**LOW-DOSE EXTRAPOLATION MODELS FOR RELIABLE HUMAN HEALTH ASSESSMENT**

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Dose response models are important tools in assessing the impact of pollutants to human health. A dose response model can be written as $f(x, \mathbf{p}) = y$, where $x$ is the chemical concentration, $\mathbf{p} = (p_1, \ldots, p_k)$ is a vector of input parameters, and $y$ is the measured effect of a chemical concentration on an organism's health. By definition no dose has no effect on health, that is $f(0, \mathbf{p}) = 0$. Parameters are estimated by fitting paired measurements of dose and response $(x_1, y_1), \ldots, (x_n, y_n)$ to the model. We often have measurements of dose response for only mid to high values of $x$. However, most exposures to a chemical concentration occur at low doses. The extrapolation is uncertain because the relationship governing how responses arise from dose is unknown. We must take this uncertainty into accout when estimating $f(x_{low}, \mathbf{p})$. Assuming a fixed error on the measure responses $y_i \pm \epsilon_i$ and $f(0, \mathbf{p}) = 0$, set inversion via interval analysis [1, 2] can be used bound the set of parameters which is consistent with the data: $\mathbf{p}_{\text{space}} = \{\mathbf{p_j} | \underline{y}_i \leq f(x_i, \mathbf{p}_j) \leq \overline{y}_i, \forall i\}$, where $\left[\underline{y}_i, \overline{y}_i\right]$ are interval bounds on the measured response. By forward propagating the set $\mathbf{p}_{\text{space}}$ along with $x_{low}$ through the dose response model bounds can be set $\underline{y}_{low} \leq f(x_{low}, \mathbf{p}_{\text{space}}) \leq \overline{y}_{low}$. This paper will make clear how this approach differs in handling uncertainty from traditional statistical estimation.

# References

[1] Ramon Moore. Parameter sets for bounded-error data. *Mathematics and Computer and Information Science*, 34:113-119, 1992.

[2] Luc Jaulin and Éric Walter. Gauranteed nonlinear parameter estimation via interval computations. *Interval Computations*, 3: 61-75, 1993.