Semi-Automated Information Extraction to Improve Scientific Knowledge Discovery in Environmental Health Science Literature

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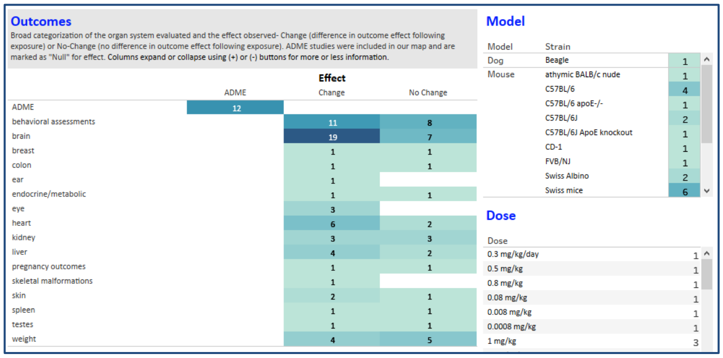
Introduction: The National Toxicology Program (NTP) at the National Institute of Environmental Health Sciences (NIEHS) conducts literature-based evaluations using systematic review methods to objectively and transparently assess the evidence that environmental substances may be associated with adverse health effects. These reviews collect information on chemicals from published scientific literature such as toxicity and health outcomes assessed, test methods, human populations or animal models, and results using a structured process (NTP 2019). Depending on the research question and the extent of available data, an evaluation may characterize the evidence in scoping reviews with interactive evidence maps (Figure 1) to identify data-poor and data-rich areas for further research, or the evaluation may integrate the evidence to reach conclusions on human health hazards associated with environmental exposures.

Conducting a review is time-consuming and resource intensive – often requiring more than 1,000 hours and $100,000 USD. As such, NTP is actively pursuing automated and semiautomated processes for information extraction (IE) and natural language processing (NLP) in our workflow to reduce time and labor-costs while maintaining quality and reproducibility for our products. The NTP is also applying IE methods to other data needs such as assessing institutional impact through citations and improving document screening and prioritization.

Figure1: Example interactive evidence map (Vinpocetine Outcomes in Animals)



Outcomes

Broad categorization of the organ system evaluated and the effect observed- Change (difference in outcome effect following exposure) or No-Change (no difference in outcome effect following exposure). ADME studies were included in our map and are marked as "Null" for effect. Columns expand or collapse using (+) or (-) buttons for more or less information.

		Effect	
	ADME	Change	No Change
ADME	12		
behavioral assessments		11	8
brain		19	7
breast		1	1
colon		1	1
ear		1	
endocrine/metabolic		1	1
eye		3	
heart		6	2
kidney		3	3
liver		4	2
pregnancy outcomes		1	1
skeletal malformations		1	
skin		2	1
spleen		1	1
testes		1	1
weight		4	5

Model

Model	Strain	
Dog	Beagle	1
Mouse	athymic BALB/c nude	1
	C57BL/6	4
	C57BL/6 apoE-/-	1
	C57BL/6J	2
	C57BL/6J ApoE knockout	1
	CD-1	1
	FVB/NJ	1
	Swiss Albino	2
	Swiss mice	6

Dose

Dose	
0.3 mg/kg/day	1
0.5 mg/kg	1
0.8 mg/kg	1
0.08 mg/kg	1
0.008 mg/kg	1
0.0008 mg/kg	1
1 mg/kg	3

Training Data: The NTP has several datasets available to share with experts to identify, develop, test, and implement new NLP/IE models relevant to systematic reviews and wants to develop environmental health relevant datasets that may inform models.

