**Constructing a Dynamic AI-Powered Knowledge Graph of the Human Biological System: An End-to-End Framework for AI Memory Encoding and Retrieval**

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**Abstract**

A dynamic knowledge graph for the human biological system is a comprehensive, evolving network of biomedical entities and relations, continuously updated by artificial intelligence (AI) agents. This paper presents an architecture that leverages AI memory encoding and retrieval mechanisms to construct and maintain a **biological knowledge graph** encompassing genes, proteins, pathways, diseases, and more. We detail how AI-driven extraction and integration of data from major databases (GenBank, UniProt, KEGG, etc.) and literature can populate the graph, and how multi-agent systems ensure **dynamic updates** with minimal human intervention. Our methodology combines **LLM-based memory systems** for encoding knowledge with graph databases (Neo4j) for structured storage, enabling efficient retrieval and reasoning. We describe an implementation using a Neo4j graph database integrated with AI models (e.g., BioBERT for text extraction and GPT-based agents for reasoning), including example Python code for automated graph updates. Emphasis is placed on **accuracy maximization**: we discuss prompt engineering techniques and validation loops that ground the AI’s outputs in verified data, reducing hallucinations and errors. We evaluate the system’s performance on maintaining up-to-date, correct knowledge and outline metrics for accuracy. This research offers an end-to-end framework for AI researchers and engineers to build scalable, accurate, and **self-updating knowledge graphs** for the entirety of human biology, bridging the gap between raw biomedical data and actionable knowledge.

**Introduction**

The human biological system is characterized by vast and complex information spanning genomics, proteomics, cellular pathways, and clinical phenotypes. Integrating this knowledge into a coherent structure is a grand challenge. Traditional biological databases and ontologies (e.g., GenBank, UniProt, KEGG) store siloed pieces of this puzzle, but researchers and AI systems often struggle to **retrieve and reason** over the collective knowledge. A **biological knowledge graph** offers a solution by representing biomedical concepts (genes, proteins, diseases, etc.) as nodes and their relationships (interactions, regulatory links, disease associations) as edges. Such graphs enable unified queries and inference across levels of biology, answering questions that span multiple domains (for instance, querying how a genetic mutation propagates through protein interaction networks to influence a disease).

Building a **dynamic knowledge graph of human biology** is necessary to keep pace with the rapid growth of data and literature. GenBank®, for example, contains over 19 trillion base pairs from 2.9 billion sequences, covering ~504,000 species. UniProt, the universal protein knowledgebase, houses more than 227 million protein sequences with functional annotations. Each year, thousands of new research articles report previously unknown gene functions, protein interactions, and clinical findings. No single static database can capture all this information in real-time. An AI-powered knowledge graph can act as a living repository: continuously ingesting new data, encoding it into a structured form, and **updating relationships** as scientific understanding evolves. This dynamic approach addresses the **necessity** of keeping biological knowledge current and interconnected, which is crucial for applications like drug discovery, precision medicine, and hypothesis generation in research.

However, creating such a comprehensive graph presents challenges in **knowledge encoding and retrieval**. AI systems, particularly large language models (LLMs), excel at processing unstructured text but may hallucinate facts or miss nuanced details. Conversely, knowledge graphs excel at precision and structured recall but require accurate input. By combining the strengths of AI and knowledge graphs, we can build a system where AI agents populate and query a graph that serves as a **long-term memory**. This memory paradigm mimics human cognition: just as humans encode information into memory and recall it to make decisions, AI agents can encode new biological knowledge into the graph and retrieve relevant facts when needed. The graph thus becomes an **externalized memory** for the AI, providing both a high-level view of complex biological networks and a fine-grained repository of verified facts.

In this paper, we focus on the design and implementation of an AI-driven dynamic knowledge graph for the entire human biological system. We detail the **AI memory encoding mechanisms** for inserting knowledge, the retrieval strategies for answering questions accurately, and the multi-agent architecture that manages dynamic updates. We emphasize strategies to **maximize accuracy**, including grounding AI outputs in the graph to filter out errors. The target audience is AI researchers and engineers (especially those in computational biology) seeking to build or leverage such systems. By outlining a full pipeline – from data ingestion and graph construction to AI-driven updates and validation – we aim to provide a blueprint for harnessing AI agents to create and maintain a **comprehensive, up-to-date biological knowledge graph**.

**Methodology**

**AI-Driven Knowledge Graphs**

A knowledge graph (KG) is a structured representation of information as a network of entities and relationships. In the context of human biology, nodes in the graph represent biological entities such as genes, proteins, metabolites, cells, tissues, diseases, and drugs. Edges represent the relations between these entities: for example, a *codes\_for* relation linking a gene to a protein, an *inhibits* relation between a drug and an enzyme, or a *located\_in* relation linking a protein to a cellular compartment. Formally, the graph can be considered a collection of triples (subject, predicate, object) that capture factual assertions (e.g., **TP53 – regulates – CellCycle**). This triple-based formalism is flexible enough to encompass diverse data and supports inferencing via graph algorithms. Knowledge graphs have proven valuable in biomedicine, enabling tasks like gene prioritization for diseases and drug repurposing by linking drugs to targets and diseases.

An **AI-driven knowledge graph** is one where artificial intelligence techniques are employed both to construct the graph and to utilize it. Rather than relying solely on manual curation (which yields high precision but is slow and labor-intensive), we incorporate **machine learning and NLP** to automate knowledge extraction. In our approach, AI agents ingest data from various sources (databases and literature) and convert it into graph entries. This involves several sub-tasks: recognizing entities (using biomedical named entity recognition), identifying relationships (using relation extraction models), and normalizing these to a consistent schema (ensuring, for example, that "TP53" in text maps to the same node as "Tumor protein p53" from UniProt). By deploying pre-trained domain-specific language models (such as **BioBERT**, a BERT model fine-tuned on biomedical text) and ontologies for entity linking, the system can parse complex scientific statements and represent them in the graph.

Crucially, the knowledge graph also serves as a **contextual memory** for AI agents. When an agent (say, a question-answering agent) needs information, it can query the KG rather than relying on its internal parametric memory alone. This retrieval step grounds the AI’s reasoning in factual data and relationships present in the graph. For instance, an agent asked about a pathway involving a certain gene can traverse the graph to find connected proteins, related pathways, and associated phenotypes, thereby constructing an evidence-based answer. In essence, the KG becomes an extension of the AI’s memory: a structured, queryable memory bank that the AI can both read from and write to. This arrangement mitigates the **forgetting problem** common in AI systems by providing persistent storage of knowledge, and it enhances **explainability** since each answer can be traced through the graph’s nodes and edges (much like following a chain of reasoning).

**AI Memory Systems for Knowledge Encoding and Retrieval**

To emulate human-like memory, our system distinguishes between **encoding** (storing new knowledge) and **retrieval** (recalling stored knowledge). We draw inspiration from cognitive memory models, which often categorize memory into *episodic memory* (specific events) and *semantic memory* (general knowledge). In our design, the **knowledge graph itself represents semantic memory** – a long-term store of generalized biomedical knowledge – while the AI agents’ transient working memory can be considered episodic (for example, an agent might temporarily hold the context of a specific research paper it’s reading).

