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Guest editorial for special issue on "ADME and Physical Properties"

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The prediction of physical properties and ADME parameters remains an area of considerable interest and challenge, despite the enormous amount of effort that has been devoted to it by multiple research groups throughout the world. During a 3 day symposium at the American Chemical Society National Meeting in San Francisco in September 2006, 25 speakers presented recent results in the area of physical property and ADME modeling. The range of topics was broad, as were the institutions represented, including speakers from the pharmaceutical industry, academia, software companies, research institutes and government.

In this issue, five of the symposium speakers share their results. Although these articles represent only a small sampling of the science on display at the symposium, they do reveal some of the diversity of the symposium, both with respect to the scientists' institutions and the topics studied. Their articles also touch on several of the major themes that emerged in the symposium. I hope therefore that in addition to providing specific information on the topics presented here, this issue serves as a snapshot of the current state of ADME and physical property prediction.

One barrier to more widespread use of computational tools is inconsistency in the performance of many models on molecules from different chemical classes. One of the themes that emerged during the symposium was therefore the estimation of prediction accuracy. In this issue, Timon Schroeter and colleagues from the Fraunhofer FIRST Institute in Berlin describe a method for assessing prediction reliability in their use of Bayesian process models for the prediction of aqueous solubility. This technique adds to the similarity-based approaches, such as presented by Igor Tetko (Institute of Bioinformatics, GSF National Research Centre for Environment and Health, Neuherberg, Germany), available to assign confidence estimates to individual predictions. The use of similarity measures for reliability analysis is also highlighted in the article by Pil Lee and co-workers from Pfizer on the prediction of metabolic stability.

Another important theme raised by Dr. Lee and other presenters is the need for carefully curated data over a large, diverse set of compounds in order to build useful global models. By using a very large set of 47,000 metabolic stability measurements, and removing compounds near the cutoff, Lee et al. were able to build a predictive classifier despite the complexity involved in metabolic stability.

In addition to models based on statistical methods and machine learning, a significant amount of the presented work was directed toward more detailed physical models, such as for solubility and protein solvation. The permeability modeling work of Matt Jacobson's group at UCSF is an excellent example of this approach. Additionally, in the physical property area, the pK_a and tautomer prediction software Epik presented by John Shelley of Schrödinger, Inc., and the SPARC property prediction software discussed by several presenters, also represent an attempt to model physical observables by better understanding the underlying atomistic phenomena like protonation.

Finally, of great importance for the pharmaceutical and chemical industries is the use of computational models by various governmental agencies, such as the US Food and Drug Administration. Said Hilal of the US Environmental Protection Agency provides an overview of the use of SPARC within the EPA.

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It was a pleasure to hear about the research going on at these diverse labs, and I would like to thank the presenters for their efforts, along with the assistance of my symposium co-organizer Matt Walker, ACS COMP program chair Wendy Cornell, financial assistance provided by Merck & Co., Inc., and Terry Stouch, Editor-in-Chief, and Naomi Portnoy, Springer, for assistance in compiling this special issue of *JCAMD*.