

## **Environmental Systems Biology Framework for Human Health Risk Analysis**

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A computational framework is under continuing development for supporting studies of human health risks from environmental factors. This involves quantifying interactions of environmental and biological systems across multiple scales of spatiotemporal extent and biological organization, through a person oriented (anthropocentric), integrated approach. The source-to-dose modeling components constitute the Modeling Environment for Total Risk studies (MENTOR), which has been applied in assessing exposures and doses to multiple chemicals. The dose-to-effect modeling components constitute the Dose-Response Information Analysis system (DORIAN), which is under ongoing development. Together, they can support comprehensive toxicity and human health risk assessment studies that merge together “traditional” environmental and toxicology knowledge with toxicogenomic information that is becoming available from genomic, proteomic, and metabonomic studies. The ultimate goal is to study personalized risks utilizing concepts and mathematical tools from environmental systems biology and toxicology. The main rationale for following an integrated approach in source-to-dose-to-effect modeling is that human health states involve interactions among multiple levels of biological organization that are in turn affected by various types of environmental factors. The genetic code for any individual can be seen as a “set of initial conditions” for a dynamic biological system that will evolve under the influence of environmental conditions that depend critically on human behavior. So, a “person-specific,” anthropocentric approach that takes into account all the above is expected to eventually improve risk characterization. This framework also supports “bi-directional” analysis by allowing not only calculations of dose and biological effect from environmental and exposure information, but also, under certain conditions, the reconstruction of environmental exposure patterns from appropriate biomarker data. DORIAN includes ebTrack, which expands the features of ArrayTrack, developed at the U.S. Food and Drug Administration (FDA) National Center for Toxicological Research (NCTR) Center for Toxicoinformatics, by incorporating modules for the analysis of proteomic and metabonomic datasets, in addition to providing additional analysis modules for gene expression data. It is complemented by an “environmental bioinformatics Knowledge Base” ([www.ebkb.org](http://www.ebkb.org)) that covers resources for all the stages in the source-to-dose-to-effect sequence.

*The viewpoints expressed in this work are solely the responsibility of the authors and do not necessarily reflect the views of the U.S. Environmental Protection Agency or its contractors.*

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