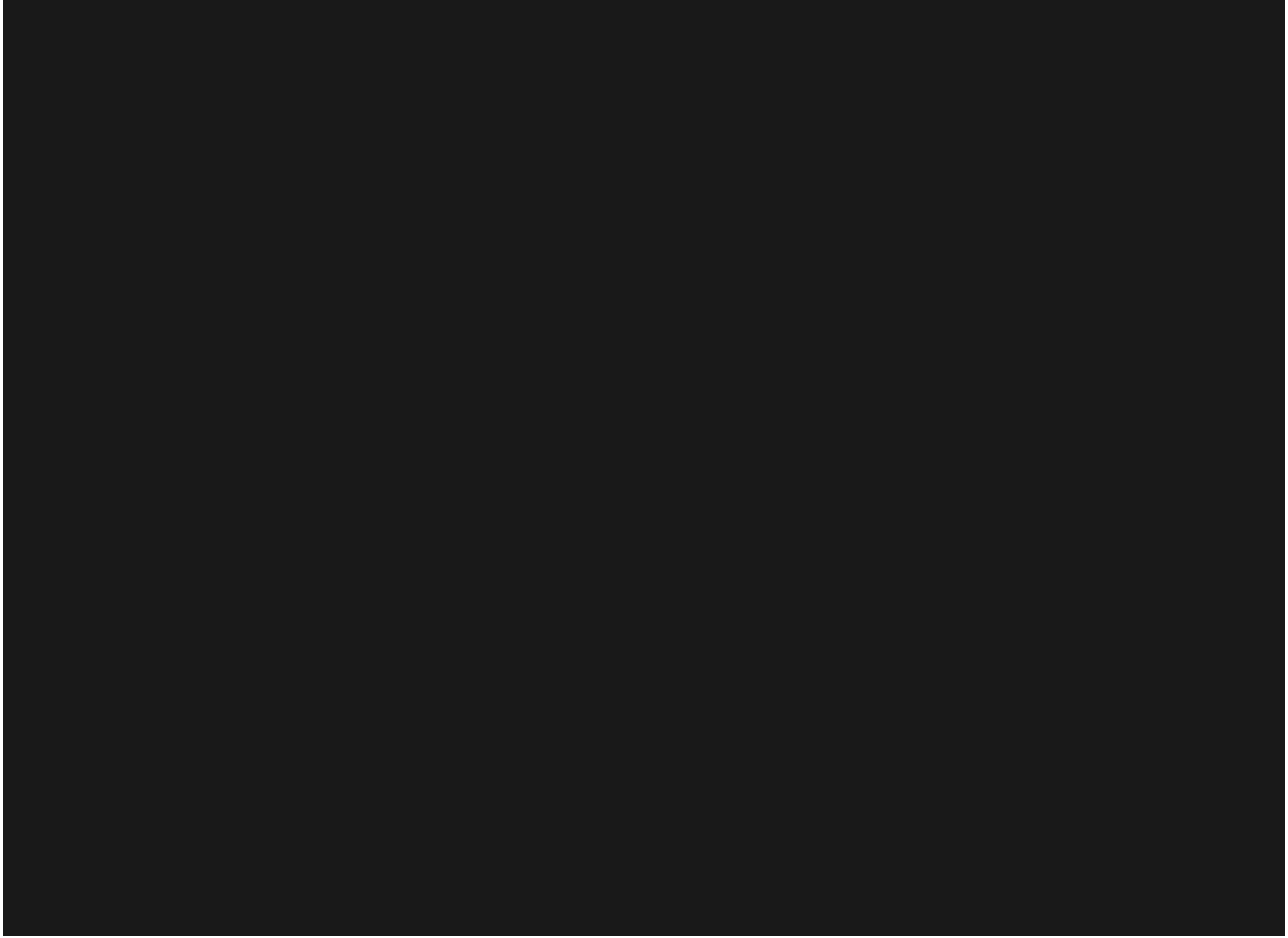
Automating Literature Research

FutureHouse

Health Research Alliance

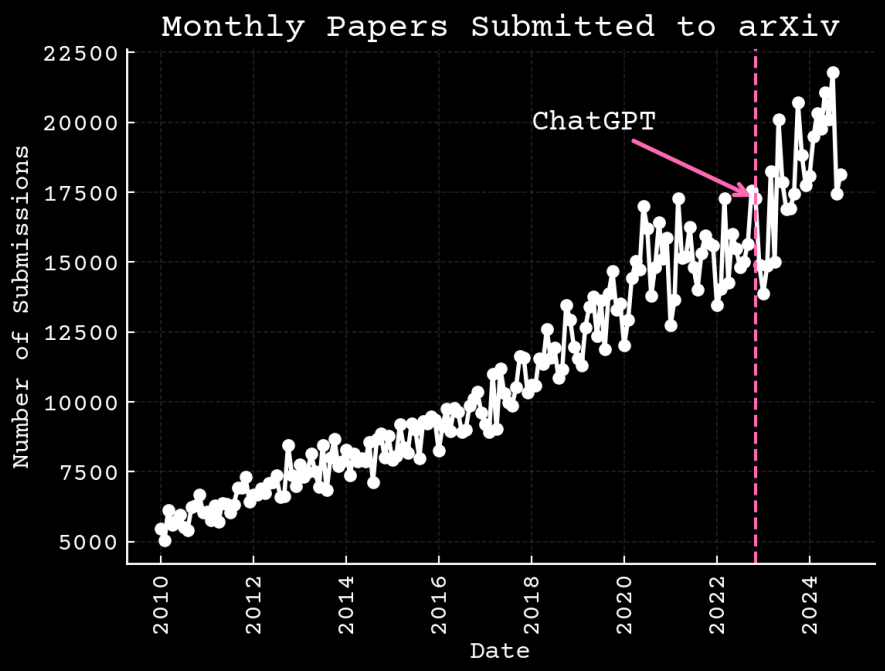
March 2025



FutureHouse Structure

- Non-profit
- Funded primarily by Eric Schmidt
- Based in San Francisco
- 20 employees

Science is changing independent of AI



Arxiv.org,10.6084/m9.figshare.17064419.v3

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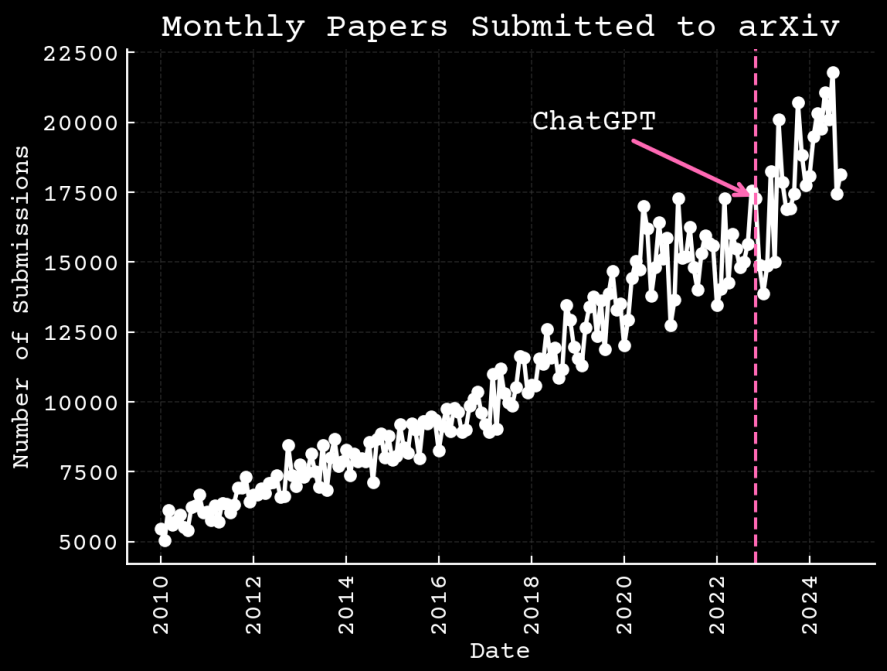

