Effective Entity Augmentation By Querying External Data Sources

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1. Drug Repositioning Can Save Lives

Patients with Castleman's disease
- ○ Rare
- ○ Potentially fatal: causes severe inflammation

Unfortunate reality:
✗ **Too rare**: no financial incentive for pharmaceutical companies to develop effective treatments

Alternative:
✓ Find an existing drug to treat Castleman's disease

Step 1: find a candidate drug

FDA-Approved Drugs

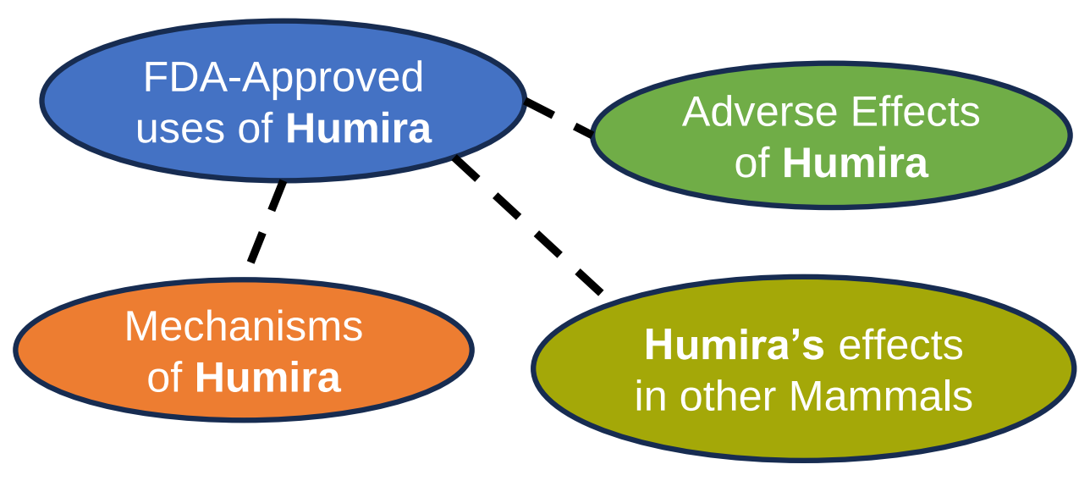
brand_name	class	uses
Humira	TNF inhibitor	rheumatoid arthritis, psoriatic arthritis …
Enbrel	TNF inhibitor	plaque psoriasis, ankylosing spondy…

Local Data Source

Biomedical Researcher

Humira is also used to treat conditions involving severe inflammation

Step 2: augment it with important information from external data sources


FDA-Approved uses of Humira
Adverse Effects of Humira
Mechanisms of Humira
Humira's effects in other Mammals

Manually Querying for External Information

Goal: Query for *data* about Humira from external sources

Challenge:
- ○ Data heterogeneity: each source = different representation
  - ○ Humira = Adalimumab = $C_{6428}H_{9912}N_{1694}O_{1987}S_{46}$ = ???
- ○ Many sources to query!