**Memory Encoding**: When new data or a new discovery becomes available, an AI ingestion agent encodes this information into the knowledge graph. This involves a pipeline of NLP: first, identify relevant entities and concepts in the input (using models like SciSpacy or BioBERT NER for genes, diseases, chemicals, etc.), then detect relations between them (using relation extraction models or prompting an LLM to output relationships). We enforce a schema derived from biomedical ontologies (such as Gene Ontology, Disease Ontology, or custom schemas) to categorize relations (e.g., *gene–associated\_with–disease*, *protein–interacts\_with–protein*). By structuring the encoding process, the agent ensures that new knowledge is added in a format consistent with existing data. The knowledge graph’s design is **ontology-driven**, meaning that entity types and relation types are pre-defined to align with biological reality (for instance, **Gene** nodes can only have a *encodes* relation to **Protein** nodes, **Drug** nodes can have a *treats* relation to **Disease** nodes, etc.). This provides a form of memory **indexing**: any new fact is stored at a precise location in a semantic network, where it can later be retrieved via its connections.

**Memory Retrieval**: AI agents retrieve knowledge from the graph using graph queries or embedding-based searches. For structured queries, a reasoning agent can use graph query languages (like Cypher for Neo4j) to find the subgraph relevant to a question. For example, to answer “What pathways is TP53 involved in?”, the agent issues a query to find all pathway nodes connected to the TP53 gene/protein node via any relation, and then filters for *pathway involvement* relations. This is analogous to recalling all facts about TP53 from one’s memory. If the query is fuzzy or the agent is uncertain how to structure it, we can use **vector retrieval**: represent the question and graph nodes in a shared embedding space and find the closest nodes (this can be done by storing text descriptions of nodes and using a similarity search). The combination of symbolic queries and vector-based retrieval ensures both **precision and recall** in memory access – precise when exact relations are known, and broad when a more associative recall is needed.

One novel approach to retrieval we incorporate is the use of **prompt-based graph reasoning**. Large language models can be prompted to reason about relationships if given a portion of the knowledge graph in textual form. We can serialize a relevant subgraph (a set of triples) into text and feed it to an LLM with a prompt like: *“Using the following knowledge, answer the question…”*. The LLM then performs reasoning with the graph facts as constraints. This method allows leveraging the generative and reasoning capabilities of LLMs while ensuring they remain grounded in the graph (the provided facts). Advanced prompting frameworks such as *Graph-of-Thoughts (GoT)* extend this idea by having the LLM generate not just linear chains of reasoning but **arbitrary graphs of thoughts**, where each “thought” (intermediate conclusion or piece of info) is a node and dependencies form edges. This is conceptually similar to how our knowledge graph operates, creating a natural synergy: the LLM can internally mimic a knowledge graph reasoning process, exploring multiple interconnected reasoning paths, which aligns well with retrieving interconnected facts from the external knowledge graph.

**Agent-Based Architecture for Dynamic Updates**

To maintain the knowledge graph as a living resource, we employ a **multi-agent system** architecture. Different AI agents are assigned distinct roles, collaborating to continuously ingest, update, and validate knowledge. This agent-based approach introduces modularity and parallelism, much like a team of experts, each focusing on specific tasks but sharing a common memory (the knowledge graph).

Key agents in our architecture include:

* **Ingestion Agent**: This agent monitors various data sources (new database releases, scientific publications, preprints, etc.). It reads inputs and extracts structured knowledge to add to the graph. For example, it might scan the latest PubMed abstracts for sentences indicating gene-disease associations. Using prompt-based extraction or fine-tuned NLP models, it identifies new relationships and encodes them into the graph. It may use small LLMs or rules for precision (e.g., a rule that looks for “X inhibits Y” patterns to catch inhibitor relationships in text). The ingestion agent is designed to be conservative – uncertain extractions are flagged for review rather than immediately added, to preserve accuracy.
* **Update/Maintenance Agent**: As the graph grows, this agent ensures consistency and handles modifications. Biological knowledge can change (e.g., a protein once thought to be linked to a disease might be disproven later). This agent uses **change detection** – comparing new data with existing graph content. If a conflict arises (say a new source contradicts a relation in the graph), the agent either updates the relation’s confidence score or appends a new node indicating an alternative viewpoint, depending on the domain practices. The maintenance agent also refines the graph structure, e.g., merging duplicate nodes referring to the same concept (synonym resolution) or removing spurious edges that were added erroneously (perhaps identified through lack of supporting evidence).
* **Query/Reasoning Agent**: This agent interfaces with end-users or other systems that query the knowledge graph. It translates user questions or analytical tasks into graph queries and orchestrates the retrieval. If a question is high-level (“What are potential therapies for disease X that target pathway Y?”), it may break it down: query the graph for all compounds affecting pathway Y, then filter those that have an edge to disease X. It can leverage the LLM’s ability to interpret natural language questions and map them to formal graph operations (through prompt templates that generate Cypher queries, for instance).
* **Validation Agent**: Ensuring accuracy is paramount, so an independent agent is tasked with verification. After the ingestion agent adds new knowledge, the validation agent cross-checks it. This could involve searching for multiple sources that support the same fact (e.g., if a paper suggests a gene interacts with a protein, check if that interaction is also reported in a database like BioGRID or IntAct). The validation agent might use an LLM with a "critic" prompt to assess the plausibility of a new triple and even retrieve snippets of text that confirm or refute it. Knowledge that passes validation is marked as high confidence, while low-confidence assertions might be tagged or queued for human expert review.

These agents communicate through the shared knowledge graph and via messaging cues. For example, when the ingestion agent adds a new node or edge, it can attach a meta-data property like needs\_validation=True which signals the validation agent to act on it. Similarly, the query agent, if it encounters an area of the graph that hasn’t been updated recently, might trigger the update agent to refresh that subgraph (for example, if a user asks about a gene, the system might ensure it has the latest info on that gene by fetching recent papers in the background).

Multi-agent frameworks like this draw on principles of distributed AI and have been shown to mimic collaborative human problem-solving. In our context, the agents work as an ensemble to keep the knowledge graph **dynamic** – always incorporating new information and correcting itself. This approach scales well: additional ingestion agents can be added for different data types (one specialized in genomic data, another in clinical trial data, etc.), all contributing to the same graph in a coordinated manner. By modularizing tasks, we also make the system more robust; even if one component fails or lags (say a certain extractor model underperforms), the overall system can compensate via validation and later correction.

**Data Sources for the Knowledge Graph**

A dynamic knowledge graph covering the entire human biological system must integrate data from a multitude of sources. We categorize these sources into structured databases and unstructured literature, both of which are indispensable.

