Staying grounded: assembling structured biological knowledge with help from large language models

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Sep 6 2023
AgBioData Webinar
Where does biological knowledge come from?

It’s the result of repeated observations.

Learning from those observations is a task in itself, but can be automated.

How may we automate:

- learning from literature?
- comparing findings?
- Integrating observations?
  - Across different studies or replicates?
  - Across different knowledge bases?
  - Across different fields and disciplines?
  - Of similar concepts, even when described in different contexts?
Background - what are current methods?

We need structured data.
Consistent data models, standards, and ontologies help but don’t do the work of structuring data for us.
How can we curate structured data from unstructured text?

- **Human experts** - a famously limited resource
- **Rule-based extractors** like SemMedDB*
  - Fairly high precision, low recall
  - Varies by domain and structure to extract
- **Enrichment** of terms and/or annotations, like MELODI**
  - Subject to publication bias
- **Neural networks** for Natural Language Processing (e.g., LSTMs)
  - Require extensive labeled training data…
  - and even then, they may overfit
- **Language models** (e.g., BERT)
  - Avoid learning the basics of language from scratch

Each method may still be effective for some use cases!

Can we translate unstructured scientific text directly into arbitrary knowledge schemas?

What if:
- Those schemas are **complex** and involve **nested subclasses**?
  - Like “each relationship between i and j where i is an object of type A and j is an object of type B but only from set C”
- We need to link to external unique identifiers?

Can Large Language Models (LLMs) like GPT-3+ help?
Bigger is better...
○ for some tasks.
○ More interesting: emergent behaviors
● Training data often unclear
○ Or may include fictitious claims
● Human-like performance, even in biomedicine
○ But without human reasoning
○ Or user ability to distinguish between human communication vs. generated text
○ See Levine et al. The Diagnostic and Triage Accuracy of the GPT-3 Artificial Intelligence Model. medRxiv (2023) doi:10.1101/2023.01.30.23285067
● Hallucinations
○ LLMs are grounded in language, not fact

Counts refer to the 202 tasks in the BIG-Bench language tech benchmark.

“Another example we produced that was outside of the scope for the present study was when asked about vaccines, GPT-3 responds, “Vaccines are not 100% effective. Vaccines can cause serious side effects. Vaccines can cause death. Vaccines are not tested for safety or effectiveness””

Figure from Bowman arXiv:2304.00612v1 [cs.CL]. (2023)
SPIRES: Structured Prompt Interrogation and Recursive Extraction of Semantics
(or, *information extraction grounded in reality*)

Populate knowledge schemas by providing structured prompts to a LLM. Parse the resulting response. Ground, map, and normalize the identifiers within using the [Ontology Access Kit](https://github.com/INCATools/ontology-access-kit).

Available through [OntoGPT](https://github.com/monarch-initiative/ontogpt):
Approach - SPIRES

Why not just tell the LLM to extract all relationships?


Predator–Prey Relationship

In Nature's plan, there is no such thing as a good or bad animal. There are only those animals that kill to eat (predators) and those that are killed and eaten (prey). It is unfair for us to judge their natural survival actions by our own ideas of what is good and bad or to decide that all predators are villains.

When the coyote chases, catches, kills, and eats the cute, furry rabbit, it is not being intentionally cruel. It is only meeting its physical need for food with whatever is available at the time. Its meal could just as easily have been a mouse, rat, or other small creature if one of these other animals had been closer or easier to catch.

Is there really any difference between a hungry mountain lion stalking, killing, and eating a deer and a hunter stalking, shooting, and taking a deer home for his family to eat? Both the mountain lion and the human hunter are predators, using the deer for food. You may think that since you are not a hunter, you are not a predator. How about the beef, pork, lamb, fish, or chicken you eat each day? Just because you do not kill the animal yourself does not make you less of a predator. You are still an animal eating the flesh of another animal to satisfy your hunger.

People usually think of predators as meat-eating mammals (carnivores), but the bird, reptile, amphibian, fish, and even plant-eating mammals (herbivores) share this characteristic. An ecological balance of predator and prey is essential to the health of the food web.