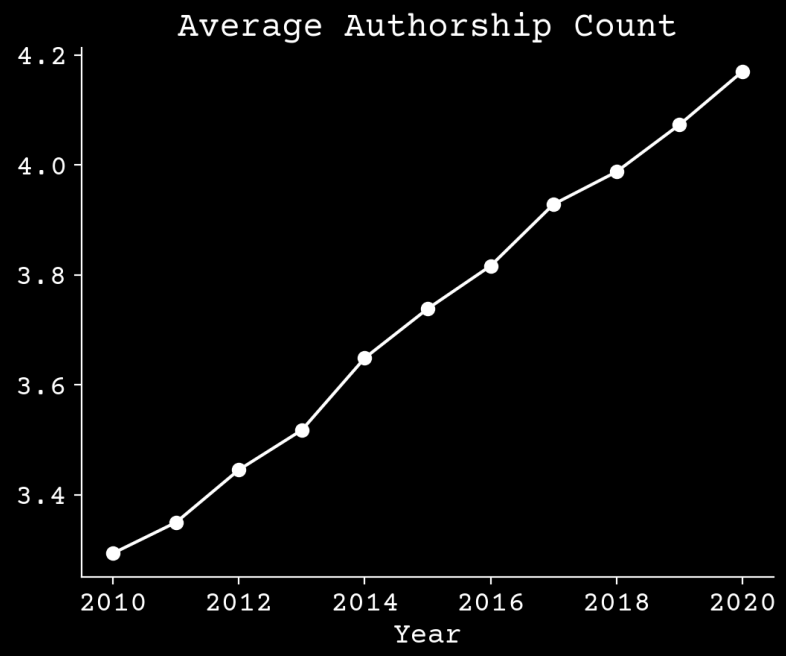

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Intellectual bottlenecks are growing

 Increasing paper count (≈5M per year)

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🧬 Larger data sets from cheaper experiments (genome at $200 per person, $1 / GB of sequencing)

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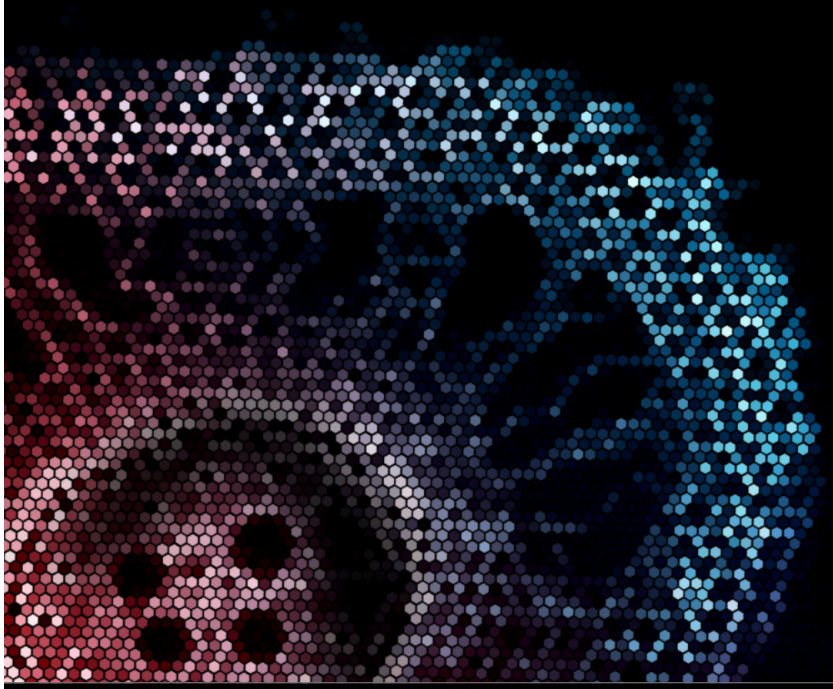
🔍Increasingly less disruptive papers (96% decline in biology)

Park, M., Leahey, E. & Funk, R.J. Papers and patents are becoming less disruptive over time. Nature 613, 138–144 (2023). https://doi.org/10.1038/s41586-022-05543-x

ion

odern science is omplex



Build a complete, mechanistic model for the brain

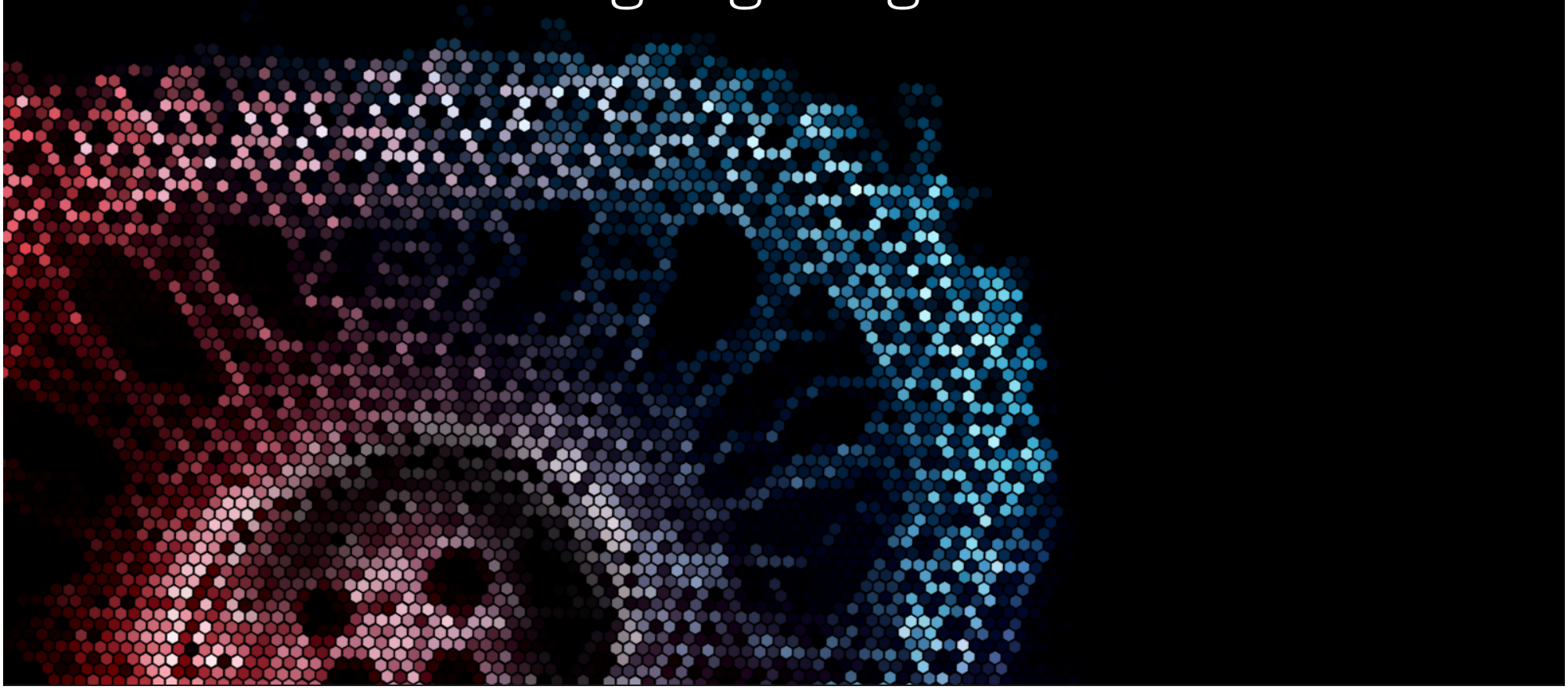
Annotate all the proteins of unknown function in the genome

Understand the function of every gene regulatory region

utureHouse

Mission

Accelerate Scientific Discovery with Language Agents



Can LLMs do science already?