**Structured Databases**: These are well-established repositories of biological information, usually curated and maintained by research consortia:

* **GenBank**: A primary nucleotide sequence database (part of the International Nucleotide Sequence Database Collaboration). GenBank provides genomic DNA sequences, mRNA sequences, and others. We use GenBank for gene and genome information, linking gene nodes to sequence data and related metadata. The sheer size of GenBank (on the order of trillions of base pairs) means we typically do not store raw sequences in the graph, but rather metadata like gene identifiers, species, and perhaps sequence length or key features. This ensures the graph knows *of* each gene and its basic attributes without ballooning in size. GenBank’s continuous updates (daily exchange with EMBL-EBI’s ENA and Japan’s DDBJ ensures worldwide coverage) make it a backbone for keeping genomic entries current.
* **UniProt**: The Universal Protein Knowledgebase is our source for protein sequences and functional annotations. UniProtKB comprises **Swiss-Prot** (reviewed, manually curated protein entries) and **TrEMBL** (unreviewed, computationally annotated entries). It includes protein-protein interactions, enzyme functions, subcellular localizations, and cross-references to other databases. In the graph, each protein is a node that may connect to gene nodes (via *encoded\_by* relations), to other proteins (*interacts\_with* edges representing physical or regulatory interactions), to pathways (*participates\_in*), and to diseases (*associated\_with* if a mutation or dysregulation is known to cause a condition). UniProt’s emphasis on quality and comprehensive coverage (with over 227 million sequences and continuous expert curation) ensures our graph has a solid proteomic foundation. Where possible, we import high-confidence interactions directly from curated sections of UniProt or related interaction databases (like IntAct or STRING).
* **KEGG (Kyoto Encyclopedia of Genes and Genomes)**: KEGG is a reference knowledge base for biological pathways and networks. It provides pathway maps that link genes and proteins to biochemical pathways, molecular complexes, and disease mechanisms. In our graph, **Pathway** nodes (from KEGG or Reactome) act as hubs connecting multiple gene/protein nodes, representing membership in a pathway. KEGG also includes orthologous groupings (KO entries) and networks of cellular processes. Incorporating KEGG allows the graph to support queries like “Which metabolic pathways is Gene X involved in?” or “What genes are in the p53 signaling pathway?”. We integrate KEGG by importing its pathway definitions and linking them to gene/protein nodes via *in\_pathway* relations. KEGG is particularly useful for functional context: it ties molecular entities to higher-level biological functions.
* **PubChem and Drug Databases**: For representing the pharmacological aspect, we draw from databases like PubChem (for chemical compounds), DrugBank, and ChEMBL. These provide information on drugs, compounds, their targets, and their mechanisms of action. In the knowledge graph, **Compound/Drug** nodes connect to protein targets (*binds* or *inhibits* relations), to disease nodes (*treats* relations if the drug is indicated for a disease), and to pathway nodes (*affects\_pathway*). This integration enables polypharmacy analysis or drug repurposing queries (e.g., find drugs that target a pathway dysregulated in a disease).
* **Disease and Clinical Databases**: Resources such as OMIM (Online Mendelian Inheritance in Man), ClinVar, or disease ontologies contribute the phenotype and disease relationships. A **Disease** node might link to Gene or Protein nodes (*causes* or *associated\_with* relations indicating a mutation causes a genetic disorder, or a gene’s dysregulation is associated with a disease). We also include Gene Ontology (GO) terms as nodes to capture functional annotations (GO biological processes, molecular functions, cellular components) associated with gene/protein nodes.

The initial construction of the graph involves importing these databases. Efforts like the RTX-KG2 project have demonstrated one way to integrate dozens of such sources into a single semantically unified graph. In our implementation, we map each source’s schema to our unified ontology. For example, KEGG pathways and Reactome pathways are both represented as Pathway nodes, even though they come from different sources; UniProt and NCBI Gene both provide gene/protein info which we merge on common identifiers.

**Unstructured Literature**: A dynamic knowledge graph must also mine the vast body of biomedical literature for facts not yet curated into databases. New discoveries often appear in research papers before making it into curated databases. Our system uses text mining to extract knowledge from sources like:

* **PubMed and PubMed Central**: We periodically scrape titles and abstracts (and full-text articles where available) for statements of relationships. Techniques include using **LLM-based extraction**: prompting a model with a sentence or paragraph and asking *“What biomedical relationships are stated here?”*. For example, given a sentence "BRCA1 interacts with PALB2 to facilitate DNA repair," the AI should output a triple (BRCA1 – interacts\_with – PALB2). Tools like spaCy’s *displaCy* or dependency parsing can also be applied to identify subject-object pairs in sentences with relationship verbs.
* **Biomedical Text Repositories**: We also consider text from clinical trial descriptions, patent literature, and biomedical news. Each of these may mention novel insights (e.g., a clinical trial might report a gene expression biomarker for a drug response).

To efficiently mine literature, we maintain a pipeline where new papers trigger the ingestion agent. Natural language processing models specialized in biomedical text (such as **BioGPT** or fine-tuned T5 transformers for relation extraction) are used. We also use **knowledge-guided extraction**: existing knowledge in the graph can help focus the extraction. For example, if the graph knows a set of proteins interact in a pathway, and a new paper mentions two of those proteins, the system can be primed to look for a direct interaction statement.

Data from literature is inherently noisier than curated database data, so we attach provenance and confidence to each extracted edge. Each edge in the graph might have attributes like source="PubMed:XXXXXX" (a reference to the publication) and a confidence score from the extractor model. This provenance allows the validation agent or even end-users to trace a fact back to its origin. It also enables a form of **continuous learning**: if a certain source repeatedly provides reliable info, the system can trust it more, whereas if an extraction is contradicted by multiple other sources or not confirmed elsewhere, the system flags it.

By combining structured and unstructured sources, our knowledge graph aims for **comprehensiveness**. The structured sources give us breadth and a solid base of verified knowledge (e.g., all human genes and proteins, known interactions and pathways up to the last curated release). The literature mining adds depth and currency, capturing the latest discoveries and niche information not yet in databases. The AI agents orchestrate the flow from these sources into the graph, ensuring that the knowledge is normalized and interconnected – for example, linking a newly discovered protein interaction from a paper to the corresponding protein nodes imported from UniProt.

**Implementation**

**System Architecture with Neo4j**

Our implementation uses **Neo4j**, a popular open-source graph database, as the core storage and query engine for the knowledge graph. Neo4j is well-suited for this task due to its ability to store billions of nodes and relationships while supporting complex graph queries with the Cypher query language. The system architecture (illustrated conceptually in text) consists of several layers:

* **Data Layer (Neo4j Graph Database)**: This is where the knowledge graph resides. We design a property graph schema: each node has labels (e.g., Gene, Protein, Disease) and properties (e.g., a Gene node might have symbol="TP53", name="tumor protein p53", chromosome=17). Relationships also have types (e.g., INTERACTS\_WITH, REGULATES) and can carry properties like confidence or evidence. We also create indexes on key properties like gene symbols or identifiers to speed up lookups, which is important when the AI agents merge new info (for example, to quickly check if a node exists).
* **AI Agents and Services Layer**: The ingestion, query, and validation agents are implemented as separate services (in Python, for instance) that communicate with Neo4j and occasionally with each other. Each agent maintains a connection to the Neo4j database (using the official Neo4j Python driver or an ORM like Py2Neo) to run queries and updates. For example, the ingestion agent might run a Cypher MERGE query to insert a new node or relation as it processes an input. The query agent might run Cypher MATCH queries to find answers or subgraphs. Agents also utilize external AI models via APIs or libraries. We integrate models in the following way:
  + **NLP Models** (for ingestion): accessible through a library or microservice. For instance, we could host a BioBERT-based relation extraction model and the ingestion agent sends raw text to it and gets back triples.
  + **LLM** (for reasoning/prompting): We can use an API (like OpenAI's GPT-4 or a local model via HuggingFace) where the query agent constructs a prompt that includes relevant graph info and the user question, then gets a response.
  + These models are containerized for scalability, meaning multiple instances can run in parallel if needed to handle large data throughput (e.g., scanning thousands of papers).
* **Orchestration and Message Bus**: A lightweight message queue (like RabbitMQ or even simple in-database job tables) is used for agents to signal each other. For example, after the ingestion agent adds data, it sends a message "new\_data\_added" with references for validation. This decoupling ensures the system is not strictly synchronous and can handle bursts of new data gracefully.
* **User Interface or API Layer**: Though not the focus of this research paper, we envision a query interface (could be a web app or an API) through which users (or automated clients) pose questions or requests. The query agent listens for these and uses the KG to respond. Having a clear API also allows integration with other pipelines (for instance, a drug discovery workflow could query this KG for target information).

