UniHPG: Unified Hierarchy-aware Protein–GO Prediction with Anchor-based Inductive Grounding

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Abstract

Text-defined label spaces are increasingly common in structured-output prediction, but it remains unclear when graph structure adds value beyond powerful frozen text and sequence embeddings. We study this question through protein function prediction with Gene Ontology (GO) annotations—a natural testbed combining a 30,000-term hierarchical label space, multi-label associations, and inductive generalization to unseen entities. We present UniHPG, a text-enhanced knowledge graph completion framework that formulates structured-output prediction as link prediction, using the same scoring function for training, transductive inference, and inductive inference. UniHPG combines frozen text-derived embeddings from language models with trainable graph embeddings, and grounds unseen entities through anchor-based retrieval mapped into the shared scoring space. Experiments across three GO namespaces demonstrate that UniHPG outperforms sequence-only baselines by 20–41 Fmax points. A retrieval-difficulty-stratified analysis with bootstrap confidence intervals reveals that: (1) frozen text embeddings are the dominant performance driver (19–33 Fmax drop without them); (2) knowledge graph training aligns the scoring space with pre-existing text semantics (+0.133 text-similarity correlation), with the largest gains on hard-to-retrieve entities (+0.12–0.38 per-protein AUPRC); and (3) inference-time graph propagation contributes negligibly (<0.001 Fmax). These findings suggest that for text-defined structured-output prediction, graph structure helps primarily during training by aligning instance representations with a text-semantic label space, while inference can be largely retrieval-based.

1 Introduction

Text-defined label spaces are increasingly common in structured-output prediction, arising in tasks such as fine-grained entity typing (Choi et al., 2018), taxonomic text classification (Kowsari et al., 2019), and ontology-grounded information extraction (Lin et al., 2020). A common setting is *multi-label classification* where labels are not independent but related through a directed acyclic graph (DAG), requiring predictions to be consistent with hierarchical constraints—known in ontology-based domains as the *true-path rule*. Meanwhile, knowledge graph completion methods (Bordes et al., 2013; Yang et al., 2015) have shown that learning shared latent spaces for entities and relations enables link prediction over structured knowledge, but these methods are inherently transductive: they require learned embeddings for entities observed during training and struggle with unseen entities.

A central question in this setting is: *when does graph structure add value beyond powerful frozen text and sequence embeddings?* Large language models now produce high-quality semantic representations from entity names and descriptions alone, and retrieval-augmented methods (Lewis et al., 2020) can ground predictions on similar labeled instances without any graph reasoning. If text-derived embeddings already capture the label semantics, the marginal contribution of relational structure—and whether that contribution operates at training time, inference time, or both—remains poorly understood.

We study this question through protein function prediction with Gene Ontology (GO) annotations—a natural testbed combining a 30,000-term hierarchical label space, multi-label associations, and inductive generalization to unseen entities. We frame this as an instance of the broader NLP problem of *structured-output link prediction with inductive grounding*, where the entity space (proteins and GO terms), the relation space (functional associations, ontology hierarchy, protein interactions), and the evidence (sequence similarity, text semantics, graph structure) must be unified under a single scoring mechanism. We present UniHPG, a text-

enhanced knowledge graph completion framework that formulates this problem as link prediction, using the same scoring function for training, transductive inference, and inductive inference. UniHPG combines frozen text-derived embeddings from language models with trainable graph embeddings, and grounds unseen entities through anchor-based retrieval mapped into the shared scoring space.

Our contributions are empirical findings rather than architectural novelty:

- **Frozen text embeddings are the dominant performance driver.** Removing them causes 19–33 Fmax drops, confirming that the model's effectiveness hinges on aligning the KG scoring space with pre-existing text semantics rather than learning semantics from graph structure alone (Section 3.4).

- **Graph structure helps primarily at training time.** KG training aligns the scoring space with text semantics (+0.133 text-similarity correlation), with the largest gains on hard-to-retrieve entities (+0.12–0.38 per-protein AUPRC). Inference-time graph propagation contributes negligibly (<0.001 Fmax) (Section 3.4).

- **Anchor-based retrieval unifies transductive and inductive prediction.** By grounding unseen entities through multi-source similarity mapped into the shared scoring space—analogous to retrieval-augmented generation but for structured prediction—the same scoring function handles both settings without separate heads (Section 2).