We can improve the result by using a more defined relationship and by grounding to a consistent set of concepts.
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People usually think of predators as meat-eating mammals (carnivores), but the bird, reptile, amphibian, fish, and some insect-eating plants are predators as well. Many plants can catch insects and even small animals.

This time, we’ve defined a schema specifically for relationships between taxa.
Why not just tell the LLM to extract all relationships?


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People usually think of predators as meat-eating mammals (carnivores), but the bird, reptile, amphibian, fish, and other cold-blooded animals are the ones the average person thinks of as predators. Eels, birds, lizards, and even a few invertebrates are known to eat fish, birds, and small mammals. The difference is only that the predator has to eat cold-blooded animals while the human predator has to eat warm-blooded animals.

Here, we’ve only used NCBITaxon and Gene Ontology - so we’re still missing some domain knowledge, but now have identifiers for concepts.
SPIRES works with a LinkML schema. (see linkml.io)
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A description of β-Catenin’s role and interactions with HSV-1
You et al. (2020) J Virol
PMID: 31801859

Title: β-Catenin Is Required for the cGAS/STING Signaling Pathway but Antagonized by the Herpes Simplex Virus 1 US3 Protein

Text: The cGAS/STING-mediated DNA-sensing signaling pathway is crucial for interferon (IFN) production and host antiviral responses. Herpes simplex virus I (HSV-1) is a DNA virus that has evolved multiple strategies to evade host immune responses. Here, we demonstrate that the highly conserved β-catenin protein in the Wnt signaling pathway is an important factor to enhance the transcription of type I interferon (IFN-I) in the cGAS/STING signaling pathway,...

GO-Causal Activity Model
GO-CAM
Template
Sediment communities from the hyporheic zone of the Columbia River along the Hanford Reach were sampled from April 30, 2014 to November 25, 2014, using sand packs deployed at three equivalent hyporheic zone locations.

A template for environmental sample metadata

Figure legend from a study of the hyporheic zone
Nelson et al. (2020) PLoS ONE
PMID: 31986180

Photo from https://commons.wikimedia.org/wiki/File:East_River_(northern_Gunnison_County,_Colorado,_USA)_ (46220745984).jpg
**Requirements:** Python 3.9 or greater.  
The `poetry` dependency toolkit for Python.  
The **Ontology Access Kit** ([https://github.com/INCATools/ontology-access-kit](https://github.com/INCATools/ontology-access-kit)).  
An OpenAI API key.

**Installation:** Clone the repository ([https://github.com/monarch-initiative/ontogpt](https://github.com/monarch-initiative/ontogpt))  
`poetry install`  
`poetry run runoak set-apikey -e openai <your openai api key>`

**To run and test:** `poetry run ontogpt extract -t mendelian_disease.MendelianDisease`  
`-i tests/input/cases/mendelian-disease-sly.txt`  
OntoGPT will download the necessary ontologies.
Next steps

See our preprint: https://arxiv.org/abs/2304.02711

- Automated KG assembly
  - Extract relations from literature,
  - Then integrate with those defined in knowledge bases,
  - And hierarchical relationships from ontologies,
  - And add predicted relationships
- Dealing with limitations
  - Reducing dependence on OpenAI
  - Avoiding hallucinations
- Improving ID mappings
- Gene enrichment analysis (SPINDOCTOR)
- Broad literature extraction
  - e.g., from PMC full-texts

OntoGPT/SPIRES performs just slightly worse than the average F1 score on the BioCreative V Chemical-Disease Relationship (CDR) task...though it requires no training or fine-tuning.
OntoGPT uses the Ontology Access Kit (OAK) for its annotators and grounders.

OAK works best with ontologies from the OBO Foundry and Bioportal.

To support use cases involving AgBioData, we can:

- Use Agroportal
- Extract plant strains and genomes by name
- Extract livestock traits and breeds
  - Vertebrate Breed Ontology (VBO) does some of this…but it’s a challenge to capture general names consistently
- Other use cases?
Thank You

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Icons ℅ the Noun Project (Made x Made; Rivercon)