**Neo4j’s role** is pivotal: it provides ACID transactions for updates (important when multiple agents update concurrently), indexes for quick retrieval, and graph algorithms if needed (Neo4j has algorithms for community detection, shortest paths, etc., which could be leveraged for advanced reasoning tasks). We design our Cypher queries to use MERGE for idempotent operations – this way, if an agent tries to add a node that already exists (same primary identifier), Neo4j will simply match the existing node, avoiding duplicates. Similarly, relationships are merged on key properties to avoid duplicating edges (or we allow duplicates but maintain a count or confidence aggregation).

A simplified example of the system’s operation: The ingestion agent reads a new article about a gene “XYZ” involved in a disease “ABC”. It extracts the triple (Gene XYZ – associated\_with – Disease ABC). The agent then executes a Cypher query to insert this into Neo4j. In Cypher pseudo-code:

cypher

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MERGE (g:Gene {symbol: "XYZ"})

MERGE (d:Disease {name: "ABC"})

MERGE (g)-[r:ASSOCIATED\_WITH]->(d)

ON CREATE SET r.source = "PubMed:12345678", r.confidence = 0.9;

This ensures that if the Gene or Disease nodes already exist, they are reused, and the relationship is either created fresh with source and confidence or found existing (where we might then update some property like an evidence count). The validation agent, on seeing this insertion (it could be triggered by a database event or by reading the message queue), then might query Neo4j to retrieve all relations between "XYZ" and "ABC" and verify if there are multiple pieces of evidence. If it finds only one (the just added one), it might flag it for manual review or attempt to corroborate via an LLM literature search. The query agent, later on, if asked "What diseases is gene XYZ associated with?", runs a MATCH (g:Gene {symbol:"XYZ"})-[:ASSOCIATED\_WITH]->(d:Disease) RETURN d.name to get the list of disease names, which would include "ABC" with maybe an annotation of evidence.

**AI Model Selection and Integration**

Selecting appropriate AI models is critical for the system’s performance. We base our choices on the type of data and task:

* **Language Models for Extraction**: For processing natural language (research papers, abstracts), we employ models like **BioBERT** (Lee et al., 2020) for named entity recognition and relation extraction. BioBERT is pre-trained on PubMed articles, which gives it a strong understanding of biomedical terminology. We fine-tune BioBERT on specific tasks such as extracting gene-disease associations or drug-target interactions, using available annotated corpora. For example, there are datasets where sentences are labeled with the relationship type they express; these can train a classifier on top of BioBERT’s embeddings. Additionally, we use rule-based or regex-based extraction for specific formats (like “X (gene) – Y (disease)” patterns in text). This hybrid approach ensures we catch straightforward mentions with high precision and use ML for the rest. We also integrate **SciSpaCy** (a version of spaCy with biomedical models) for quick entity detection (genes, chemicals, etc.) and linking to identifiers (it has functionality to resolve entities to UMLS concepts, which can link to nodes in our graph).
* **Knowledge Graph Embeddings (KGE)**: While not explicitly an agent, we incorporate an AI technique to embed the entire knowledge graph into a vector space. We use algorithms like ComplEx or TransE to generate embeddings for each node/relation type. These embeddings serve two purposes: (1) to support similarity search (for example, find nodes that are similar to a given node, which could hint at novel associations), and (2) to predict new links (link prediction can suggest probable new edges that the ingestion agent might have missed, effectively giving the system a way to propose hypotheses). For instance, if the KGE suggests a high probability that Protein A interacts with Protein B (because they have many common neighbors and features in the embedding space), the system can flag this and perhaps search literature for evidence. Integration of KGE is done offline in batches – we periodically retrain embeddings as the graph grows, and store these in a vector index for query. This is an example of **memory compression** – the high-dimensional graph is “compressed” into dense vectors that the AI can use for fast reasoning.
* **Large Language Models (LLMs)**: For the reasoning and query agent, we leverage large language models (like GPT-4 or open models such as LLaMA2 fine-tuned on instruct tasks) to interpret queries and to validate/generate text. The LLM is prompted with a combination of user query and relevant knowledge graph content. We design **prompt templates** for different tasks. For example:
  + *Query interpretation prompt*: “You are a biomedical expert AI with access to a knowledge graph. The user asks: '{user question}'. Break this down into graph queries or steps.” – The LLM might output a plan or even Cypher code. We found that providing a few examples of natural language to Cypher translation in the prompt helps the model generate correct queries. If the model produces Cypher, the query agent can execute it on Neo4j and then format the results.
  + *Validation prompt*: “The knowledge graph has added a fact: Gene XYZ is associated with Disease ABC. How strongly is this supported by current evidence?” – The LLM can be tasked to search its training (or use a tool to query literature) and respond with a judgment. If connected to tools (like a retrieval plugin that searches PubMed), the LLM’s response can be more factual.
  + *Graph reasoning prompt*: We can present a subgraph as text (like a list of triples or a summarized description of a network around certain nodes) and ask the LLM a question requiring multi-hop reasoning. This tests the system’s ability to combine symbolic and neural reasoning. For instance, provide all genes in pathway X that are linked to disease Y, and ask the model to draw a conclusion (perhaps which gene is a potential drug target). By giving the exact known relations, we force the LLM to derive answers only from those, enhancing accuracy.

Integration of LLMs is done via API calls within the agent code. We ensure to include **guardrails**: if the LLM returns an answer that contradicts the graph (e.g., mentions a relation not present), the agent can double-check. The knowledge graph thus acts as a truth filter – any final answer is cross-verified against it for consistency. This reduces the risk of hallucination from the LLM because the graph provides a factual backbone.

**Code Snippets: AI-Driven Graph Updates**

Below, we include an illustrative Python code snippet that demonstrates how an AI agent might update the Neo4j knowledge graph after extracting information. In this simplified scenario, suppose our ingestion agent has processed a scientific sentence and identified two proteins that interact: **BRCA1** and **PALB2** (a known interaction involved in DNA repair). The agent will update the graph to reflect this protein-protein interaction:

python

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from neo4j import GraphDatabase

# Neo4j connection settings (assuming Neo4j is running and accessible)

uri = "bolt://localhost:7687"

user = "neo4j"

password = "your\_password" # replace with actual password

# Connect to the Neo4j database

driver = GraphDatabase.driver(uri, auth=(user, password))

# The extracted information

protein1 = "BRCA1"

protein2 = "PALB2"

relation\_type = "INTERACTS\_WITH"

source\_pubmed\_id = "32123347" # example PubMed ID as source

confidence\_score = 0.95 # example confidence

# Function to add interaction to Neo4j

def add\_interaction(tx, p1, p2, source, confidence):

tx.run(

"""

MERGE (a:Protein {symbol: $prot1})

MERGE (b:Protein {symbol: $prot2})

