Development of an Approach to Evaluate Multi-ion Toxicity to Aquatic Organisms

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Overview

• Historical Perspective: Membrane Potential
• Recent Developments: Major Ion Toxicity (MIT) Model
• Importance of Speciation in the MIT Model
• Conclusions
Hodgkin and Huxley (1939) succeeded in “inserting micro-electrodes into the giant axons of squids (Loligo forbesi)” to record membrane potential between the axoplasm and the external medium.
“Professor Hodgkin and Professor Huxley, who worked together, were able to devise a system of mathematical equations describing nerve pulse.”

Goldman-Hodgkin-Katz (GHK) Equation
Recent Developments

• Elevated **TDS/Conductivity** cause physiological stress to aquatic organisms.

• For assessing **multi-ion toxicity (MIT)** for major ions USEPA (2011) set an aquatic life benchmark of 300 μS/cm.

• Expected to be technologically difficult and costly to achieve.

• It is important that benefits are actually realized.
Effect of Conductivity on *Ceriodaphnia dubia* 48-hr Mortality

*Conductivity level generally protective of *C. dubia*

Mount et al. (1997) *C. dubia* dataset

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MIT Framework: Generalized Approach

Biotic Ligand Model (BLM)*

*National Freshwater Quality Criteria for Cu based on BLM (EPA, 2007)
MIT Framework: Generalized Approach

Major Ion Toxicity (MIT)

TDS or Conductivity

Na⁺  K⁺  Ca²⁺  Mg²⁺
Cl⁻  SO₄²⁻  HCO₃⁻

Major Ions

Voltmeter

Extracellular Fluid

Cell
Rationale for Approach: Electrochemical Gradients

Nernst Equation, $V_m$:

$$V_m = \frac{RT}{zF} \ln \frac{[K^+]_o}{[K^+]_i}$$

... applies to single ions

Notation:
- $i = \text{inside} \& \ o = \text{outside}$
- $R = \text{Universal Gas Constant}$
- $T = \text{Absolute Temperature}$
- $F = \text{Faraday Constant}$
- $z = \text{valence}$
Goldman-Hodgkin-Katz (GHK) Equation

Use GHK Eq. to evaluate \( V_m \) for an ion mixture:

\[
V_m = \frac{RT}{F} \ln \left( \frac{p_K [K^+]_o + p_{Na} [Na^+]_o + p_{Cl} [Cl^-]_i}{p_K [K^+]_i + p_{Na} [Na^+]_i + p_{Cl} [Cl^-]_o} \right)
\]

Function of:
- Inside and Outside Concentrations
- Ion Permeability Coefficients \( (p_K, p_{Na}, p_{Cl}) \)

HYPOTHESIS: organism survival is related to membrane potential \( (V_m) \) in a dose-dependent manner
Mitigation of NaCl Toxicity by a Trace Level Addition of CaSO₄

Loeb et al. (1902) F. heteroclitus dataset
Model Application to the Daphnid Dataset

**DATASET:**
C. *dubia* (2,119 treatments), Mount et al., 1997

**FOUR MODEL FORMULATIONS:**

<table>
<thead>
<tr>
<th>MODEL</th>
<th>SPECIATION</th>
<th>ION INTERACTIONS (II)</th>
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<tr>
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</tr>
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</tbody>
</table>
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Mount et al. (1997) *C. dubia* dataset
Example Model Calibration Results (MODEL 4)

% Survival versus Membrane Potential ($V_m$)

% Survival +/- 1 Std Dev versus Membrane Potential ($V_m$)

Mount et al. (1997) C. dubia dataset

$V_{m50} = -7.7 \text{ mV}$
Response Independent of Composition

% Survival vs TDS for *C. dubia*

% Survival vs $V_m$ for *C. dubia*

TDS LC50s vary widely for individual ions or salts but converge to a single dose response curve based on calculated membrane potential.

Mount et al. (1997) *C. dubia* dataset

$V_{m50} = -7.7 \text{ mV}$
Predicted versus Measured LC50 Results (as TDS*)

Concentrations w/o IIs (MODEL 1)

\[ V_{M,50} \text{-BASED TDS}^* \text{ (mg/L)} \]

\[ \text{OBSERVED TDS}^* \text{ (mg/L)} \]

\[ R^2 = 0.55 \]

\[ N = 72 \]

Concentrations w/ IIs (MODEL 2)

\[ V_{M,50} \text{-BASED TDS}^* \text{ (mg/L)} \]

\[ \text{OBSERVED TDS}^* \text{ (mg/L)} \]

\[ R^2 = 0.83 \]

\[ N = 71 \]

Mount et al. (1997) C. dubia dataset
Predicted versus Measured LC50 Results (as TDS*)

Activities w/o IIs (MODEL 3)

Activities w/ IIs (MODEL 4)

Mount et al. (1997) C. dubia dataset
Conclusions

• As a first approximation
  • Survival is related to membrane potential in a dose-dependent manner, and
  • The results can be used to predict acute effect levels (as TDS*) with wide variations in composition
  • Using activities versus concentrations does not markedly alter model predictive ability

• Future testing and development needed.
  • Apply model to data for additional organisms
  • Apply model to chronic effects data
  • Explore joint but independent action effects due to membrane potential and osmolarity
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References


References