LAB-Bench: Measuring Capabilities of Language Models for Biology Research

Jon M. Laurent, Joseph D. Janizek, Michael Ruzo, Michaela M. Hinks, Michael J. Hammerling, Siddharth Narayanan, Manvitha Ponnapati, Andrew D. White, Samuel G. Rodriques *arXiv:2407.10362*, 2024

Existing benchmarks

MMLU-Pro

1. As of 2017, how many of the world's 1-year-old children today have been vaccinated against some disease?

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MMLU-Pro

1. As of 2017, how many of the world's 1-year-old children today have been vaccinated against some disease?
2. Find the logarithm of 3^2

Lab-Bench Questions

Not textbook knowledge

Ans: “[ANSWER]**B**[/ANSWER]”

SeqQA

Query: What is the AA encoded at position 15 in the longest ORF contained within the sequence <REDACTED>? A) Insufficient... B) Pro **C) Asparagine** D) H E) Leucine

Ans: “To find the correct answer...[ANSWER]**E**[/ANSWER]”

LitQA

Query: Active olfactory receptor genes increase their contacts with greek island regions by what factor in mouse olfactory neurons? A) 2.0 fold B) 1.7 fold C) 3.0 fold **D) 2.7 fold** E) Insufficient... F) 27 fold

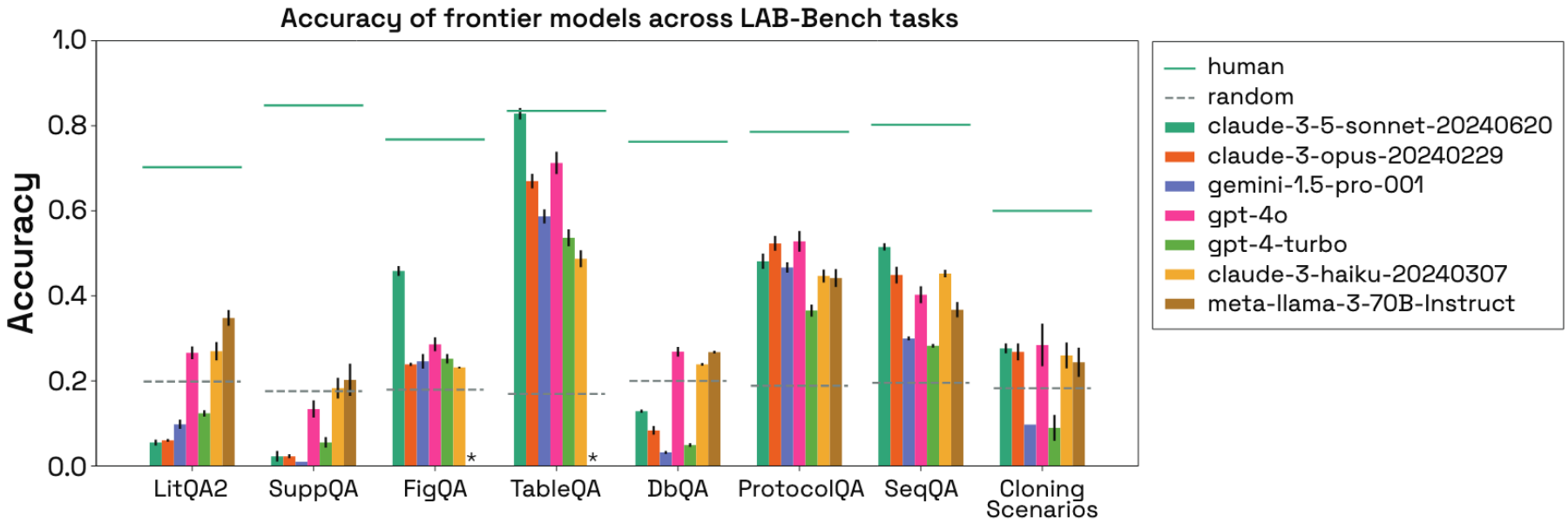
Ans: “[ANSWER]**B**[\ANSWER]”

Cloning Scenarios

Query: I have three plasmids with sequences pLAB-CTU: <REDACTED>, pLAB-gTU2E: <REDACTED>, pLAB-CH3: <REDACTED>. I combined all three plasmids together in a Golden Gate cloning reaction with Esp3I. The resulting plasmid expresses Cas9 protein as well as a targeting gRNA. What gene does the gRNA target? A) Insufficient...
B) Yeast SCL1 C) Human PRC3 D) Human SCL1 E) Yeast PRC3

Ans: “To determine the gene...answer is:\n[ANSWER]**D**[/ANSWER]”

Human baselines exceed LLMs



LitQA2 Question

Which three residues with evolutionary divergence in the G domains of RAS isoforms also impose selectivity constraints of pan-KRAS non-covalent inhibition?

GPT-4 Response (prompted to cite)

The three residues with evolutionary divergence in the G domains of KRAS, HRAS, and NRAS isoforms that impose selectivity constraints for pan-KRAS non-covalent inhibition are Thr35, Asp38, and Glu37. It has been observed that these three amino acids significantly influence the binding affinity and selectivity of potential non-covalent inhibitors, thereby determining the efficacy of different therapeutic strategies targeting the RAS isoforms (Hunter et al., 2015). The understanding of these residues' evolutionary conservation and differences across isoforms can aid the development of more effective pan-RAS inhibitors (Lu et al., 2016).

