Journal of Medicinal Chemistry Editorial

J. Med. Chem. **2010,** *53,* 1–2 **1**
DOI: 10.1021/jm901774n

Computational Studies, Virtual Screening, and Theoretical Molecular Models

The *Journal of Medicinal Chemistry* (Journal) continues to receive a large number of manuscripts involving computational studies. A number of these have been truly outstanding papers that are highly recognized within the medicinal chemistry community and that make the Journal the leading international journal for publication of first-class computational medicinal chemistry research.

This Editorial summarizes current key requirements for manuscripts containing computational studies. Full details are provided in the Scope and Editorial Policy of the Journal (current revision, January 2010) and the Guidelines for Authors, sections 2.3.5 and 2.3.6. In addition, this Editorial attempts to clarify general acceptance criteria for computational manuscripts that might occasionally be overlooked or misunderstood.

In order to ensure high quality standards and a high level of consistency in evaluating computational studies, the Journal has established an internal prereview process to which all computational manuscripts are subjected, as described in the editorial "Computational Chemistry Publications in the *Journal of Medicinal Chemistry*" in the April 24, 2008, issue of the Journal. Furthermore, criteria have been formulated that define the suitability of computational manuscripts for the Journal. The Journal specifically encourages submission of studies falling into the following manuscript categories:

(1) Practical applications of established computational methods including experimental data, in particular, experimental evaluation of computational predictions.
(2) Substantially novel methods along with evidence for utility in medicinal chemistry and significant potential for advancing the field. Methods must be described clearly and comprehensibly.
(3) Computational analyses of publicly available databases or data sets that provide unexpected or provocative insights into topical problems and advance medicinal chemistry knowledge.

It should also be noted that QSAR/QSPR studies must adhere to the requirements stated in the Guidelines for Authors and in the editorial "QSAR/QSPR and Proprietary Data" (June 15, 2006, issue of the Journal), which were formulated in collaboration with the *Journal of Chemical Information and Modeling*.

The internal prereview process determines whether or not a computational submission falls into manuscript categories 1−3 and, in addition, whether the following general acceptance criteria i−vi are met:

(i) Manuscripts reporting the application of existing computational methods including QSAR/QSPR methods are only considered in combination with novel and significant experimental data.
(ii) Computational manuscripts must be presented in an accessible and lucid style that can be appreciated by a wide medicinal chemistry audience.
(iii) The use of proprietary data for computational studies is not acceptable. Please refer to the Guidelines for Authors for full details and note that these regulations are not specific to the Journal but apply to all American Chemical Society journals. This is the case because the use of proprietary data is inconsistent with the ACS Ethical Guidelines to Publication of Chemical Research. Occasionally, computational studies based on large corporate data sets might provide compelling insights not obtainable otherwise. In an exceptional case, if it is demonstrated that no public domain data exist to enable comparable studies, the Editor-in-Chief might consider relaxing the data deposition requirement. However, it is expected that such instances will be rare.

Current submissions to the Journal that combine computational and experimental studies (manuscript category 1) can broadly be divided into two types: (a) virtual screening studies and (b) computational analyses guiding and/or rationalizing experimental SAR studies. Both types of manuscript are relevant for the Journal. However, such manuscripts must meet the following requirements:

(iv) When manuscripts combine computational and experimental studies, both components must be significant. For example, computational analyses are not automatically validated by addition of a minor experimental component and vice versa. Furthermore, there must be a direct and logical link between the experimental and computational investigations. "Decorating" experimental SAR analysis with modeling or reporting computations that are unrelated to the experiments is not acceptable. Furthermore, overinterpretation of computational studies, conclusions drawn from molecular models as if they represent experimental data, speculations or hypotheses treated as facts, or the discussion of details that fall into the error margins of calculations must be avoided. Claims made on the basis of calculations that do not have proper and standard statistical support are not acceptable.

In collaboration with the *Journal of Chemical Information and Modeling*, the Journal has further refined acceptance criteria for virtual screening manuscripts:

(v) In order to validate virtual screening hits obtained from any source, proof of dose-response behavior, confirmation of IC_{50} or K_i values, and controls for nonspecific or artificial inhibition (i.e., proof of reversibility, detergent controls, etc.) must be provided. For active compounds, identity and purity data consistent with the Scope and Editorial Policy must be submitted. For active compounds obtained from external sources, evidence of purity should be provided.

Published on Web 12/11/2009

The majority of current submissions combining synthetic/SAR studies and computational analyses apply established computational methods to rationalize binding data and/or predict compound binding modes. Many of these manuscripts report "double-hypothetical" molecular models such as complexes obtained by docking of active compounds into homology models of target proteins. In order to assess the current state-of-the-art of such investigations and their intrinsic accuracy limitations, one might consider, for example, the results of a recent community-wide initiative to predict the structure of a receptor−ligand complex in a "blind test" setting (Michino et al. *Nat. Rev. Drug Discovery* **2009**, *8*, 455). Clearly, computational analysis plays an important role in the interpretation of experimental data and in providing insights that are not readily available from experiment. However, care must be taken to ensure scientific rigor of predictions including hypothetical binding modes and conclusions drawn from them:

(vi) Detailed computational studies based on theoretical models of protein−ligand complexes that go beyond current accuracy limitations of hypothetical models are strongly discouraged. If modeling studies are identified in manuscripts focusing on experimental SAR analysis that do not meet the standards and required computational rigor of the Journal, the manuscripts will be returned without peer review.

We look forward to the continued submission of high-quality computational manuscripts that will further advance the medicinal chemistry field. Computational innovation and studies that seamlessly integrate computation and experiment with clear utility for medicinal chemistry are highly encouraged. Thank you to our authors, reviewers, and editorial advisory board members who help to ensure the high standards of computational publications in the Journal.

Jürgen Bajorath
Senior Editor