PTML-LDA applied to allosteric modulators

Abstract

The allosteric modulator performs the function of allosteric regulation, which indirectly increases or decreases the effect of an agonist or antagonist on a cellular receptor by activating a catalytic site on the protein[1]. Allostery can both cause diseases and this involves synthesizing drugs with higher selectivity and less toxicity, to fit into the primary active center (orthosteric) of the biological objectives, in order to induce a therapeutic effect[2]. In this study we have employed Perturbation Theory (PT) ideas and Machine Learning techniques (ML) to seek a PTML model of the ChEMBL database for allosteric modulators. In this case, the Linear Discriminant Analysis (LDA) has been used to develop this model. This aims to predict the probability of allosteric activity for more than 20000 preclinical tests, leading to very good results of statistical parameters: Specificity Sp = 87.61 / 87.51% and sensitivity Sn = 75.18 / 75.35 % in training / validation series.

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[1] Monod, J.; Wyman, J.P.: *On the nature of allosteric transitions*: *A plausible model*. *Journal of Molecular Biology* 1965, **12**, 88-118.

[2] Nussinov, R.; Tsai, C. J.: Allostery in disease and in drug discovery. *Cell* **2013**, 153, 293-305.