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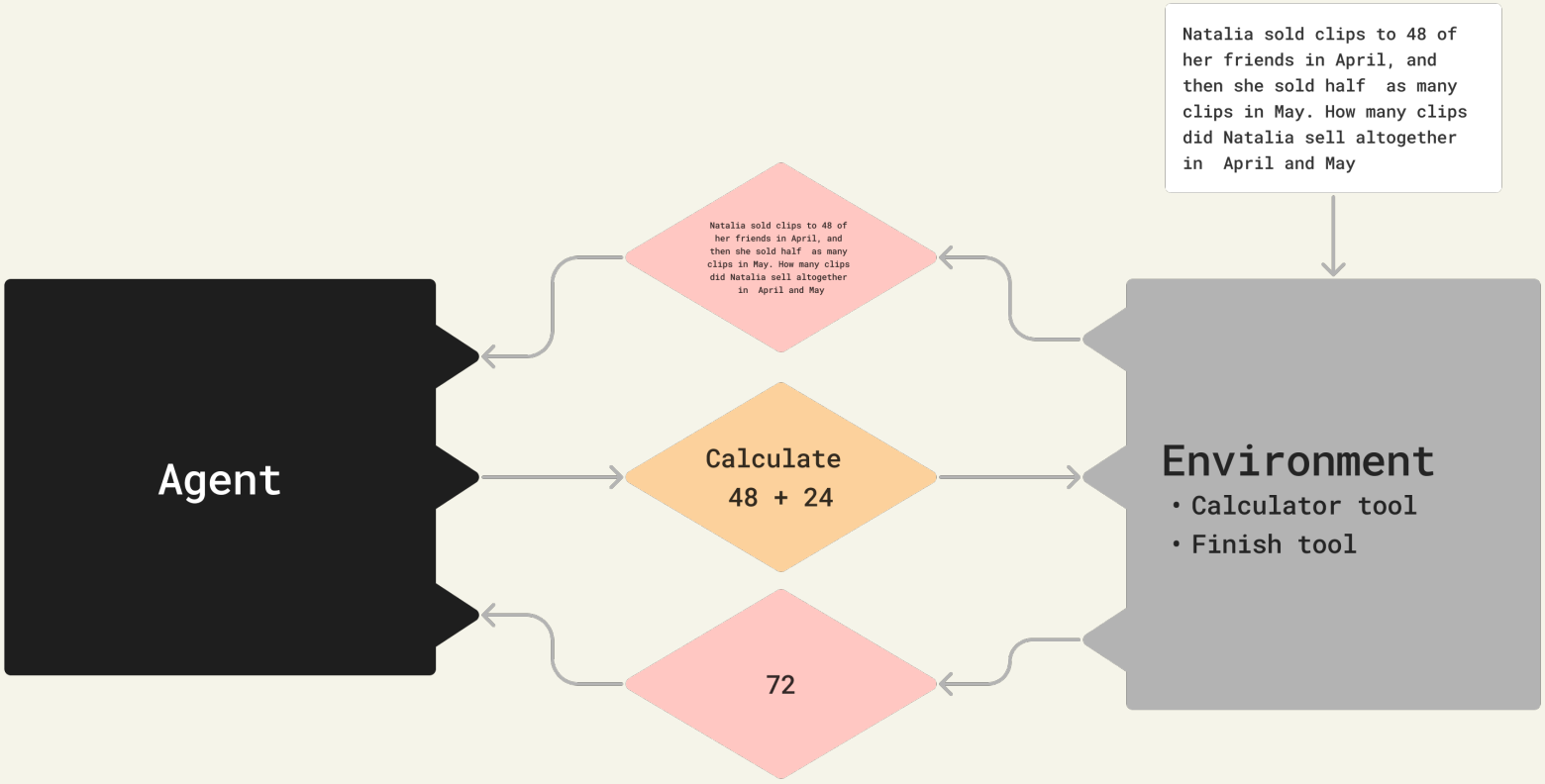
Wrong, hallucinated references

PaperQA Agent Response

Three key residues in the G domains of RAS isoforms that affect KRAS inhibitor selectivity have been identified:

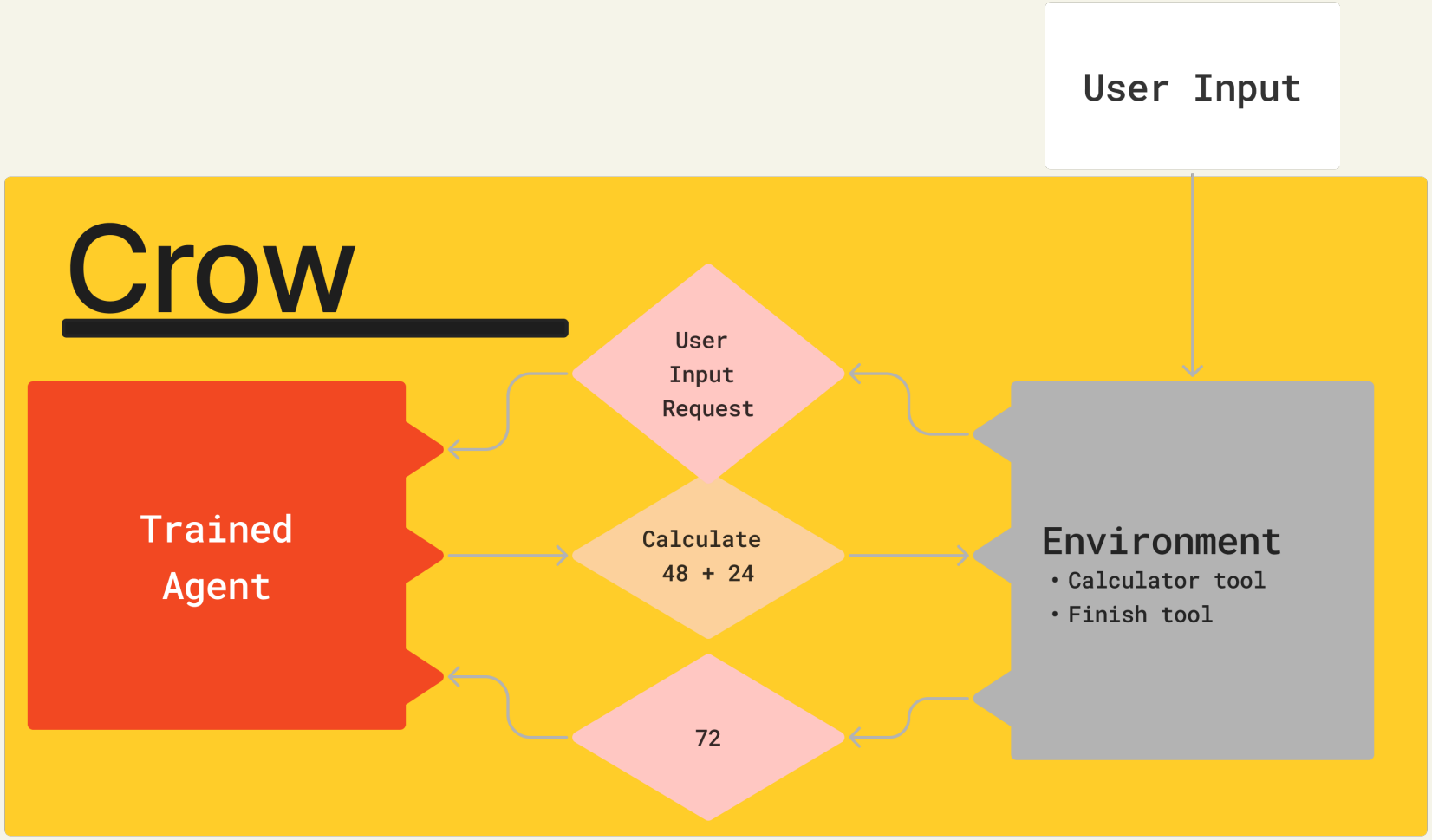
1. H95 (in the α3 helix): In KRAS this position contains histidine (H), while it is leucine (L) in NRAS and glutamine (Q) in HRAS. H95 exerts orthosteric (direct) effects on inhibitor selectivity (kim2023pankrasinhibitordisables pages 3-4, parker2018thekrasnras pages 5-7).
2. P121: This position contains proline (P) in both KRAS and NRAS, but alanine (A) in HRAS. P121 has allosteric (indirect) effects on selective inhibition (kim2023pankrasinhibitordisables pages 3-4, parker2017themostoncogenic pages 28-33).
3. S122 (in loop 8): This position varies across all three isoforms, with serine (S) in KRAS, threonine (T) in NRAS, and alanine (A) in HRAS. Like P121, S122 contributes to selectivity through allosteric effects (kim2023pankrasinhibitordisables pages 3-4, parker2018thekrasnras pages 7-9).