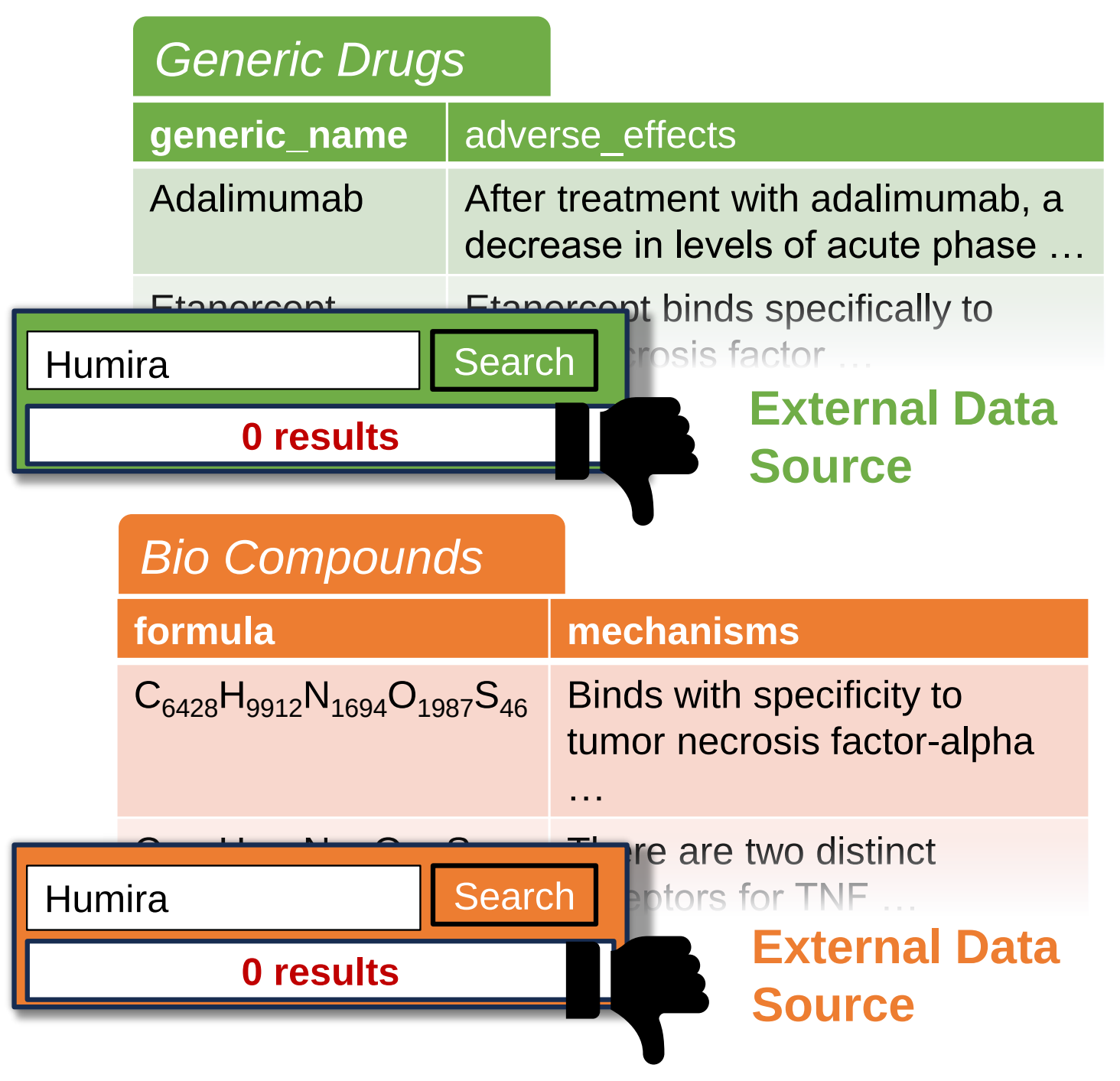
FDA-Approved Drugs

brand_name	class	uses
Humira	TNF inhibitor	rheumatoid arthritis, psoriatic arthritis …
Enbrel	TNF inhibitor	plaque psoriasis, ankylosing spon…

Local Data Source

Can Humira treat *Castleman Disease*?

Biomedical Researcher



Generic Drugs

generic_name	adverse_effects
Adalimumab	After treatment with adalimumab, a decrease in levels of acute phase …
Etanercept	Etanercept binds specifically to …osis factor …

