structure with unique substituents from both molecules. This structure could then be evolved further by fixing the core—another feature that can be done at anytime—and then using the program to evolve other fragments of the structure. This is a major strength of the program, as it allows the user to control the selection of the molecules and their evolution. One quickly realizes the power of the program for generating medicinally relevant molecules with predefined physical properties.

The *Molecule Evoluator* is a fun, easy to learn desktop tool that can be used by medicinal chemists to create patentably distinct molecules. One of its most valuable attributes is that it allows the user to fine-tune the molecular evolution process at each stage of iteration. It is a low-cost solution for generating ideas that your research team will enjoy using.

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