MERGE (a)-[r:INTERACTS\_WITH]->(b)

ON CREATE SET r.source = $source, r.confidence = $conf

ON MATCH SET r.source = coalesce(r.source, $source)

""",

prot1=p1, prot2=p2, source=f"PubMed:{source}", conf=confidence

)

# Use a write transaction to ensure atomicity

with driver.session() as session:

session.write\_transaction(add\_interaction, protein1, protein2, source\_pubmed\_id, confidence\_score)

print(f"Added interaction: {protein1} --[INTERACTS\_WITH]--> {protein2}")

driver.close()

In this snippet, we connect to Neo4j and execute a Cypher query via the Python driver:

* MERGE (a:Protein {symbol: $prot1}) will find or create a Protein node with the given symbol (here "BRCA1").
* Similarly for b:Protein {symbol: $prot2} ("PALB2").
* MERGE (a)-[r:INTERACTS\_WITH]->(b) finds or creates an INTERACTS\_WITH relationship from a to b.
* The ON CREATE SET clause sets the source and confidence properties when the relation is first created, labeling it with provenance (PubMed ID of a paper) and a confidence score assigned by the extraction model.
* ON MATCH SET r.source = coalesce(r.source, $source) is a way to ensure if the relationship already existed we don’t overwrite an existing source (coalesce will keep the existing one if present). In a more sophisticated version, we might append the source to a list, or maintain a count of evidence. But for simplicity, we only set it if it was null.

This code is representative of how the ingestion agent interfaces with the graph database. After running, the graph now has two protein nodes connected by an INTERACTS\_WITH edge. If we later query Neo4j (via the browser or via code) for BRCA1’s interactions, we’d find PALB2 as a neighbor with that edge, and we could see the source property indicating where that knowledge came from.

Another scenario: suppose an LLM agent receives a question "Which proteins interact with BRCA1?" The agent might translate that to a Cypher query:

cypher

Copy

MATCH (p:Protein {symbol:"BRCA1"})-[:INTERACTS\_WITH]->(partner:Protein)

RETURN partner.symbol;

The Python code to execute this query could be:

python

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query = '''

MATCH (p:Protein {symbol: $sym})-[:INTERACTS\_WITH]->(partner:Protein)

RETURN partner.symbol AS interacting\_protein;

'''

with driver.session() as session:

result = session.run(query, sym="BRCA1")

partners = [ record["interacting\_protein"] for record in result ]

print(f"Proteins interacting with BRCA1: {partners}")

This would output the list of symbols (including "PALB2" from our earlier insertion, and any others known in the KG). The agent can then use this list to formulate an answer or to perform further reasoning (e.g., find if those partners are involved in specific pathways, etc.).

**Data Ingestion, Processing, and Validation Methods**

Ensuring data quality during ingestion is as important as the extraction itself. Our ingestion pipeline consists of multiple processing and validation steps:

1. **Pre-processing**: Raw data from each source is converted to a standardized format. For databases, this might mean reading CSV or XML dumps and converting them to Python objects or intermediate JSON. For literature, it means cleaning the text (removing references, handling special characters, etc.). We also utilize existing identifiers where possible. For instance, when ingesting a UniProt entry, we use its UniProt ID as a key in the graph. When processing text, if we see a gene name like "BRCA1", we map it to an official gene ID (using resources like NCBI Gene or HGNC) to maintain consistency – this avoids the graph having duplicate nodes for the same entity under slightly different names.
2. **Entity Disambiguation and Mapping**: A critical step in processing is ensuring that entities extracted from unstructured text map to the correct existing nodes (or new nodes if truly novel). We maintain a dictionary of known aliases for genes/proteins, diseases, etc., derived from databases (e.g., UniProt provides gene names and synonyms, Disease Ontology provides alternative names for diseases). The ingestion agent uses this to normalize entities. If it encounters an unknown term, it might consult an ontology service or leave the entity marked as tentative. Unresolved entities could be passed to a human curator or a more powerful LLM for identification.
3. **Schema Enforcement**: As knowledge is processed, we enforce the constraints of our knowledge graph schema. For example, if an extraction yields a relation "Protein X – expressed\_in – Tissue Y", we ensure that "expressed\_in" is a valid relation type between a Protein node and a Tissue node. This prevents logical errors like attaching a protein directly to a disease with a wrong relation (the correct chain might be gene mutation causes disease, or protein dysfunction causes disease, etc., but we wouldn't directly connect a protein to a disease without specifying the context). We use a schema definition (possibly in a JSON or a set of Python classes) that lists allowed node types and edges. The ingestion code references this schema and drops or corrects any fact that doesn’t conform. This is an important validation step to maintain **semantic consistency**.
4. **Post-ingestion Validation (Automated)**: Once new data (nodes/edges) is added to the graph, the validation agent runs automated checks. Some of these include:
   * **Duplication Check**: Ensure that we haven’t created redundant duplicate nodes. We rely on the MERGE strategy to prevent exact duplicates, but partial overlaps can occur (e.g., two nodes with the same name but one labeled Gene and one labeled Protein when they should be unified). The validation agent queries for suspicious cases (like identical names or IDs across types that might indicate a merge needed).
   * **Consistency Check**: Verify that each new edge has reasonable endpoints. For instance, if a relation type is *phosphorylates*, the source should be a protein (kinase) and target also a protein or enzyme. If we found a mismatch, it indicates an extraction error (or extremely novel biology that the schema didn’t predict, which would be rare). Such edges might be removed or quarantined.
   * **Supporting Evidence Check**: If a fact was extracted from text, the agent tries to find if that fact exists in the curated databases or at least in multiple publications. This can be done by querying the graph itself (maybe the same relation exists via another source) or by doing a quick literature search (perhaps using an API to a search engine or even scanning a local corpus of text). The idea is to boost confidence in facts that have multiple support and flag those that are singletons (especially if coming from a less reliable source).
5. **Human-in-the-loop Verification**: Despite automation, we include an option for expert curation. The system can produce a report of new or low-confidence assertions (edges, or even entire new nodes for concepts like a newly discovered gene). Domain experts or curators can review these periodically. The interface for this might be a simple list or a graphical view of subgraphs that were recently added, along with their sources. Curators’ feedback (approve/reject/edit) is then fed back into the system. Over time, as the AI models improve and trust in them grows, the reliance on human oversight can decrease, but in a high-stakes domain like biomedicine, having expert review for critical pieces (like a potential new drug-disease link) is valuable.
6. **Continuous Learning and Updates**: The pipeline is continuous. We schedule periodic re-processing of certain data. For example, each month, re-ingest the latest UniProt release to catch updates or new proteins. For literature, subscribe to alerts (RSS feeds or APIs) for specific keywords so we process new papers as they come. Each cycle of ingestion and validation improves the graph. Also, when our knowledge graph embedding is retrained on the updated graph, it might highlight new connections which loop back as potential knowledge to verify (closing a feedback loop where the graph helps identify what it might be missing about the real world).

Throughout these steps, **accuracy maximization** is the guiding principle. By layering multiple checks (schema, evidence, expert review) on top of the AI’s raw output, we reduce the chance of inaccuracies propagating. This multi-tiered validation echoes the practice in manual curation (where a fact is typically reviewed by multiple curators). Indeed, automated systems can present preliminary extractions, and human curators can focus their efforts where the AI is least certain. This synergy between AI and human expertise leads to a higher overall accuracy in the knowledge graph than either alone.

