Proposing 5-Steps Rule Is a Notable Milestone for Studying Molecular Biology

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ABSTRACT

In this current minireview, the cradle of the “5-steps rule” or “5-step rules”, along with its essence and advances, has been recalled. Born in 2011, its impacts on molecular biology are both substantial and rapid, fully indicating the “5-steps rule” is no doubt a remarkable and profound milestone in molecular biology.

1. INTRODUCTION

Since it was proposed in 2011, the “5-steps rule” or “5-step rules” has been widely used in molecular biology, both theoretical and experimental. Its original source was usually referred by citing a review paper for celebrating the 50th anniversary year of Journal of Theoretical Biology [1].

Interestingly, no such a clear-cut term as “5-step” can be found in the entire aforementioned paper. Why? This is because: it is the idea of the “5-steps rule” that would become crystal clear after carefully reading through the whole paper. Accordingly, the paper [1] is actually the cradle of the “5-steps rule”.

2. THE ESSENCE OF 5-STEPS RULE

In order to quantitatively predict, or develop a useful predictor for, a molecular biology system, the following five guidelines should be observed: 1) select or construct a valid benchmark dataset to train and test the predictor; 2) represent the samples with an effective formulation that can truly reflect their intrinsic correlation with the target to be predicted; 3) introduce or develop a powerful algorithm to conduct the prediction; 4) properly perform cross-validation tests to objectively evaluate the anticipated prediction accuracy; 5) establish a user-friendly web-server for the predictor that is accessible to the public. The predictors established in compliance with these steps have the following notable merits: a) crystal clear in logic development; b) completely transparent in operation; c) easily to repeat the reported results by other investigators; d) with high potential in stimulating other predictors; e) very convenient to be used by the majority of experimental scientists.
3. RESULT AND DISCUSSION

It is without exaggeration to say that the “5-steps rule” has been used at a very deeper levels of many molecular biology systems, as clearly and remarkably indicated by a series of the following reports: 1) “prediction of S-sulfenylation sites [2], 2) “identify phosphohistidine sites in proteins by blending statistical moments and position relative features [3], 3) “identify tyrosine sulfation sites by incorporating statistical moments” [4], 4) “prediction of S-sulfenylation sites using statistical moments [5], 5) “reveal active compound and mechanism of shuangsheng pingfei san on idiopathic pulmonary fibrosis [6], 6) “exploring DNA-binding proteins by integrating multi-scale sequence information” [7], 7) “predict splice junctions with interpretable bidirectional long short-term memory networks” [8], 8) “identify hydroxylation sites in proteins by extracting enhanced position and sequence variant feature” [9], 9) “a sequence model for identifying S-palmitoylation sites in proteins” [10], 10) “a sequence-based model for identifying S-prenylation sites in proteins” [11], 11) “a two-level computation model based on deep learning algorithm for identification of piRNA and their functions [12], 12) “deep learning-based recombination spots prediction by incorporating secondary sequence information coupled with physio-chemical properties” [13], 13) “a study for therapeutic treatment against Parkinson’s disease” [14], 14) “identifying DNA N(6)-methyladenine sites in rice genome using continuous bag of nucleobases” [15], 15) “identifying enhancers using hidden information of DNA sequences” [16], 16) “identifying molecular functions of cytoskeleton motor proteins using 2D convolutional neural network” [17], 17) “identifying cancer targets based on machine learning methods” [18], 18) “identifying DNase I hypersensitive sites using multi-features fusion and F-score features selection” [19], 19) “an improved bioinformatics tool for identifying DNA 6mA modifications” [20], 20) “identify lysine crotonylation sites by blending position relative statistical features” [21], 21) “identifying RNA N6-methyladenosine sites using deep learning mode” [22], 22) “detecting formylation sites from protein sequences using K-nearest neighbor algorithm” [23], 23) “identification of DNA N6-methyladenine sites in the rice genome by intelligent computational model” [24], 24) “calcium pattern assessment in patients with severe aortic stenosis” [25], 25) “identifying FL11 subtype by characterizing tumor immune microenvironment in prostate adenocarcinoma” [26], 26) “a sequence-based tool for the prediction and analysis of quorum sensing peptides” [27], 27) “evaluate the stability of tautomers: susceptibility of 2-[(Phenylimino)-methyl]-cyclohexane-1,3-diones to tautomerization based on the calculated Gibbs free energies” [28], 28) “prediction of lysine formylation sites using the composition of k-spaced amino acid pairs” [29], 29) “a two-level sequence-based predictor for identifying nuclear receptors and their families” [30], 30) “a two-layer predictor for identifying proteases and their types” [31], 31) “classifying anticancer peptides using discriminative intelligent model” [32], 32) “a tool for protein physicochemical descriptor generation” [33], 33) “model feedback in lung cancer” [34].

It is instructive to point out that in the systems of molecular biology there exist many multi-label ones where each of the individual constituents or samples considered may need two or more labels for distinction. For this kind of multi-label systems, two kinds of metrics are needed: one is the global set of metrics to indicate the global accuracy of the prediction method or predictor developed, while the other is the local metrics to indicate its local accuracy [35]. For the concrete mathematical formulations of the two sets of metrics, as well as their biological implications, refer to a recent paper [36].

4. CONCLUSION AND PERSPECTIVE

The “5-steps rule” has played substantial roles in stimulating in-depth studies of molecular biology, both theoretical and experimental. It is indeed a remarkable and profound milestone for molecular biology.

Although at the present the reports in this regard from theoretical scientists are more than those from experimental scientists, it is anticipated that, with more experimental data available in future, this kind of reports from experimental scientists will be increasing as well. Particularly, the combined reports between experimental and theoretical approaches, or their compliments to each other, will increasingly appear.

It is anticipated that more impacts will be realized by the “5-steps rule”, as indicated by some very
impressive papers [35-41] and a series of very recent papers (see, e.g., [42-59]).

CONFLICTS OF INTEREST

The author declares no conflicts of interest regarding the publication of this paper.

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