What is an agent?



Agent: trained, makes decisions

Environment: untrained, has tools, state


User Input
Crow
User
Input
Request
Trained
Agent
Calculate
48 + 24
Environment
• Calculator tool
• Finish tool
72

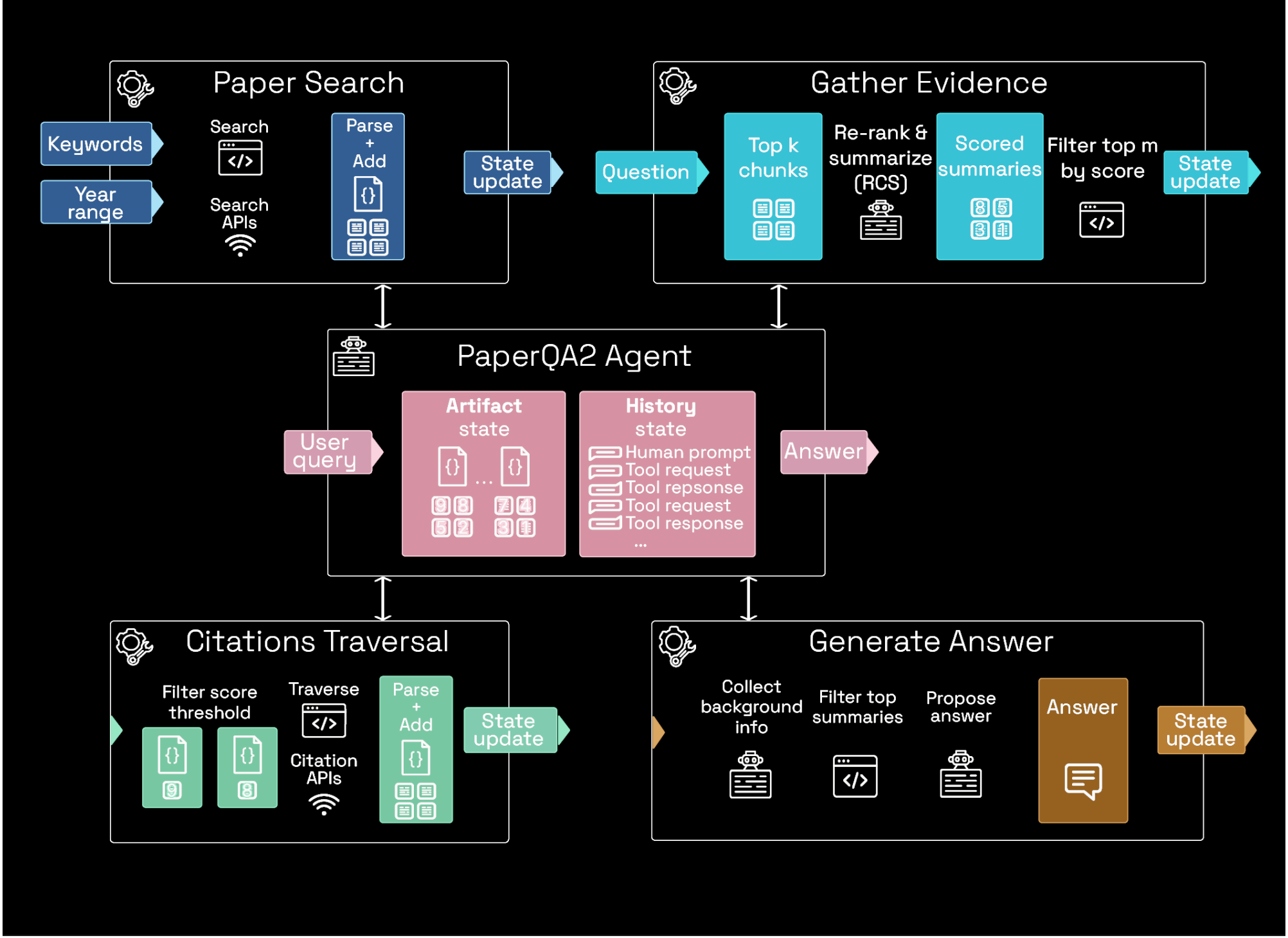
Crows

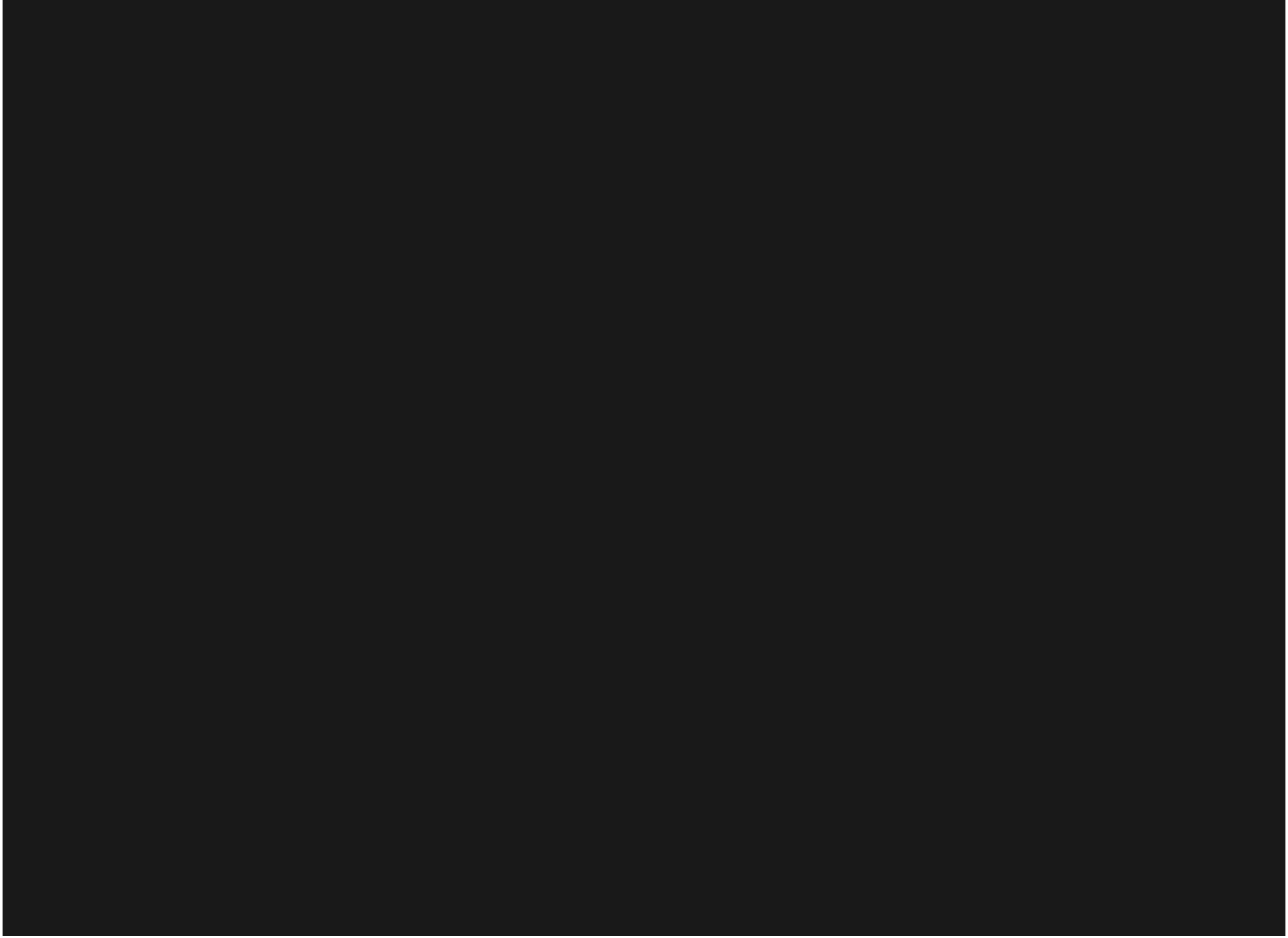
	Environment	Key Tools
PaperQA	Literature Research	Search, Citation Traversal
ProteinCrow	Designing novel proteins	AlphaFold2, Molecular Dynamics
ChemCrow	Designing new molecules	Retrosynthesis, self-driving robotic lab