**Accuracy Considerations**

**Ensuring High Accuracy in Knowledge Representation**

Accuracy in a biomedical knowledge graph means that each represented fact is correct and up-to-date according to current scientific understanding. Given the involvement of AI in curating this graph, we implement several methods to ensure high accuracy:

* **Provenance Tracking**: Every piece of information in the graph is tagged with its source. Whether it came from a curated database (trusted) or an NLP extraction from a paper (to be verified), this provenance is recorded (as seen in our code snippet using PubMed IDs). This allows the system to differentiate between various confidence levels. For example, a protein–protein interaction backed by a peer-reviewed database (IntAct or BioGRID) and multiple papers is considered high confidence. In contrast, an interaction extracted from a single paper by the AI has lower confidence. When the graph is queried for critical reasoning (like identifying drug targets), the system can preferentially use high-confidence subgraphs, or at least present confidence alongside answers. Provenance also aids manual verification – an expert can directly inspect the source of any given edge.
* **Consensus and Cross-Verification**: The system attempts to cross-verify new facts against existing knowledge. If an AI agent extracts a new gene-disease link, the validation agent checks if that link (or something related) exists in any authoritative source. We utilize cross-database checks (e.g., if a new disease association is found, check OMIM or ClinVar if they mention that gene). In cases where data is conflicting, we might represent both claims in the graph but annotated with context (for instance, an edge could have a property indicating “controversial” or listing both supporting and refuting evidence). But for delivering answers or making decisions, the agent may ignore facts that lack consensus.
* **Temporal Validity**: Knowledge can change over time (medical reversals, new consensus in science). We incorporate timestamps and versioning. Each edge can have a last\_updated property. If an edge hasn’t been updated or confirmed in a long time, and newer data suggests a change, the system can mark the old info as possibly outdated. For example, consider nutritional biology: at one time “Vitamin E supplements reduce cardiovascular risk” might have been a claim in literature, but later studies refuted it. Our graph could keep the early claim but mark it as refuted by later evidence, ensuring that outdated or superseded info is not treated on par with current consensus. Agents handling queries about vitamin E would then either not mention the refuted claim or explicitly say it's been disproven.
* **Logical Constraints and Reasoners**: We use logical constraints to catch impossible or highly unlikely facts. For example, if the graph by mistake had a cycle like Gene -> Protein -> same Gene (which in biology, a gene encodes a protein, but a protein doesn’t encode a gene), that’s a violation of biological logic. We enforce constraints like “a gene cannot be its own product” or “a compound cannot treat a disease that is actually a side effect of the compound” using a rule-based reasoner or integrity constraints. Some can be enforced at data entry (as in the schema enforcement step), but others might need a reasoner pass. We could use technologies like OWL ontologies and a reasoner (e.g., Pellet or HermiT) for more complex ontology constraints (though integrating that with Neo4j may require export to a triple store or something; instead, we implement simpler custom checks in Python for performance).
* **Continuous Evaluation**: The system is regularly evaluated against known benchmark questions or datasets. For example, we might use a set of known facts (from a resource like WikiData or validated sets of triples from literature) as test queries. The accuracy is measured in terms of precision (what fraction of the graph’s answers or contents are correct) and recall (how much of the known knowledge the graph has captured). One can use standard information extraction metrics if we have ground truth triples: if the graph is treated as the output of an extraction process, we can compute precision/recall/F1 against a gold standard like the BioCreative workshop datasets (which often have sets of known gene-disease or protein interactions from curated data).

**Prompt Engineering Strategies for AI Agents**

When using LLMs as part of the agent toolkit, careful prompt engineering is essential to guide the model towards accurate and relevant outputs. We adopt several strategies:

* **Grounding Prompts in Data**: We always provide context from the knowledge graph to the LLM, rather than asking open-ended questions. For instance, instead of prompting “What does gene TP53 do?”, we gather key facts from the graph (interactions, pathways, diseases) and include them in the prompt: “TP53 is a tumor suppressor gene. It interacts with proteins X, Y, Z and is involved in apoptosis. Based on these facts, describe its role.” By giving the LLM factual scaffolding, we reduce its chance to hallucinate and ensure any elaboration it provides is anchored to known data. This *grounded generation* technique is akin to retrieval-augmented generation (RAG), where the KG serves as the retrieval source.
* **Controlled Generation with Templates**: For tasks like converting a question to a Cypher query or extracting triples from text, we use prompt templates with few-shot examples. For example:

css

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User question: "What pathways involve BRCA1?"

Cypher query: MATCH (g:Gene {symbol:"BRCA1"})-[:PARTICIPATES\_IN]->(p:Pathway) RETURN p.name;

User question: "Which diseases are associated with BRCA1 mutations?"

Cypher query: MATCH (g:Gene {symbol:"BRCA1"})-[:ASSOCIATED\_WITH]->(d:Disease) RETURN d.name;

User question: "<<actual user question>>"

Cypher query:

Providing 2-3 examples in the prompt teaches the model the pattern. We also explicitly instruct the model to only provide the query and nothing else, to avoid extraneous text. This way, the output can be directly used by the system.

* **Role Instruction and Self-Consistency**: We might instruct the LLM with a role (e.g., “You are an expert biomedical knowledge base that only states facts supported by the data given.”). This sets the tone. Additionally, we can use the self-consistency technique – posing a query multiple times with slight prompt variations or using the model’s temperature to generate multiple reasoning paths, then aggregate answers. In a QA setting, for example, we might get the model to produce 5 possible answers with explanations and then have another process (or the model itself) cross-verify which answer is most consistent with the knowledge graph evidence.
* **Graph-of-Thoughts Prompting**: As referenced earlier, we can encourage the model to structure its reasoning. A prompt might say: “Break down your reasoning step by step, and list the entities and their relationships you use at each step.” This effectively gets the model to enumerate a reasoning graph or chain, which we can then check against the KG. If at any step it introduces an entity or relation not in the KG, that’s a point to intervene (either query the KG for it, or note that the model is assuming new info). This method aligns with the Graph-of-Thoughts concept, turning the prompt into a request for an *explainable path*. Not only does this maximize accuracy by keeping the model in check, but it also provides interpretability of the AI’s answer – a desirable feature for researchers and engineers trusting the system.
* **Preventing Overconfidence**: We craft prompts to make the model admit uncertainty when appropriate. For instance, if a prompt is given without enough context, we include a line like “If the knowledge provided is insufficient to answer conclusively, say 'I don’t know based on given data.'” and include that in the few-shot examples. Ensuring the model knows it’s acceptable (or required) to defer to the knowledge limits is key to avoid it guessing and potentially outputting incorrect info as if it were fact.

**Evaluation Metrics and Feedback Loops**

To systematically evaluate and improve the knowledge graph system, we define metrics at both the data level and the application (query) level, and implement feedback loops to use evaluation results for refinement.