External Data Source

Bio Compounds

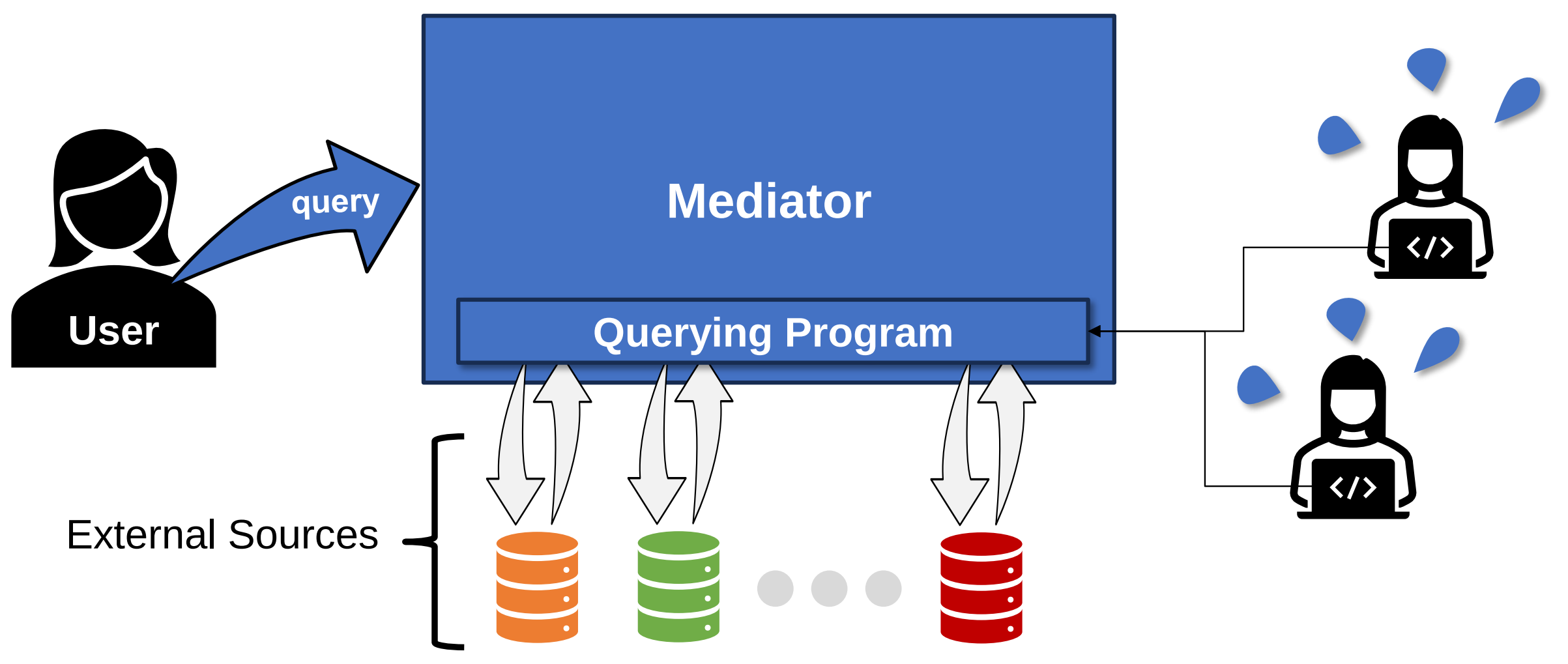
formula	mechanisms
$C_{6428}H_{9912}N_{1694}O_{1987}S_{46}$	Binds with specificity to tumor necrosis factor-alpha …
	There are two distinct …ptors for TNF …

External Data Source

2. Existing Work: Write Querying Programs By Hand

Use a **mediator** instead:
1. User specifies some *local* entity for augmentation (e.g., Humira)
2. Mediator returns entity augmented with *external* information

Mediator gathers external information using its own **Querying Program**



A lot of work for programmers
- ○ Write querying programs *for each* external source
- ○ Fix programs whenever sources change

Delayed entity augmentation
- ○ Takes time to build and maintain query programs
- ○ Users must wait for time-sensitive information

In an NIH-funded consortium of such systems (~14)
Just one system has…
- ○ 73 external sources
- ○ Millions of entities

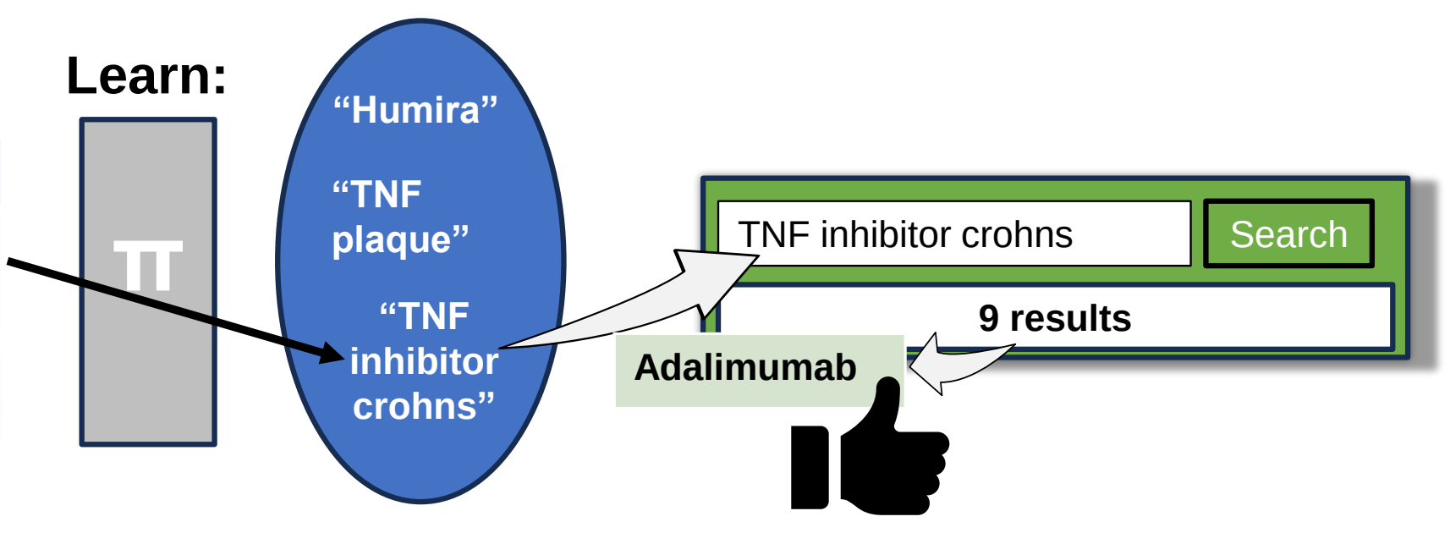
Total: US$923 million per year for development and maintenance