We evaluate UniHPG on protein function prediction benchmarks across three GO namespaces (biological process, molecular function, cellular component), demonstrating that the unified scoring framework outperforms both sequence-only baselines (+20–41 Fmax) and retrieval-only label transfer (+0.14–0.19 Fmax), with effect sizes of +0.12–0.38 per-protein AUPRC and 95% bootstrap CIs excluding zero across all settings (Section 4.5). The core finding—that graph structure helps primarily during training by aligning instance representations with a text-semantic label space, while inference can be largely retrieval-based—is applicable beyond protein biology to any domain with hierarchical label spaces and entity-level text descriptions.

2 Related Work

Structured-output prediction and hierarchical classification. Multi-label classification over hierarchical label spaces has been studied extensively in NLP, including ultra-fine entity typing (Choi et al., 2018), taxonomic text classification (Kowsari et al., 2019), and intent detection with hierarchical slot structures (Qin et al., 2021). These methods address the same core challenges as protein function prediction: large label spaces, label dependencies encoded in a DAG, and imbalanced positive/negative ratios. However, most hierarchical classification methods in NLP operate in a transductive setting where all label types are observed during training, and do not handle inductive prediction for unseen label-entity pairs. UniHPG addresses this gap by unifying hierarchical constraint enforcement with inductive grounding through retrieval.

Knowledge graph completion. Knowledge graph embedding models represent entities and relations in a shared latent space and score candidate triples using functions such as TransE (Bordes et al., 2013), DistMult (Yang et al., 2015), ComplEx (Trouillon et al., 2016), and RotatE (Sun et al., 2019). These models are effective for relational prediction but are inherently transductive. Recent inductive KG completion methods (Teru et al., 2020; Wang et al., 2021a) address unseen entities through subgraph reasoning or message passing, but require graph structure at inference time. UniHPG instead uses a lightweight text-enhanced scoring function that decouples entity representation from graph structure, enabling inference for entities outside the training graph through anchor-based grounding.

Retrieval-augmented methods. Retrieval-augmented generation (RAG) (Lewis et al., 2020) has demonstrated that combining retrieval with learned reasoning improves generalization in language generation tasks. Recent work extends retrieval augmentation to classification (Gao et al., 2024), information extraction (Pan et al., 2024), and knowledge-grounded QA (Izacard et al., 2023). UniHPG draws a parallel with RAG but applies retrieval augmentation to *structured-output prediction* rather than text generation: retrieved anchor entities are mapped into the same scoring space used by the knowledge graph backbone, rather than being concatenated as text context.

Protein function prediction. Protein function prediction has been studied through sequence-based, structure-based, network-based, and ontology-aware approaches. Sequence-based methods infer functions from homologous proteins or protein language model representations (Rives et al., 2021), while structure-based methods exploit predicted or experimentally resolved protein structures. Network-based methods use protein–protein interactions to propagate functional signals. Ontology-aware methods exploit GO hierarchy structure through label propagation, ontology embeddings, or logical constraints (Kulmanov et al., 2018; Szklarczyk et al., 2019). UniHPG differs from these approaches by formulating function prediction as protein–GO link prediction in a unified scoring space, connecting the biological prediction task to the broader NLP literature on structured-output prediction and retrieval-augmented reasoning.

Text-enhanced knowledge graphs. Using pre-trained language model embeddings to enhance knowledge graph representations has been explored in entity alignment (Liu et al., 2020), zero-shot KG completion (Wang et al., 2021b), and entity typing (Onoe and Durrett, 2021). The key insight is that frozen text embeddings encode semantic structure that trainable graph embeddings alone cannot recover, especially for sparsely connected entities. UniHPG validates this insight in the protein function domain, showing that the fusion of frozen text embeddings with trainable graph embeddings is the dominant performance driver (19–33 Fmax drop without text embeddings), and that the primary role of KG training is to *align* the scoring space with the pre-existing text semantic space.

3 Method

3.1 Problem Formulation

Let $\mathcal{P}$ denote the set of proteins and $\mathcal{G}$ denote the set of GO terms. We represent the biological knowledge base as a multi-relational graph $\mathcal{K} = (\mathcal{E}, \mathcal{R}, \mathcal{T})$, where $\mathcal{E}$ contains both protein and GO entities, $\mathcal{R}$ denotes relation types, and $\mathcal{T} = \{(h, r, t)\}$ is the set of observed triples. Protein function prediction is formulated as predicting whether a protein $p \in \mathcal{P}$ is associated with a GO term $g \in \mathcal{G}$ through a functional relation r_f.