**Evaluation Metrics:**

* *Data-level Metrics*: For the knowledge graph content itself, we measure:
  + **Precision of Extracted Facts**: We sample a set of edges added by the AI (especially from literature) and have domain experts or reference databases confirm if they are true. Precision is the fraction of sampled edges that are correct. Our goal is to keep precision very high (because false knowledge can mislead downstream usage), ideally above 90%. A drop in precision triggers a review of the extraction pipeline.
  + **Coverage/Recall**: This is harder to quantify because we don’t have a complete ground truth of “all facts.” Instead, we focus on important subsets: e.g., all known gene-disease associations in OMIM as of a certain date should be present in the graph (recall against OMIM). If recall is low, it means the ingestion pipeline missed known facts, prompting us to find why (maybe a parsing issue or missed synonyms).
  + **Consistency Metrics**: How many constraint violations are present (ideally zero)? If any appear, it’s a sign of error. We also track duplication rates (no duplicate nodes ideally, minimal duplicate edges except where they represent multiple evidence).
  + **Growth and Update Latency**: How quickly do new publications get reflected in the graph? If our goal is a “live” knowledge base, we might measure the average time from a paper’s publication to it being processed and relevant info added. A shorter latency is better for keeping current.
* *Application-level Metrics*: For queries and reasoning tasks using the graph:
  + **Question Answering Accuracy**: We maintain a benchmark set of questions (some simple like “What is the function of gene X?”, some complex like “Find a potential drug that could treat disease Y by targeting pathway Z”). We know the expected answers (via experts or existing literature). We then run our system (query agent + KG) to answer them and measure accuracy (correct/incorrect).
  + **Efficiency**: Query execution time is measured for complex multi-hop queries, to ensure the system is responsive. If certain queries are too slow, we might need to add indexes or redesign the query strategy (maybe precompute some common paths).
  + **User feedback**: If this system is used by researchers, their feedback (ratings on answer helpfulness or correctness) can serve as a metric. Even if not publicly deployed, we can simulate users by asking experts to evaluate answers.

**Feedback Loops:**

* **Automated Feedback**: Results from the evaluation can directly loop into system improvement. For instance, if precision of extraction on a particular relation type is low, we analyze those errors and adjust the model or add rules. If recall for a known dataset (like OMIM gene-disease) is low, we specifically feed more data or tweak the NER to catch those cases.
* **Active Learning**: The system can actively seek feedback on uncertain predictions. Suppose our KGE predicts a new relation (drug A treats disease B with high probability) that’s not in the graph. The system can treat this as a question and attempt to validate it – essentially querying its internal model. It could generate a hypothesis statement and search literature for evidence. If found, it adds it; if not, maybe down-weight that belief. Over time, this self-questioning improves the graph.
* **Human-in-loop Feedback**: As mentioned, any human corrections (like a curator deleting a wrong edge or adding a missed one) are fed back as supervised data to the AI models. For example, if curators often correct a certain type of false relation, the system can learn to avoid extracting that pattern (maybe the model was confused by co-occurrence of terms in text as an actual relation).
* **Prompt Iteration**: We A/B test different prompt strategies using the evaluation questions. If one style of prompt yields more accurate answers (which we measure via QA accuracy), we adopt it. This is an iterative process; LLM behavior can be unpredictable, so empirical testing guides prompt refinement.

By continuously evaluating with these metrics and closing the loop from evaluation to system update, we strive to **maximize accuracy** not just at initial deployment, but throughout the lifecycle of the knowledge graph. The dynamic nature of the system extends to learning from its mistakes and user interactions, embodying a form of continual learning.

**Discussion**

**Challenges and Limitations**

Building a dynamic, AI-curated knowledge graph of the entire human biological system is an ambitious endeavor fraught with challenges:

* **Scalability and Performance**: The volume of biological data is enormous. Even though Neo4j and similar graph databases can handle billions of nodes/edges, querying across such a vast graph might become slow, and updates might face throughput limits. We must carefully optimize queries (using indexes, caching frequent query results, using summary nodes for high-degree nodes to avoid traversing thousands of edges naively). Additionally, as the graph grows, memory and storage requirements escalate. Partitioning strategies or sharding the graph (for example, by subdomain like genomics vs. proteomics) might be necessary, but that introduces complexity in cross-domain queries.
* **Data Integration and Schema Evolution**: Integrating heterogeneous data sources means dealing with inconsistent identifiers, formats, and sometimes conflicting information. While we set an initial ontology for the graph, biology is complex and our schema might need to evolve. For instance, new types of entities (e.g., regulatory RNAs, microbiome species interacting with the human host) might become relevant. The system should be adaptable to incorporate new node or relation types without a complete redesign. This is non-trivial because adding new types can require re-training NLP models or adjusting existing data. Maintaining a unified schema that’s both comprehensive and not overly rigid is a continual challenge.
* **Accuracy vs. Coverage Trade-off**: Aggressively automated ingestion can maximize coverage of knowledge (recall), but risks introducing incorrect information (lowering precision). Conversely, a very conservative approach (e.g., only include facts confirmed by multiple sources) might miss important novel insights. Balancing this trade-off is difficult. We addressed it by multi-tier confidence and validation, but ultimately some false positives might slip through or some true but new facts might be omitted until confirmed. The system’s usefulness could be impacted by these choices – a researcher might prefer completeness at the cost of a few errors, while a clinical application might demand near-perfect accuracy at the cost of being slightly outdated.
* **Maintaining Currency**: Keeping the graph updated in near real-time with new discoveries is challenging in practice. There could be a lag in obtaining full-text papers (some are behind paywalls or not immediately available). Some data like clinical trials outcomes or latest genomic variants might not be published openly right away. Also, the process of re-training models or re-running extraction on new data continuously is computationally intensive. We need to ensure the pipeline can run incrementally – ideally processing only new information rather than reprocessing everything. But incremental updates risk missing context (e.g., a new fact might be better understood in the context of all knowledge). We mitigate this by scheduling periodic full re-processing (like a nightly or weekly batch to re-read recent papers with the latest model).
* **AI Model Limitations**: The AI agents and models themselves have limitations. LLMs might still hallucinate or misunderstand queries, especially if they venture outside the domain of the provided context. Domain-specific models like BioBERT are strong at certain tasks but may miss others (BioBERT might not catch very subtle context that a human would). And models can have biases – perhaps overrepresenting well-studied genes and underrepresenting rare diseases. There’s also the risk of error propagation: if the model mis-extracts a fact and it enters the graph, it could then mislead other agents or future extractions (as the system might assume it’s true unless caught by validation).
* **Interpretability and Trust**: While knowledge graphs are more interpretable than black-box models (since one can trace relationships), the involvement of AI in constructing the graph can raise trust issues. Users may question how a particular fact got in the graph. We addressed this with provenance and explanations, but users (especially clinicians) might still be cautious about trusting an AI-curated knowledge source. Building trust will require demonstrating a track record of accuracy and perhaps giving users tools to input corrections or annotations to the graph themselves (making it a community-curated resource with AI assistance).
* **Privacy and Ethical Concerns**: If the knowledge graph were to incorporate patient-specific data or medical records (to personalize the knowledge for an individual), there would be significant privacy issues. In our current scope, we mainly use public data and published knowledge, so privacy is not a major concern. But any extension toward personalizing or integrating patient data must consider data governance, anonymization, and compliance with regulations (like HIPAA, GDPR). Even with public data, licensing issues can arise (some databases have restrictions on use; we have to ensure that integrating data from various sources complies with their licenses).
* **Multi-Agent Coordination**: Having multiple agents introduces complexity in coordination. There could be race conditions (two ingestion agents adding overlapping knowledge simultaneously, potentially duplicating before they see each other’s updates) or conflicts (one agent’s update inadvertently triggers a rule in another that flags it). We rely on transactions and a message bus to synchronize, but designing these interactions is complex and prone to edge cases. Ensuring that, for example, the validation agent doesn’t delete or undo something the ingestion agent is in the middle of adding requires careful ordering or versioning of operations.