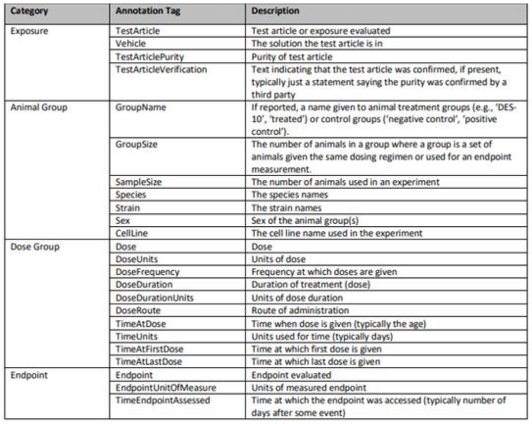
NIST SRIE: NTP hosted the 2018 Systematic Review Information Extraction (SRIE) track for the National Institute for Standards and Technology (NIST) Text Analysis Conference (TAC). For this challenge, NTP manually curated training and test data sets of 100 articles each by tagging mentions and groups of mentions relevant to IE in published animal studies (Figure 2).

Health Outcomes Data Set: NTP is preparing a data set of 1000 articles manually tagged at the full text level for health outcomes based on content in the title, abstract, and full text.

Systematic Reviews: NTP has access to 664 articles with extracted terms, but without location information that could be used in distant supervision.

Uterotrophic Data set: NTP has developed a data set of 670 articles tagged on six study protocol criteria considered minimal requirements to distinguish high-quality animal studies conducted according to regulatory guidelines (Kleinstreuer et al. 2015).

Figure2: SRIE Track data tagging scheme



Category	Annotation Tag	Description
Exposure	TestArticle	Test article or exposure evaluated
	Vehicle	The solution the test article is in
	TestArticlePurity	Purity of test article
	TestArticleVerification	Text indicating that the test article was confirmed, if present, typically just a statement saying the purity was confirmed by a third party
Animal Group	GroupName	If reported, a name given to animal treatment groups (e.g., 'DES-10', 'treated') or control groups ('negative control', 'positive control').
	GroupSize	The number of animals in a group where a group is a set of animals given the same dosing regimen or used for an endpoint measurement.
	SampleSize	The number of animals used in an experiment
	Species	The species names
	Strain	The strain names
	Sex	Sex of the animal group(s)
	CellLine	The cell line name used in the experiment
Dose Group	Dose	Dose
	DoseUnits	Units of dose
	DoseFrequency	Frequency at which doses are given
	DoseDuration	Duration of treatment (dose)
	DoseDurationUnits	Units of dose duration
	DoseRoute	Route of administration
	TimeAtDose	Time when dose is given (typically the age)
	TimeUnits	Units used for time (typically days)
	TimeAtFirstDose	Time at which first dose is given
	TimeAtLastDose	Time at which last dose is given
Endpoint	Endpoint	Endpoint evaluated
	EndpointUnitOfMeasure	Units of measured endpoint
	TimeEndpointAssessed	Time at which the endpoint was accessed (typically number of days after some event)

Challenges with Adoption of NLP

1. Methods advancement requires environmental health relevant datasets that are costly to develop. Approaches are needed for online models that self-improve with use, and generating training data from usage without impacting curation workflows (e.g., without requiring tagging of all negative or positive mentions).

2. Existing methods lack context awareness. Literature assessment workflow needs to identify relevant context of terms not just identify terms somewhere in the paper. For example, a chemical may be used as an anesthetic, part of laboratory procedures, or an experimental treatment, exposure, or control. Methods to derive context and allow experts to provide context to models are needed.

3. Improvements are needed in handling mentions that are similar to but not specifically found in training sets, as well as for extracting complex concepts (e.g., timing of exposure / endpoints) that are not contiguous but rather have long spans and multiple subphrases.

4. Existing methods are not adept at extracting statistical results and assigning those results to the correct endpoints.

5. Advances in grouping extracted entities are needed. Environmental health assessments gather data from multiple evidence streams - epidemiological studies, non-human animal studies, and *in vitro* and mechanistic data. These all require data to be sorted and grouped. For example, a single animal study may investigate effects of exposure to one or more chemicals by evaluating multiple endpoints, on several health categories, in one or more species or experimental models. It is critical that semi-automated data extraction approaches consider and maintain the complex structure of the data being extracted.

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