Learn the Mediator Online

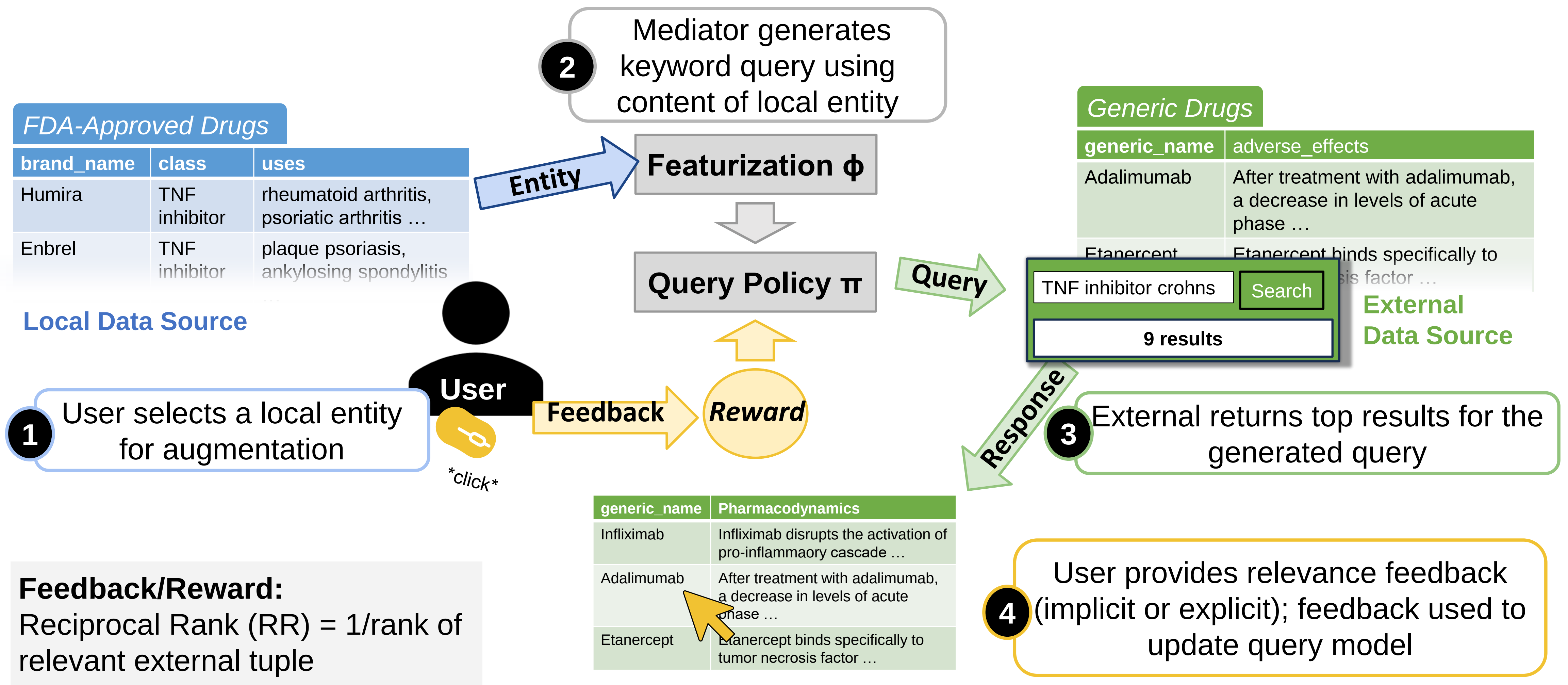
FDA-Approved Drugs

brand_name	class	uses
Humira	TNF inhibitor	rheumatoid arthritis, psoriatic arthritis …
Enbrel	TNF inhibitor	plaque psoriasis, ankylosing spondylitis …

