

Perspective on the US Army's Uses for Predictive Models of Acute Oral Toxicity

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Army and Chemicals: It's Complicated

Battlefield Warfighter Needs	Military Enterprise Needs
<p data-bbox="79 529 909 565">Intelligence Preparation of the Battlefield</p> <ul data-bbox="142 572 909 765" style="list-style-type: none">What chem/bio threats existWhere do chem/bio threats existWhat is the risk of incapacitationWhat are the appropriate countermeasures <p data-bbox="79 796 417 832">Small Unit Needs</p> <ul data-bbox="142 836 823 1023" style="list-style-type: none">Sensors to identify chemical/biologicalWhat are the likely acute symptomsWill this lead to incapacitationWhat is appropriate countermeasure	<p data-bbox="981 529 1792 565">Military Materials Design and Production</p> <ul data-bbox="1006 572 1875 818" style="list-style-type: none">Kill new chemical entities early in developmentMove toxicity testing earlier in developmentMethods that use only structure for tox screeningDecrease testing costsIncrease testing throughput

OBJECTIVE: DECIDE FASTER

My Role At the US Army

- Objective
 - To get the Army (and our partner Agencies) the best models and tools to DECIDE FASTER
 - Intelligence Preparation of the Battlefield, Emergency Response, and Enterprise Needs (platforms, weapons, materials)
- Approach
 - Technology Development
 - Basic and applied research portfolio in Artificial Intelligence
 - Ethical, Legal, Social Implications of AI
 - AI to predict toxicity using only structural information or read-across
 - Fill model and needs gaps
 - Technology Enabling
 - Work with others outside Army to develop applied research products
 - Acquire open source and freely available tools
 - Technology Transfer
 - Develop predictive AI and model platforms that use existing data and structural information to make predictions that enable the Army to DECIDE FASTER

What Do We Need from QSAR Models?

- Open source and freely available are most useful
- Need the data used to train, test, and validate
- Why?
 - Need to be able to validate that the tool does what it says through code examination
 - AI/Models and Bias
 - Need to identify potential sources of bias and outcomes of any bias to mitigate impact on decisions
 - Operational Security (OpSec)
 - Need to ensure we understand what the software might communicate with, how it communicates, and what it communicates with
 - We seek to build software systems that enable end-users to use these models
 - Typically academic models lack a GUI – our end users expect a GUI experience

Our Challenges with Computational Models

- Army chemistries tend to be unique
 - Energetics and explosives tend to have a large number of C-N bonds
 - Thus, many of our chemistries fall outside the domain of applicability of most models
 - We have unique mixtures as a result
- De novo chemical-biological interactions are generally necessary
 - Docking and 3-D models tend to not perform that great (in general)

Where Are Moving?

- “Industrial” Side
 - Structures to perform early structural screening
 - Identify potential toxicity liabilities (human and environmental) early in development
 - Tradespace analysis
 - Potential for readiness impacts
 - Environmental toxicity in endangered species may close training sites until cleaned up
 - Understanding and forecasting liabilities of legacy contaminants
- Intelligence side
 - Inform about potential toxicity of chemicals that may be encountered on the battlefield
 - Urban warfare significantly increases the list of potential chemicals
 - Inform about potential chemicals that may be used as emerging chemical warfare agents
 - Inform about potential PPE that may be required, or how targeting may impact environmental conditions that may degrade operations
 - Example: Hitting this building may cause release of XYZ chemical that may cause severe respiratory distress in local population
 - Lead to secondary mobility issues due to emergency response workers in the area
 - Warfighters may require PPE to prevent exposure that would degrade readiness

Things to Remember

- Army develops chemicals and materials for warfighter use
- Army interests in toxicology span multiple fields
 - Public health
 - Occupational health
 - Environmental health
 - Intelligence Preparation of the Battlefield
- Army is interested in acquiring and fielding new computational technologies to meet its varied needs
- Models need to be open source, with all of the data used for training, testing and validation made available
 - To ensure works as advertised
 - To understand potential biases
 - Operational Security
- Army chemistries tend to be different from commerce chemical and pharmaceutical industry
- Army is also interested in being able to identify potential liabilities from ALL chemicals
 - Forecast potential use of chemicals as weapons
 - Forecast potential outcomes from targeting

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