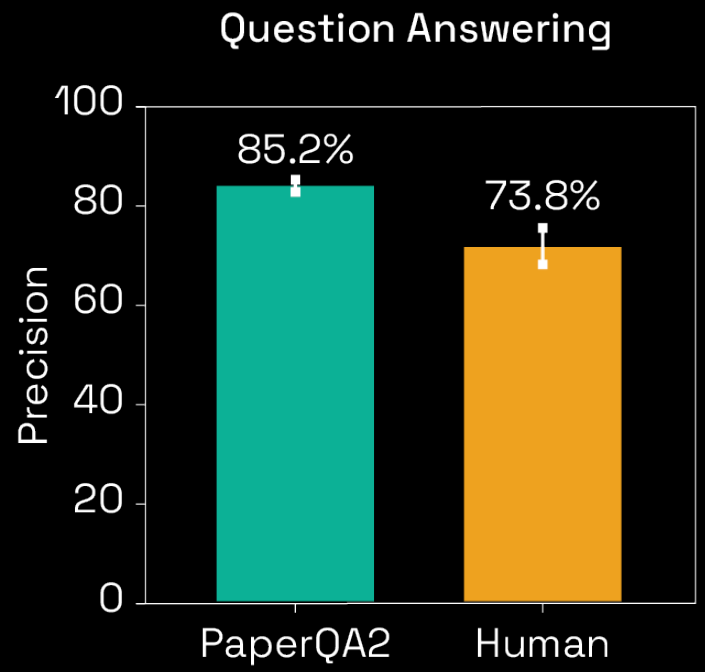
PaperQA: an agent for literature research

Language agents achieve superhuman synthesis of scientific knowledge

Michael D. Skarlinski, Sam Cox, Jon M. Laurent, James D. Braza, Michaela Hinks, Michael J. Hammerling, Manvitha Ponnapati, Samuel G. Rodriques, Andrew D. White *arXiv:2409.13740*, 2024

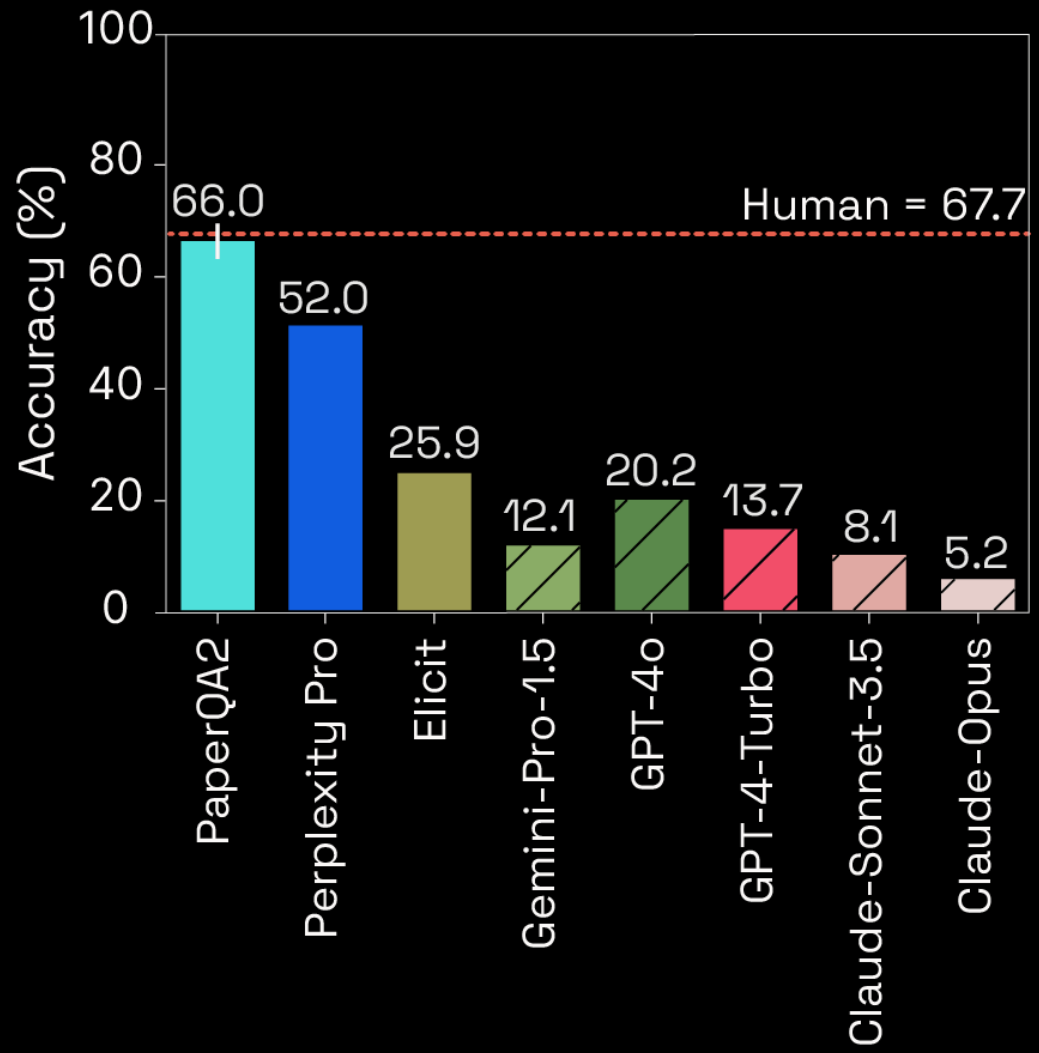

Paper Search
Keywords
Year range
Search
Search APIs
Parse + Add
State update
Gather Evidence
Question
Top k chunks
Re-rank & summarize (RCS)
Scored summaries
Filter top m by score
State update
PaperQA2 Agent
User query
Artifact state
History state
Human prompt
Tool request
Tool repsonse
Tool request
Tool response
Answer
Citations Traversal
Filter score threshold
Traverse
Citation APIs
Parse + Add
State update
Generate Answer
Collect background info
Filter top summaries
Propose answer
Answer
State update