Local Data Source



3. Online Autonomous Querying



FDA-Approved Drugs

brand_name	class	uses
Humira	TNF inhibitor	rheumatoid arthritis, psoriatic arthritis …
Enbrel	TNF inhibitor	plaque psoriasis, ankylosing spondylitis …

Local Data Source

1 User selects a local entity for augmentation

2 Mediator generates keyword query using content of local entity

3 External returns top results for the generated query

4 User provides relevance feedback (implicit or explicit); feedback used to update query model

Generic Drugs

generic_name	adverse_effects
Adalimumab	After treatment with adalimumab, a decrease in levels of acute phase …
Etanercept	Etanercept binds specifically to …sis factor …

External Data Source

generic_name	Pharmacodynamics
Infliximab	Infliximab disrupts the activation of pro-inflammatory cascade …
Adalimumab	After treatment with adalimumab, a decrease in levels of acute phase …
Etanercept	Etanercept binds specifically to tumor necrosis factor …

Feedback/Reward:
Reciprocal Rank (RR) = 1/rank of relevant external tuple

4. Challenges

A balancing act:

Short-Run Success: should learn sufficiently effective queries quickly
- ○ Users must remain engaged with the system

Long-Run Success: should continue to improve over time
- ○ Methods should not waste feedback
- ○ Avoid underfitting

Online setting: only know the quality of terms tried
- ○ Exploration: try new queries that *may* be better
- ○ Exploitation: use queries known to be good

5. Dataset-Level (Linear UCB)

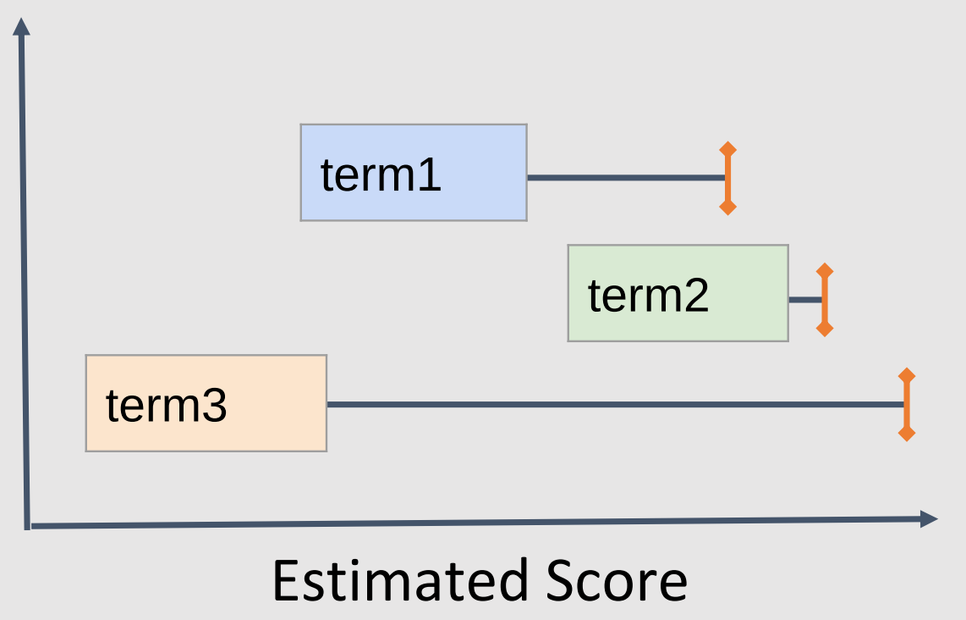
ϕ(inhibitor) **score** = $\theta_0 1\{\text{high IDF}\} + \ldots + \theta_n \text{term\_freq.}$

Learn Θ = $(\theta_0, \theta_1, \ldots, \theta_n)$ over *all* entities

Θ may underfit = poor long-run performance

linUCB
derive upper confidence bound on estimated scores

score = score + λ*UBC



6. Hybrid

Idea: When Θ overfits, diversify with more models!

