A short note on Structure-activity relationship.

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Abstract

The development of molecular Structure-activity relationships (SARs) is an important approach for facilitating hit discovery in the early stages of drug discovery. SAR is important in many aspects of drug discovery, from primary screening to lead optimization. Work with SARs begins with identifying whether SARs are in fact present in a collection of molecules and their associated activities, attempting to elucidate the details of one or more SARs, and then disseminating this information. Use to make structural changes to optimize characteristics or activities. Fundamentally, understanding the SARs of different molecules enables rational exploration of chemical space that is essentially infinite if there are no signposts. The development of chemical series is always the simultaneous optimization of several physicochemical and biological properties.

Keywords: Structure-activity relationships, Virtual Screening, Drug discovery; Structure-activity landscape.

Introduction

Structure-activity relationships (SARs) for a given set of molecules allows one to rationally explore chemical space and develop a chemical series optimizing multiple physicochemical and biological properties simultaneously, for instance, improving potency, reducing toxicity, and ensuring sufficient bioavailability. In silico methods allow rapid and efficient characterization of SARs and facilitate building a variety of models to capture and encode one or more SARs, which can then be used to predict activities for new molecules. By coupling these methods with in silico modifications of structures, one can easily prioritize large screening decks or even generate new compounds de novo and ascertain whether they belong to the SAR being studied. Computational methods can provide a guide for the experienced user by integrating and summarizing large amounts of preexisting data to suggest useful structural modifications. This chapter highlights the different types of SAR modeling methods and how they support the task of exploring chemical space to elucidate and optimize SARs in a drug discovery setting. In addition to reviewing modeling algorithms, we briefly describe how databases can be used as sources of SAR data to inform and improve studies of SAR trends. We also review common modeling techniques used to encode SAR, recent work in structure-activity landscapes, the role of SAR databases, and alternative approaches to studying SAR data without explicit model development [1,2].

One approach is to consider fragments as the basis for SAR exploration. This is not without precedent, as substructure-based models having been developed that are useful for both prediction and interpretation. One approach to study SAR using fragments is to develop an "R-group QSAR" model. The goal of this model is to determine if SAR exists and, if so, how different R groups affect it. Starting with a set of molecules, perform R

Group decomposition to generate a set of backbones and associated substituents. Given a scaffold, we can create an R-group matrix with the observations as the rows and the R-groups, R1, R2, Rn as the columns [3]. The matrix element is set to 1 if the ith molecule contains the jth substituent. From this R-group abundance matrix, along with the observed molecular activities, predictive models can be developed. Most of these R group matrices are small, so some form of linear regression is probably best. However, it is clear that this approach has many limitations. First, many of the scaffolds have very few observations, making it impossible to build a reliable model. Second, most R-group matrices are sparse because not all permutation points are evenly filled. Also, a binary incidence matrix may not be the best input for a linear regression model. One way to approach this is to replace each of the n columns with n×d columns. Where d represents a d-dimensional real-valued descriptor vector derived from the structure of the corresponding R group. For frameworks with more than two permutation points, this can lead to R group matrices with more columns than rows. Even otherwise, such matrices usually have a large number of featur. Despite these problems, linear regression models can be developed for scaffolds with a sufficient number of observations and relatively few permuted points. In such cases, the predictive

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accuracy of the model is not a priority. Rather, we are interested in whether the model is statistically significant. The hypothesis is that such a model represents the real relationship between displacement and observed activity. This allows us to provide rankings for individual series. Clearly, this approach is not very useful for a diverse set of structures [4].

Structure-activity relationship analysis is a complex process that can be enhanced by computational techniques. This article describes a simple tool for SAR analysis with a graphical user interface and a flexible approach to molecular data entry. This application allows the calculation of molecular similarity represented by the Tanimoto index and the Euclidean distance, and the determination of activity cliffs using the structure-activity landscape index. Calculations are performed pairwise on the reference connection and any other connection or all possible pairs in the data set. The results of SAR analysis are visualized using two types of charts. Applicability is demonstrated by analyzing a series of COX2 inhibitors related to isoxicam. This tool is available online: A Sample manual and input files are included [5].

Conclusion

It is clear that computational methods play an important role in the drug discovery process. While there has been some debate about the actual value added of these models, it is clear that much can be gained from these methods when used properly, along with proper testing and control methods, addressing how the large amounts of data generated by the development of modern high-throughput experimental techniques and large-scale chemical structure databases enable scientists practicing computational techniques to explore the wealth of structure-activity data becoming more and more important.

References

1. Tong W, Welsh WJ, Shi L, et al. Structure-activity relationship approaches and applications. Environ Toxicol Chem. 2003;22(8):1680-95.
2. Shulgin AT, Sargent T, Naranjo C. Structure–activity relationships of one-ring psychotomimetics. Nature. 1969;221:537-41.
3. Topliss JG, Edwards RP. Chance factors in studies of quantitative structure-activity relationships. J Med Chem. 1979;22(10):1238-44.
4. Hasdenteufel F, Luyasu S, Hougardy N, et al. Structure-activity relationships and drug allergy. Cur Clin Pharmacol. 2012;7(1):15-27.
5. Sutherland JJ, O'Brien LA, Weaver DF. A comparison of methods for modeling quantitative structure activity relationships. J Med Chem. 2004;47(22):5541-54.

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