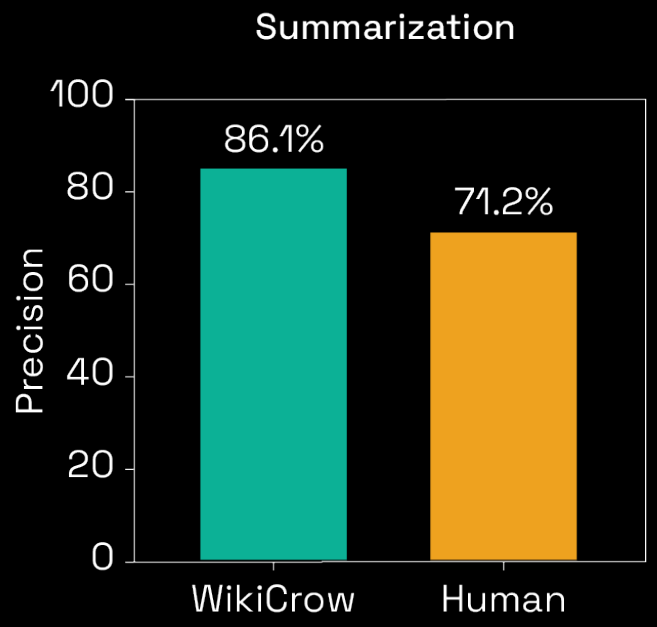




Better at answering questions than PhD biology experts

Accuracy vs Precision

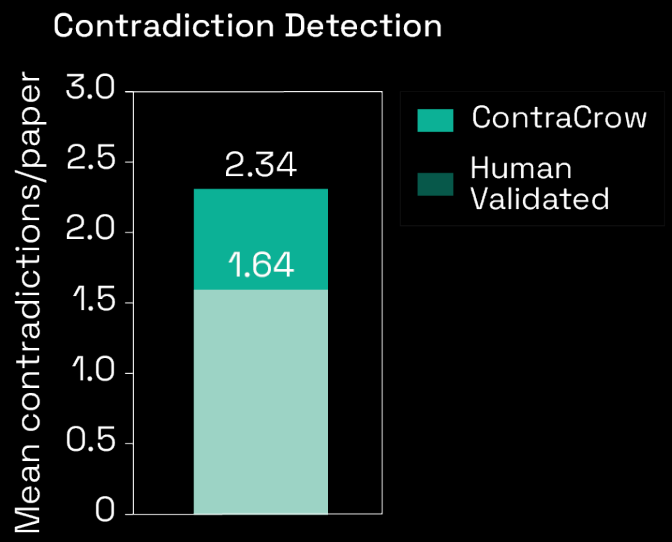




Better than human written Wikipedia articles

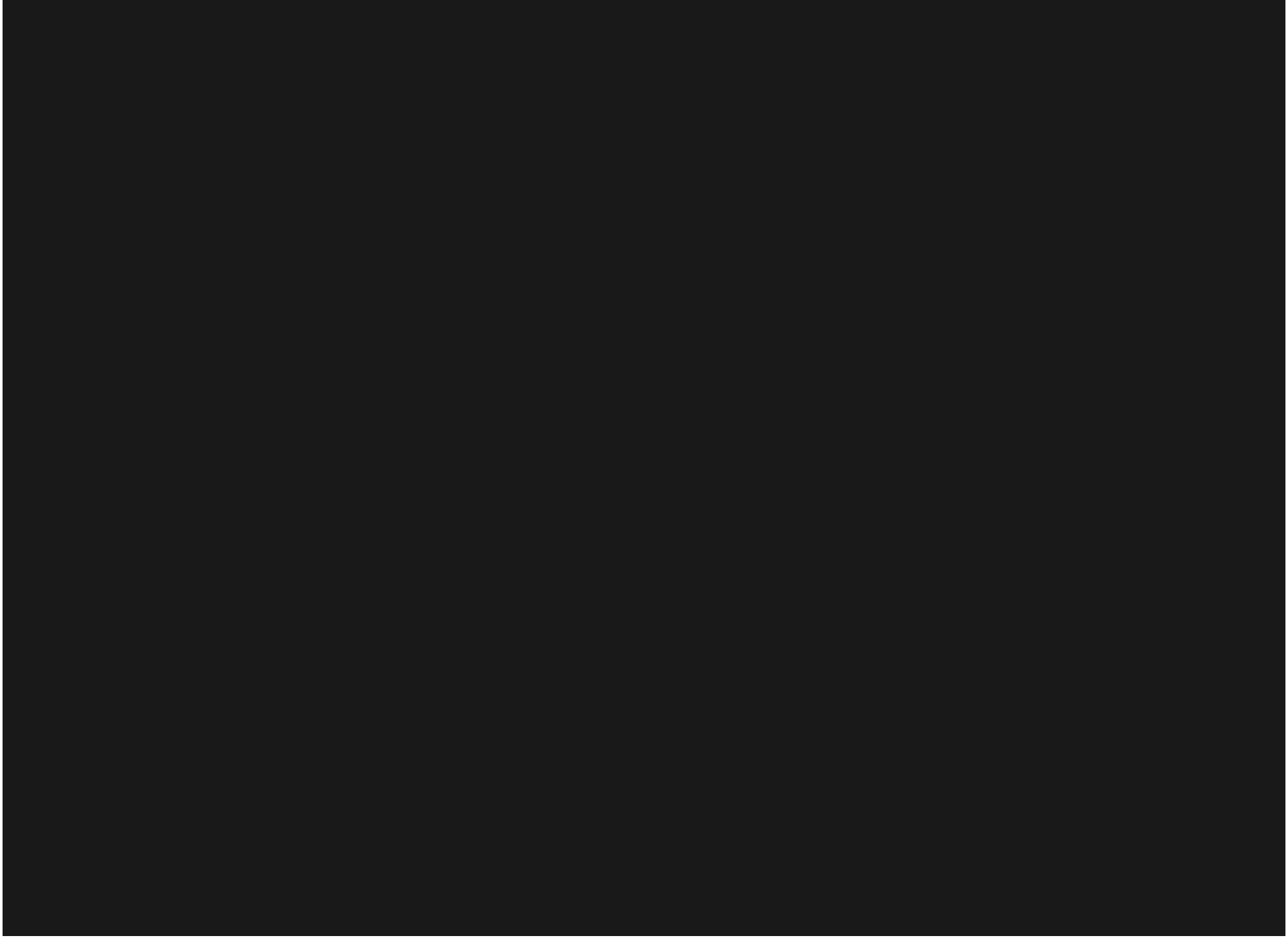
Difference between PaperQA and Wikipedia

	WikiCrow	Wikipedia
Unsupported Breakout (total)	23	42
Reasoning Issues	12	26
Attribution Issues	10	16
Trivial Statements	1	0



