

The Implementation of an Expert System to Search for Novel Substances Acting on Serotonergic and Glutamatergic Systems.

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As part of an academia-based platform [1] to discover substances acting on serotonergic or glutamatergic systems as potential new antidepressant or anxiolytic drugs, an expert system recognizing potential activity of new compounds was developed. Both receptor systems are among the most diversified, so we focus our attention only on targets implicated in depression and anxiety, i.e.: serotonin transporters (SERT), 5-HT_{1A}, 5-HT₆ and 5-HT₇ receptors and metabotropic glutamate (mGlu) receptors of group II (mGluR₂, 3) and III (mGluR₄, 7, 8).

The expert system [2] uses Bayes classification [3] as a methodology, MOLPRINT 2D fingerprints as structure representation and is run under Canvas [4]. In general, the system is based on databases of known ligands for the above targets, and is trained in supervised learning setting on correlations between fingerprints and activities. Bayes classification is a simple probabilistic classifier which assumes that presence of some feature is independent on the presence of another. It is especially useful for classification of arguments described by multidimensional variables (like fingerprints [5]). As a result the system indicates compounds potential activity as boolean value. For example, the 5-HT₇ module (based on 470 known ligands) shows 72,7% and 98,6% efficacy in recognizing active and inactive compounds from internal test sets.

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[1] www.cns-platform.eu/index.html

[2] Hemmer M.: *Expert systems in chemistry research*, CRC Press, Boca Raton, 2008.

[3] Jajuga K.: *Pattern Recognition* 19 (5) (1986), 413.

[4] Canvas, version 1.3, Schrödinger, LLC, New York, NY, 2010.

[5] Sastry M., Lowrie J. F., Dixon S. L., Sherman W.: *J. Chem. Inf. Model.* 50 (2010), 771.