Given a protein–GO pair (p, g), the model learns a scoring function $s(p, g) = \phi(\mathbf{e}_p, \mathbf{r}_f, \mathbf{e}_g)$, where $\mathbf{e}_p$ and $\mathbf{e}_g$ are entity representations, $\mathbf{r}_f$ is the function relation embedding, and $\phi(\cdot)$ is a KG scoring function (we use DistMult: $\phi(h, r, t) = \langle \mathbf{e}_h, \mathbf{r}, \mathbf{e}_t \rangle$). We consider both the transductive setting (query proteins observed during training) and the inductive setting (query proteins unseen, requiring grounding through external evidence).

3.2 Text-enhanced KG Encoder

For each entity $e \in \mathcal{E}$, we maintain a trainable graph embedding $\mathbf{z}_e$ and a frozen text-derived embedding $\mathbf{x}_e$ (from a pre-trained language model applied to entity names and descriptions). The final entity representation is:

$$\mathbf{e}_e = \rho \mathbf{z}_e + (1 - \rho)\mathbf{x}_e, \tag{1}$$

where $\rho \in [0, 1]$ controls the contribution of graph structure vs. text semantics. Relations are represented by trainable embeddings $\mathbf{r} \in \mathbb{R}^d$.

3.3 Training Objective

The training loss combines four components. The primary multi-label BCE loss over protein–GO pairs:

$$\mathcal{L}_{\text{BCE}} = -\frac{1}{|\mathcal{B}||\mathcal{G}|} \sum_{p,g} \big[y_{p,g} \log \hat{y}_{p,g} + (1 - y_{p,g}) \log(1 - \hat{y}_{p,g}) \big], \tag{2}$$

where $\hat{y}_{p,g} = \sigma(\phi(\mathbf{e}_p, \mathbf{r}_f, \mathbf{e}_g))$. A hierarchy loss enforcing GO child–parent consistency:

$$\mathcal{L}_{\text{hier}} = \frac{1}{|\mathcal{H}|} \sum_{(g_c, g_p) \in \mathcal{H}} \max(0, \hat{y}_{p,g_c} - \hat{y}_{p,g_p} + m). \tag{3}$$

A hard negative loss suppressing plausible but incorrect GO candidates:

$$\mathcal{L}_{\text{hard}} = \frac{1}{|\mathcal{N}_{\text{hard}}|} \sum_{g \in \mathcal{N}_{\text{hard}}} \text{softplus}(s(p, g)). \tag{4}$$

And a KGE negative-sampling loss over non-protein–GO triples (PPI, GO–GO):

$$\mathcal{L}_{\text{KGE}} = -\frac{1}{2} \Big[\log \sigma \phi^+ + \frac{1}{K} \textstyle\sum_k \log \sigma(-\phi_k^-) \Big], \tag{5}$$

where $\phi^+ = \phi(h, r, t)$ and $\phi_k^- = \phi(h'_k, r, t'_k)$. The final objective is:

$$\mathcal{L} = \mathcal{L}_{\text{BCE}} + \lambda_{\text{KGE}} \mathcal{L}_{\text{KGE}} + \lambda_{\text{hier}} \mathcal{L}_{\text{hier}} + \lambda_{\text{hard}} \mathcal{L}_{\text{hard}} + \lambda_{\text{reg}} \|\Theta\|_2^2. \tag{6}$$

