

INTEGRATING ENVIROINFORMATIC AND BIOINFORMATIC APPROACHES FOR THE SYSTEMATIC ANALYSIS OF ENVIRONMENTALLY RELATED HUMAN HEALTH RISKS

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In the past, assessing the human impact on the environment, and the subsequent impact of environmental change on human well-being, was typically performed on a “stressor by stressor basis,” e.g. for groups of “related” chemical compounds, present in a given environmental medium (e.g. atmosphere, groundwater, etc.) and typically associated with a single exposure route (e.g. inhalation, ingestion, dermal absorption, etc.). Although this practice has evolved over time to allow considerations of multimedia contaminants, the focus has primarily remained on contaminant- and route-specific risk characterizations. In recent years, however, a major change has been taking place, through the development of “person-oriented” (i.e. anthropocentric) approaches and models, that aim to account for total (“cumulative” and “aggregate”) exposures of individuals (or of populations consisting of such individuals), to co-occurring stressors (i.e. mixtures of chemical, biological and radiological agents).

These new integrated, “systems-based,” approaches focus on individual humans, real or “virtual”, with well defined physiological, socioeconomic, behavioral, etc. attributes, and take into account how the detailed activities of these individuals in space and time affect (a) their “personal microenvironments,” and their corresponding exposures to stressors, and (b) the physiological and biochemical processes determining biologically relevant dose and eventually biological effect (e.g. uptake rates; metabolic rates and pathways; toxicodynamics). Proceeding a major step further, person-oriented approaches currently aim to take advantage of information on genetic and other factors that determine the highly variable individual susceptibility to environmental stressors. Current advancements in toxicoinformatic (genomic, transcriptomic, proteomic, metabonomic etc.) technologies and data are successfully used to provide quantitative understanding of the intra- and inter-individual variability in responses to various environmental factors, thus eventually giving rise to “personalized” risk assessments.

The US Environmental Protection Agency (USEPA) has established a multifaceted “university partnership” with EOHSI, that supports a continuing research effort to develop, evaluate and apply an integrated modeling and database framework for probabilistic analyses of the complete “environmental health sequence”. This effort, over the past seven years, has resulted in the evolution of two complementary software “systems of model and data components,” operating on customized Linux clusters: the Modeling ENvironment for Total Risk studies (MENTOR), that addresses the “source-to-dose” steps, and the DOse-Response Information Analysis system (DORIAN), for the biological “dose-to-effect” steps.

Various problem-specific implementations of this framework have been developed and applied to a wide range of environmental issues in the USA, including: regional/multiscale ozone and airborne particulate matter (PM) control; urban/local scale inhalation exposures to complex mixtures of co-occurring ozone, PM, and air toxics; contaminant releases from forest and urban

fires; groundwater contamination; multimedia and multipathway exposures to mixtures of metals/metalloids (Hg, Cd, Cu, As, etc.) and their compounds, to pesticides, to organic solvents, to water chlorination by-products, etc. Special focus has been on novel methods for systematic simplification of complex models and for uncertainty analysis and reduction. Up-to-date information on publications and on scientific developments related to the above efforts, is posted regularly on the web site of the Computational Chemodynamics Laboratory of EOHSI (www.ccl.rutgers.edu) and at www.EnvironmentalBioinformatics.org.

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