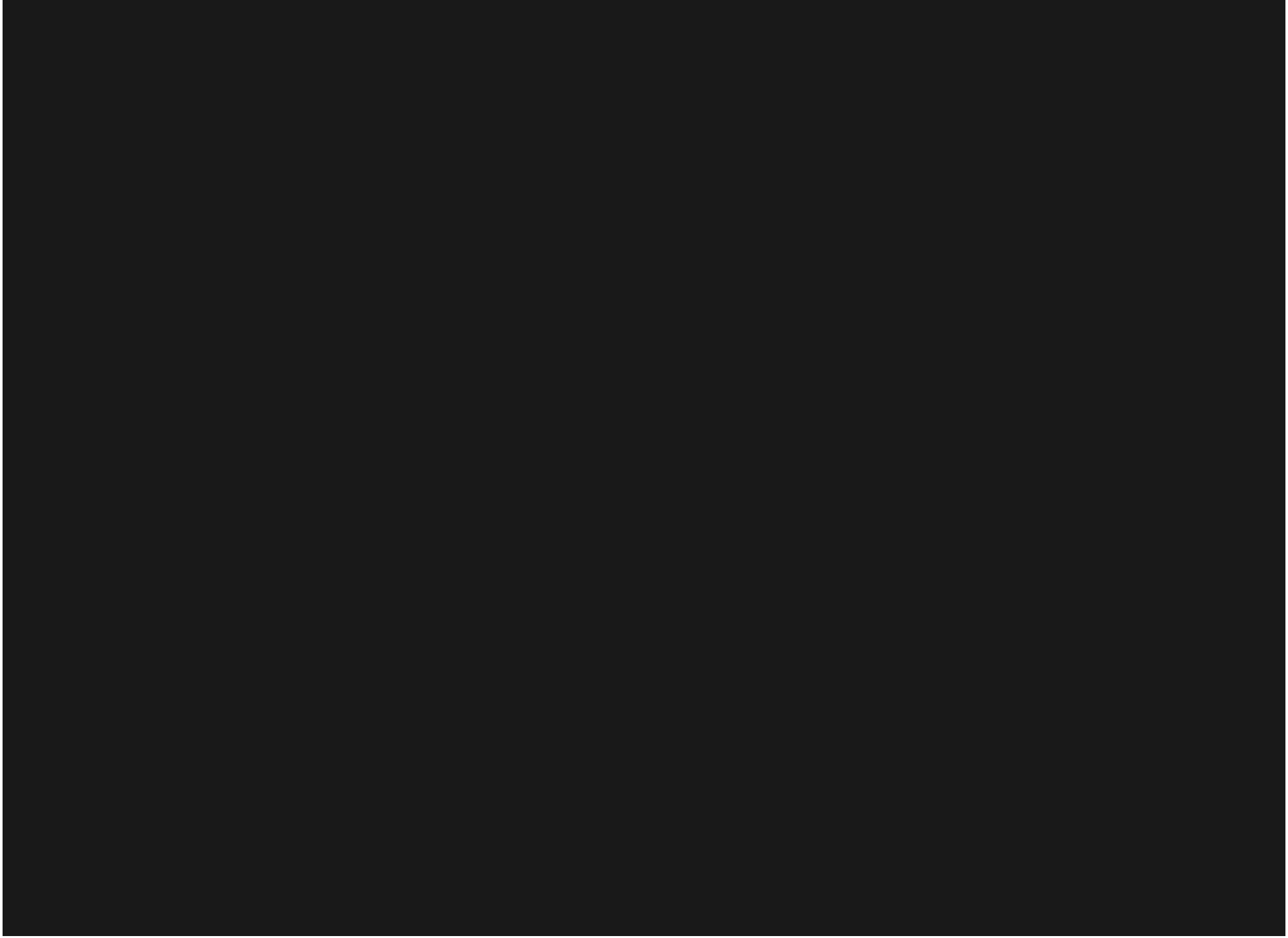
Can detect if a claim is contradicted anywhere in literature

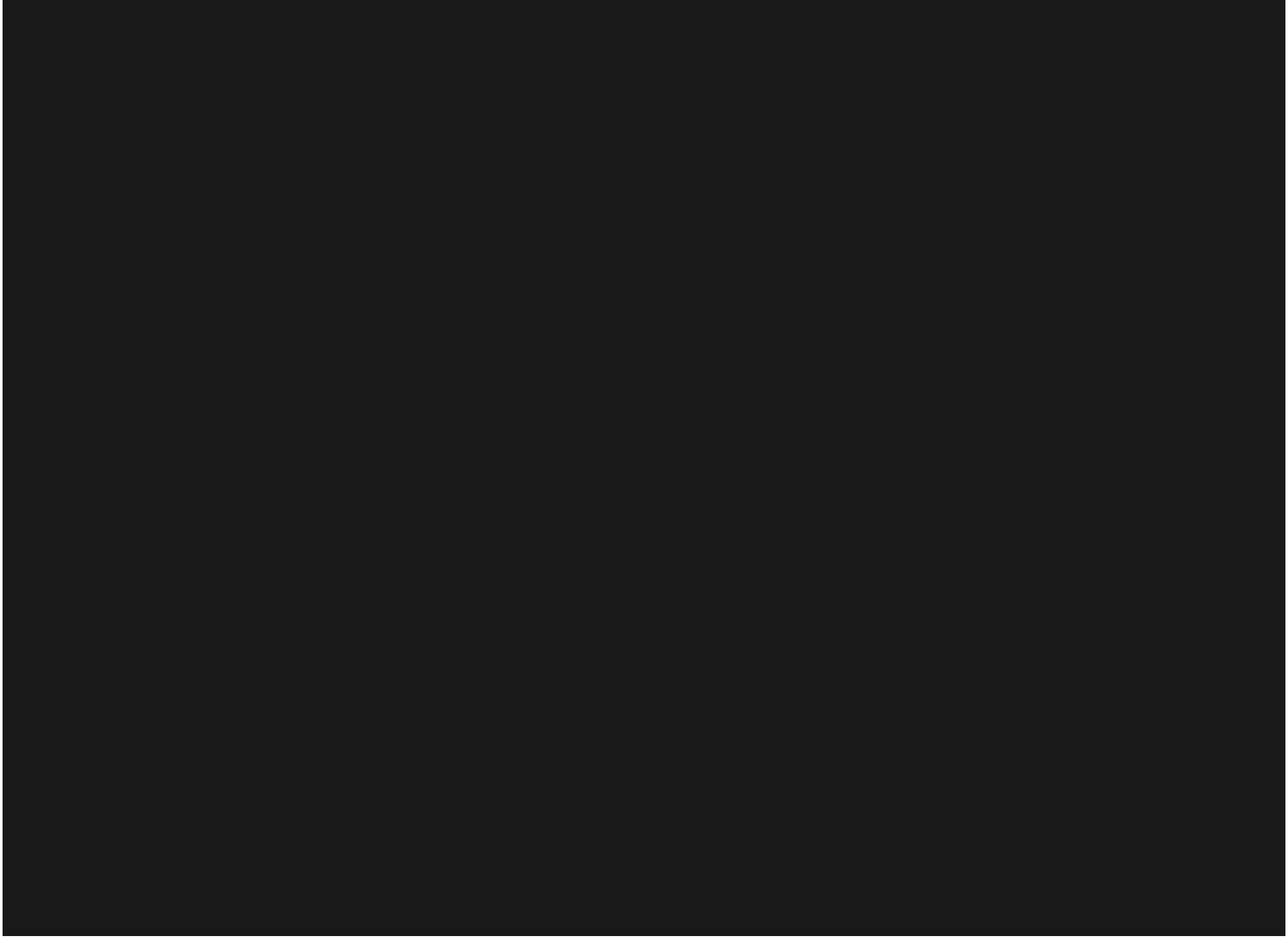
Applications



WikiCrow

1. Wikipedia articles for all 19,255 protein-coding genes
2. Succeeded on 17,269
3. Wikipedia had 3,639, so gain of 13,630
4. 48 Hours





Literature Research Agent Scale

Tasks per minute:	25
Wiki page for all diseases	every 3.5 days
All arxiv papers per week	25,000 papers / month

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Wiki page for all diseases	every 3.5 days
All arxiv papers per week	25,000 papers / month
Check for contradictions (10x)	6.3M papers / year
All Wikipedia (10x)	every 3 weeks

Progress on Accuracy