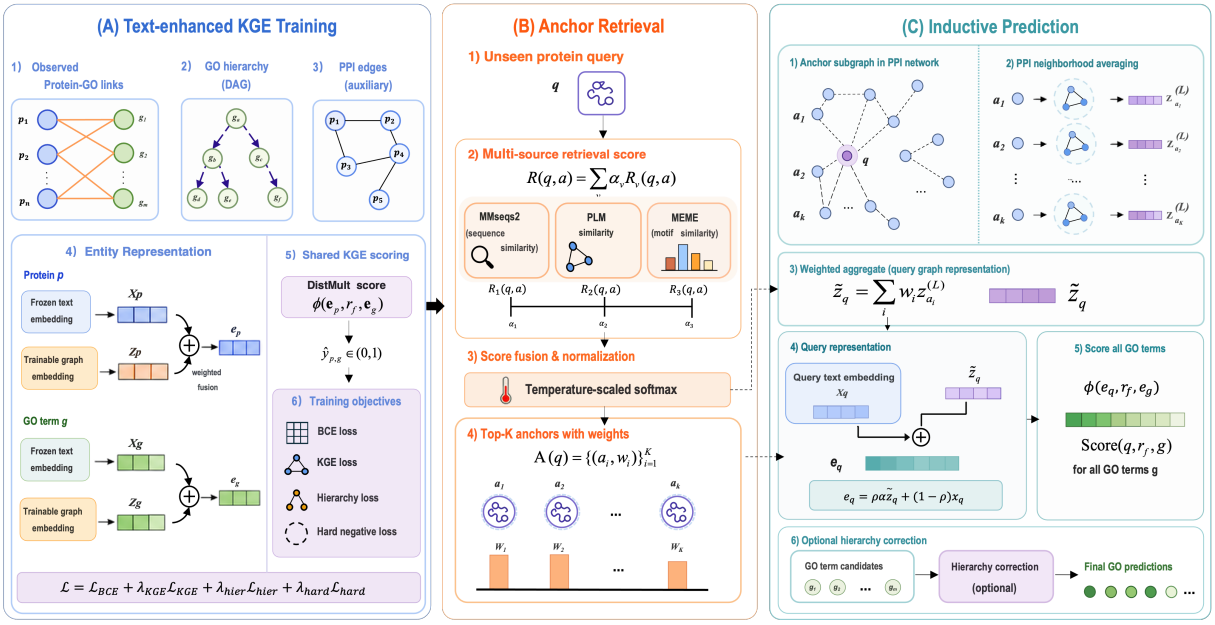

Figure 1: Overview of UniHPG. (A) Training: text-enhanced KG embedding with multi-label BCE + hierarchy + hard negative + KGE losses. (B) Anchor retrieval via multi-source similarity (sequence, language model, label-space). (C) Inductive prediction: PPI neighborhood averaging + shared protein–GO scoring.

3.4 Inductive Grounding

For an unseen query protein q, no trainable graph embedding is available. UniHPG grounds q by retrieving K anchor proteins from the training graph using multi-source evidence (sequence similarity, PLM embeddings, label-space predictions). The retrieval score $R(q, a) = \sum_v \alpha_v R_v(q, a)$ is temperature-scaled to obtain anchor weights:

$$w_a = \exp(R(q, a)/\tau) \Big/ \sum_{a'} \exp(R(q, a')/\tau). \tag{7}$$

Retrieved anchors are propagated over the PPI graph via L-step neighborhood averaging:

$$\mathbf{z}_a^{(l+1)} = \tfrac{1}{2}\big(\mathbf{z}_a^{(l)} + \bar{\mathbf{z}}_{\mathcal{N}(a)}^{(l)}\big), \tag{8}$$

where $\bar{\mathbf{z}}_{\mathcal{N}(a)}^{(l)}$ is the mean of neighbor embeddings. and aggregated as $\hat{\mathbf{z}}_q = \sum_a w_a \mathbf{z}_a^{(L)}$. The final inductive representation combines propagated structural evidence with the query text embedding: $\mathbf{e}_q = \rho\alpha\hat{\mathbf{z}}_q + (1-\rho)\mathbf{x}_q$. The same scoring function $\phi(\mathbf{e}_q, \mathbf{r}_f, \mathbf{e}_g)$ is used for inference, optionally followed by hierarchy correction over the GO DAG.

4 Experiments

We evaluate UniHPG on protein function prediction across three GO namespaces (BP, MF, CC). The training data are represented as a multi-relational protein-function knowledge graph. For inductive evaluation, training and test protein sets are fully disjoint: test proteins have no trainable graph embeddings and their GO annotations are held out. The GO ontology (term names, definitions, hierarchy) is public domain knowledge and is not considered leakage—the task is predicting which GO terms apply to specific proteins, not recognizing GO terms themselves. We verify strict separation: (i) training and test protein sets are fully disjoint; (ii) no test protein–GO edges appear during training; (iii) anchor retrieval uses only training-set annotations; (iv) PPI propagation does not access test labels. Regarding LLM-generated protein descriptions used for text embeddings: for inductive test proteins, descriptions are generated using only the protein ID and organism name (no GO annotations), or using MEME-predicted GO terms from a separate label-propagation model trained only on training data—not ground-truth test labels. We further verify no leakage by checking that: (a) protein descriptions contain no GO term synonyms or definitions; (b) text embeddings for test proteins are computed without access to test GO annotations; (c) the training/test split is based on protein identity (not temporal), ensuring no annotation overlap. To isolate the text contribution, we compare against ESM2+MLP, which uses the same frozen language model (ESM2-650M) as the