Start: one Θ_{ALL} for all entities
Over Time: create new Θs for entities that Θ_{ALL} doesn't work for:

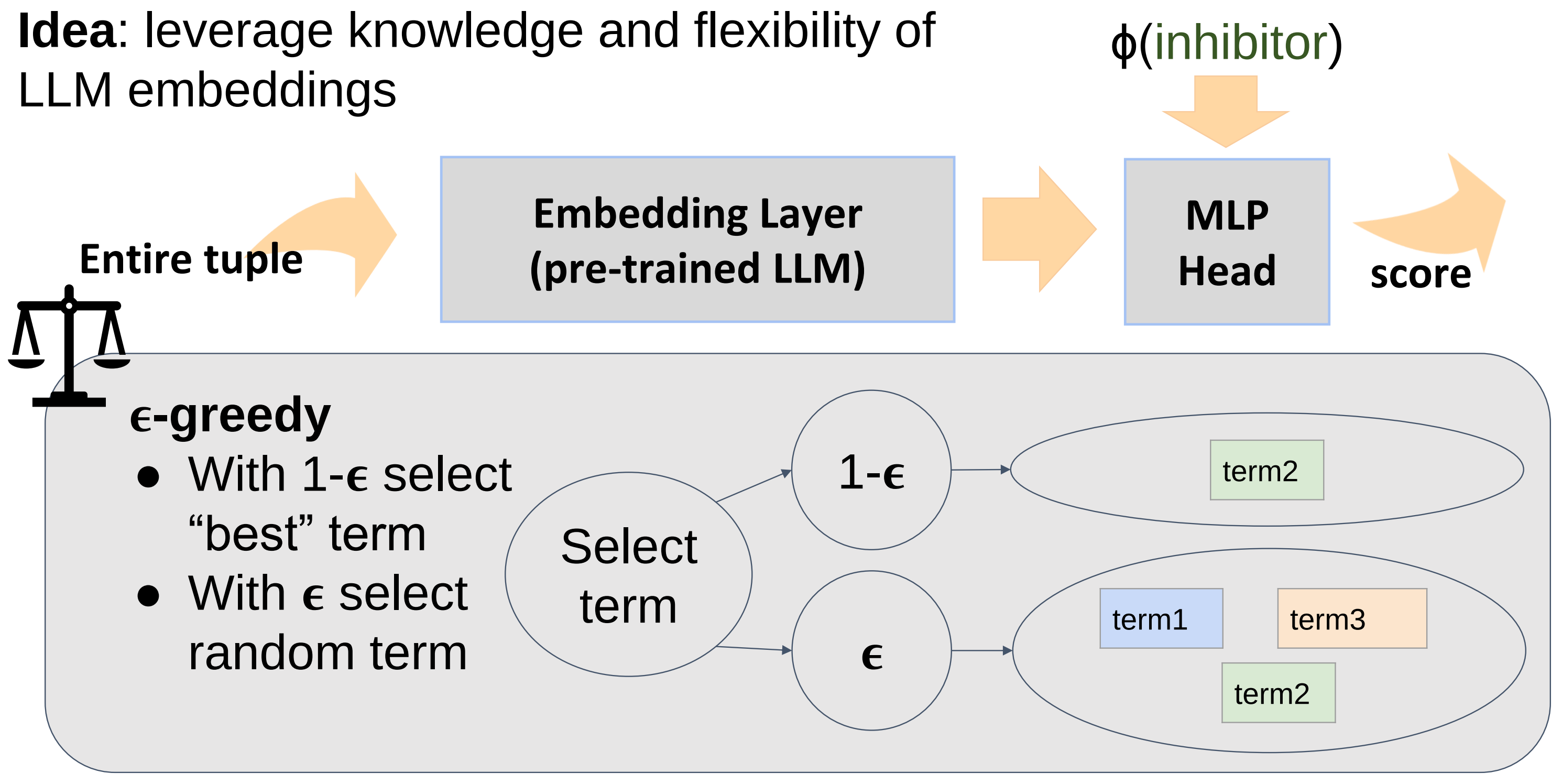
$$\Theta = (\Theta_{ALL}, \Theta_{Humira}, \ldots, \Theta_{Vyvanse})$$

Learn over all other terms

Learn over terms ∊ Humira

7. Leveraging LLM Priors (Longformer)

Idea: leverage knowledge and flexibility of LLM embeddings



ϵ-greedy
- With 1-ϵ select "best" term
- With ϵ select random term

8. Experimental Simulation (Dataset-Level vs. Longformer vs. Hybrid)

Simulate feedback with ground truth | **1 interaction** = 1 feedback cycle | Query length = 4 terms | 95% Confidence region for MRR (avg. over 5 runs)

