

Computational Model of the Hypothalamic-Pituitary-Gonadal Axis to Predict Biochemical Adaptive Response to Endocrine Disrupting Fungicide Prochloraz

M. Breen^{1,2}, D.L. Villeneuve³, G.T. Ankley³,
K.H. Watanabe⁴, M.S. Breen⁵, A.L. Lloyd², and R.B. Conolly¹

¹National Center for Computational Toxicology, US EPA, RTP, NC, USA

²Biomathematics Program, Department of Statistics, North Carolina State University, Raleigh, NC, USA

³Mid-Continent Ecology Division, US EPA, Duluth, MN, USA

⁴Department of Environmental and Biomolecular Systems, Oregon Health & Science University, Beaverton, OR, USA

⁵National Exposure Research Laboratory, US EPA, RTP, NC, USA

There is increasing evidence that exposure to endocrine disrupting chemicals can induce adverse effects on reproduction and development in both humans and wildlife. Recent studies report adaptive changes within exposed organisms in response to endocrine disrupting chemicals, and altered dose response and time-course (DRTC) behaviors to minimize the effects caused by stressors. We are developing a mechanistic mathematical model of the hypothalamic-pituitary-gonadal (HPG) axis in female fathead minnows to predict DRTC for endocrine disrupting fungicide prochloraz. The model includes several feedback regulatory loops to analyze the adaptive response to endocrine stress from exposures to the fungicide prochloraz. Experiments were performed using adult fathead minnows with an 8-day exposure and 8-day recovery phase, and multiple samples were collected during both phases. Computer simulations were performed to compare the model-predicted DRTC with experimental data. This model characterizes the mechanisms underlying the adaptive response to refine DRTC behavior for prochloraz, and helps us better understand whether exposures pose health risks. *This work was reviewed by the U.S. EPA and approved for publication but does not necessarily reflect Agency policy.*

M. Breen was supported by the NCSU/EPA Cooperative Training Program in Environmental Sciences Research, Training Agreement CT833235-01-0 with North Carolina State University.