**Future Improvements and Applications**

The current system lays a foundation, but there are several avenues for enhancement and broader application:

* **Incorporation of Reasoning Engines**: We can integrate formal reasoning engines or even emerging neuro-symbolic methods to derive new knowledge from the existing graph. For example, applying inductive logic programming on the graph could find rules like “if gene A interacts with gene B and gene B is associated with disease X, then gene A might also be associated with disease X” – essentially hypothesis generation. These can then be tested or used to guide lab experiments. Some frameworks (like AMIE for rule mining in KGs) could be applied to our data to unearth such patterns.
* **Integration with Simulation and Dynamic Data**: The knowledge graph currently represents mostly static facts. But biology has dynamic aspects (gene expression levels, patient vital signs, etc.). In the future, linking the KG with temporal data or simulation models could be powerful. For instance, integrating gene regulatory network models or metabolic simulations, and using the KG as a scaffolding for parameters or structure. AI agents could then not only store factual knowledge but also do *what-if reasoning* by running simulations (e.g., simulate what happens to a metabolic pathway if an enzyme is inhibited, using the network from the KG). This moves towards a “digital twin” of the human biological system, where static and dynamic knowledge merge.
* **User Feedback Loops and Crowdsourcing**: To scale verification, we might allow domain experts globally to contribute. A platform built on the KG could let researchers query and also submit new findings or corrections, which the AI agents then verify and incorporate. Essentially a wiki-like model but with AI guardians that ensure consistency and integration. This could accelerate the growth of the graph and engage the scientific community in curating knowledge with AI assistance.
* **Enhanced Multi-Modal Data**: Our focus was on textual and structured data, but there is a wealth of imagery and omics data (like histology images, protein 3D structures, gene expression matrices). Future expansions could include linking to image data nodes or summary features (e.g., a node for a cell type could link to an image of that cell, or a protein node could link to its 3D structure file or an embedding of it). AI agents that handle images (like deep learning models for pathology) could contribute insights (e.g., “protein X is expressed highly in these tissue images”) which then become facts in the graph (“Protein X – high\_expression\_in – Tissue Y”). This would make the knowledge graph a multi-modal hub of information.
* **Domain Expansion and Generalization**: While we target human biology, the approach can extend to other domains or across domains. For example, comparative biology graphs linking human genes to model organism genes and phenotypes could aid translational research (using animal model data to infer human outcomes). Or applying a similar AI-driven KG approach to other fields (like an AI-curated knowledge graph of materials science, as SciAgents did for materials). The general framework of AI agents + knowledge graph + continuous learning can be ported with domain-specific adjustments.
* **Real-world Applications**:
  + *Drug Discovery*: Pharmaceutical companies can use such a KG to find new drug targets by traversing the graph for under-explored connections between drugs, genes, and diseases. With link prediction, the system might suggest “drug A could interact with protein B” which researchers can then validate in the lab.
  + *Clinical Decision Support*: In a hospital setting, a clinician could query the system for patient-specific insights, e.g., “Does this patient’s combination of mutations have any known treatment?” The graph could connect those mutations to pathways and known drug sensitivities. Realizing this in practice would require incorporating patient genomic data and clinical data nodes securely, as well as rigorous validation, but it’s a future direction.
  + *Educational Tool*: For medical and biology education, an interactive KG browser powered by AI could be a great tool. Students could ask complex questions (“Explain how a mutation in gene X can lead to symptom Y”) and get answers with a graphical explanation path through the KG. This leverages the graph for explanation – something static textbooks struggle to do dynamically.
* **Improved Natural Language Interfaces**: While our query agent can handle natural language via LLMs, future improvements could allow the system to engage in dialogue. Instead of one-shot Q&A, it could ask clarifying questions (using the KG to narrow down what the user might be asking) and present answers in a conversational manner. This would make the knowledge graph more accessible to those not familiar with graph queries – essentially hiding the complexity behind a chat interface that still guarantees factuality through the underlying KG. Recent advances in conversational AI agents combined with retrieval (ChatGPT plugins with data, etc.) point towards this possibility.

In conclusion, the dynamic knowledge graph we have built is not an end, but a beginning – a platform that can continuously improve and expand with both algorithmic advances and community input. Its potential impact spans scientific research acceleration, enhanced clinical decision-making, and democratization of complex biomedical knowledge through AI-powered tools.

**Conclusion**

We presented a comprehensive framework for constructing a **dynamic, AI-driven knowledge graph** encompassing the entire human biological system. This work marries the strengths of knowledge graphs – structured, transparent, and interlinked representations of data – with the power of AI agents that can learn, extract, and reason. By implementing a multi-agent architecture, we enable continuous ingestion of new biological knowledge and upkeep of a vast graph that would be infeasible to maintain manually. Key innovations include treating the knowledge graph as an **external memory** for AI, using **AI memory encoding and retrieval techniques** to populate and query this memory. Our methodology emphasizes accuracy at every step: from careful NLP extraction with biomedical language models to multi-layer validation and prompt engineering that grounds AI reasoning in the graph’s facts. The implementation with Neo4j demonstrates that current graph databases can handle the scale and complexity of this task, and our Python integration examples illustrate how AI models interface with the graph to effect updates in real-time.

The results underscore that such an AI-curated knowledge graph can remain **up-to-date and reliable**, provided that robust feedback loops and quality controls are in place. In doing so, we effectively create an evolving map of human biology – one that can be traversed by algorithms and researchers alike to generate insights. This system has broad implications: scientists can discover non-obvious connections (e.g., linking genes to diseases through intermediate pathways) by traversing the graph or by asking the AI to find paths; clinicians can receive answers that are backed by a chain of evidence through the graph, increasing trust in AI-driven recommendations; and AI systems themselves can avoid the pitfalls of purely parametric knowledge by consulting an authoritative graph memory, thereby reducing errors like hallucinations.

For AI researchers and engineers, our work serves as a case study in integrating **symbolic and neural AI**. We show that it’s not only feasible but advantageous to embed large language models and other AI components within a knowledge-rich context. The knowledge graph acts as a scaffold that gives structure to otherwise unstructured intelligence, resulting in a system that is greater than the sum of its parts – combining statistical learning with logical reasoning. We also highlight practical considerations in deploying such systems, from ensuring data consistency to handling the evolving nature of scientific truth.

In summary, building a dynamic knowledge graph of human biology with AI agents is a significant step toward managing and utilizing the deluge of biomedical data. It creates a living repository of knowledge that grows and adapts, much like the science it aims to represent. While challenges remain, our research demonstrates a viable path forward. We encourage further exploration and refinement of this approach, as well as its application to other domains where knowledge is vast and ever-changing. The synergy of AI and knowledge graphs heralds a new era of intelligent knowledge management – one where **accuracy, scalability, and dynamism** come together to accelerate discovery and innovation.

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Example Code Below:

A screenshot of a computer program

Description automatically generated

A screen shot of a computer program

Description automatically generated

A screenshot of a computer program

Description automatically generated

A screenshot of a computer program

Description automatically generated

if \_\_name\_\_ == "\_\_main\_\_":

    main()