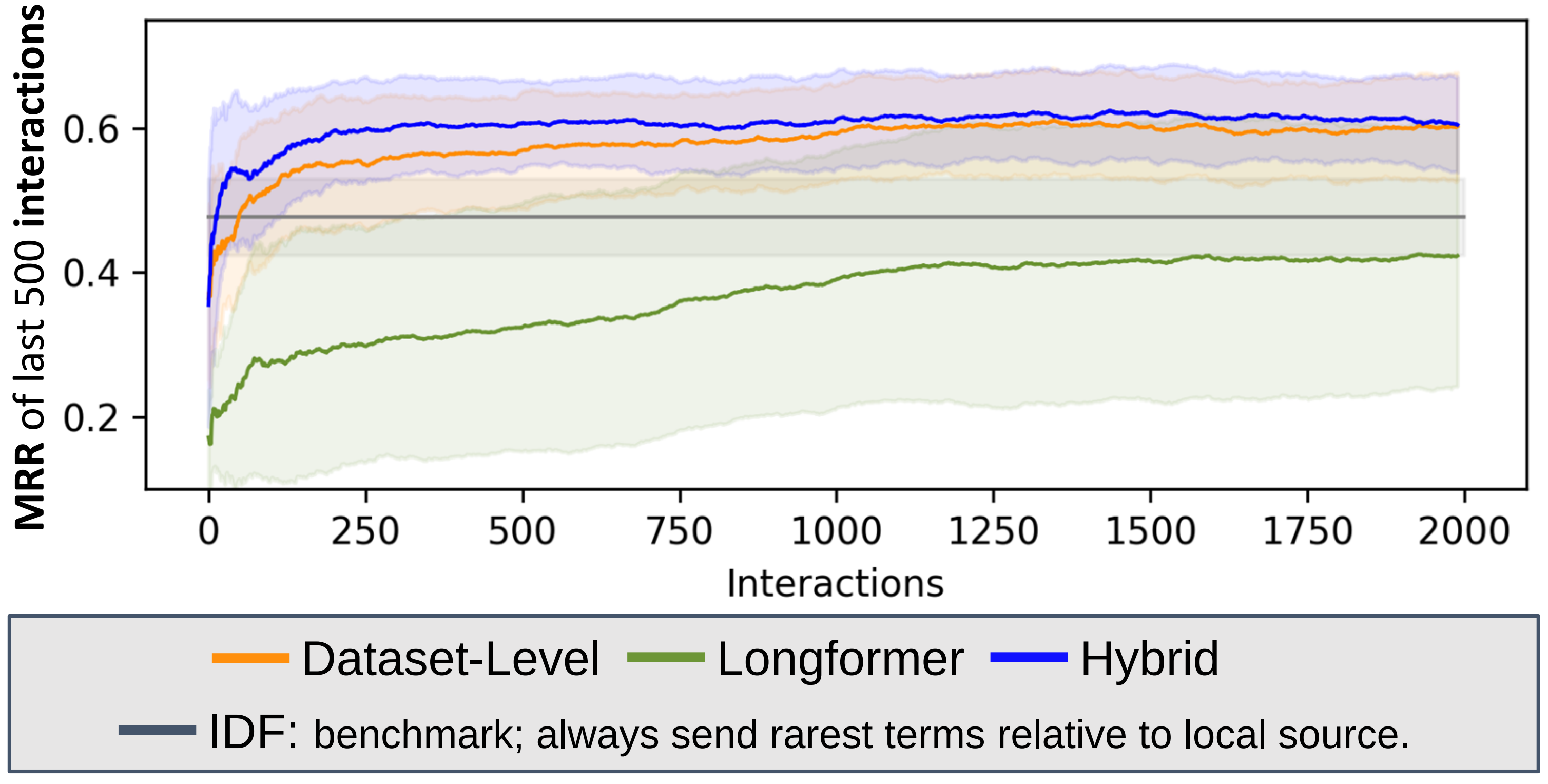
Model Comparison

Dataset-Level
- Good short-run performance
- Bad long-run performance

Longformer
- High variance in performance
- Slower to learn

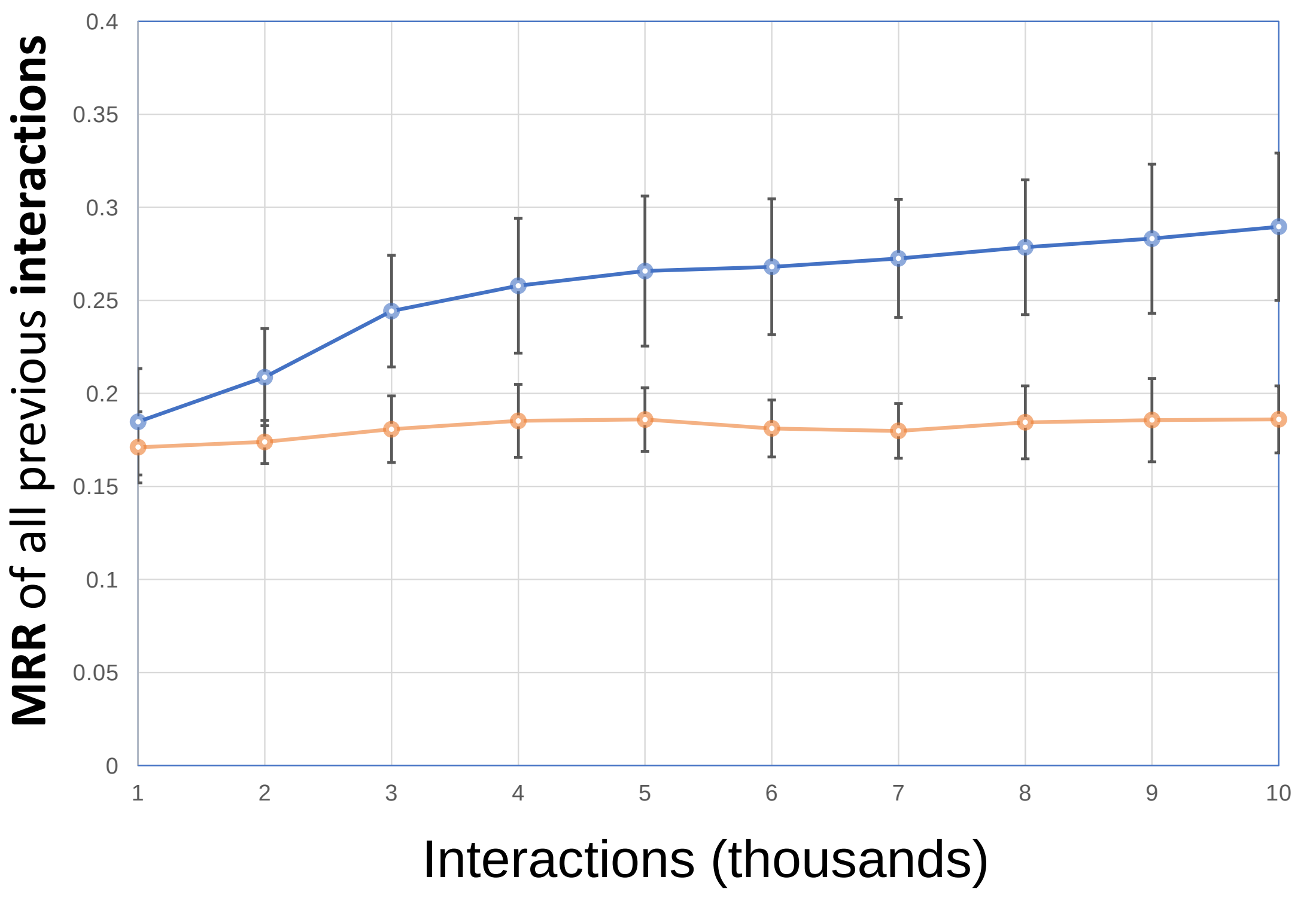
Hybrid
- Statistically insignificant increase over dataset-level

ChEBI



Dataset-level < Hybrid
- Hybrid significantly outperforms Dataset-Level over the same series of 10k tuples.
- Hybrid continues to learn over time = better long-run performance

CORD-19



See our paper for results over more datasets and query lengths. Also see additional techniques,

Term Borrowing: expand the kind of queries we can build *over time* as we interact with the external source
- Supervised: use terms from known external matches
- Unsupervised: find terms that allow us to discover new matches

Dynamic Query Length: adjust to the "sweet-spot" query length for external sources using a simple technique

LLaMA: use LLaMA as a pretrained model (as an alternative to Longformer)