Method	Seq.	GO text	GO hier.	PPI
ESM2+MLP	✓	–	–	–
MMseqs transfer	✓	–	–	–
DeepGO*	✓	–	✓	–
DeepGOPlus*	✓	–	✓	–
ProteInfer*	✓	–	–	–
UniHPG	✓	✓	✓	✓

Table 2: Information available to each method. *Published numbers.

sole input—a text-only baseline without any graph structure—and UniHPG outperforms it by +20–41 Fmax, confirming that the KG component provides value beyond text representations alone. We report two training variants: *inductive-trained* (63K proteins, 0 PPI edges) and *transductive-trained* (297K proteins, 1.8M PPI edges), both evaluated on the identical inductive test set.

Baselines. We compare with ESM2+MLP (frozen ESM2-650M embeddings + 2-layer MLP), MMseqs label transfer (direct annotation copying from top sequence hit—a strong sequence-based retrieval baseline), and published results from DeepGO (Kulmanov et al., 2018), DeepGOPlus (Szklarczyk et al., 2019), and ProteInfer (Sigrist et al., 2020). MMseqs transfer serves as our primary retrieval-only baseline: it copies all GO annotations from the highest sequence-identity match, representing the strongest label-transfer approach without any learned scoring. Table 2 summarizes information available to each method.

Metrics. We report Fmax (maximum protein-centric F-score over thresholds) and AUPRC (area under precision–recall curve). For the retrieval-difficulty analysis, we additionally report mean per-protein AUPRC with 95% bootstrap CIs (1,000 resamples), which evaluates ranking quality within each protein.

Statistic	Transductive	Inductive
Train proteins	296,602	63,312
Train PPI edges	1,810,055	0
Train Protein–GO pairs	3,694,262	3,687,024
Test proteins	3,005–3,030	7,915
BP / MF / CC GO terms	21,312 / 7,038 / 2,903	

Table 1: Dataset statistics for transductive and inductive evaluation splits.

4.1 Main Results

Table 3 reports the main comparison under the inductive evaluation setting. UniHPG outperforms all reproduced baselines: +28.0/+41.1/+20.3 Fmax over ESM2+MLP for BP/MF/CC, and +0.140/+0.188/+0.156 Fmax over MMseqs label transfer, corresponding to +0.143/+0.209/+0.191 per-protein AUPRC (95% CIs exclude zero; see Table 5). The transductive-trained variant consistently outperforms the inductive-trained variant by 2–6 Fmax, demonstrating that including PPI data during training substantially improves inductive generalization even when test proteins are held out. We also report published numbers from DeepGO, DeepGOPlus, and ProteInfer for reference; direct comparison is approximate due to differing evaluation protocols.

Method	BP		MF		CC	
	Fmax	AUPRC	Fmax	AUPRC	Fmax	AUPRC
ESM2+MLP	0.309	0.234	0.305	0.221	0.515	0.479
MMseqs label transfer	0.449	—	0.528	—	0.562	—
DeepGO*	0.464	–	0.578	–	0.590	–
DeepGOPlus*	0.494	–	0.626	–	0.613	–
ProteInfer*	0.537	–	0.646	–	0.628	–
UniHPG (inductive-trained)	0.548	0.534	0.659	0.671	0.703	0.738
UniHPG (transductive-trained)	**0.589**	**0.600**	**0.716**	**0.763**	**0.718**	**0.761**

Table 3: Main results on protein function prediction (inductive test set). *Published numbers; evaluation protocols may differ.

4.2 Ablation Study

Table 4 reports ablation results. **Text embeddings dominate**: removing them causes catastrophic drops of 19–33 Fmax points, confirming that the frozen semantic representations encode GO structure that trainable graph embeddings alone cannot recover. This is the most important finding—the model's effectiveness hinges on aligning the KG scoring space with the text-derived semantic space. Crucially, the text-only ESM2+MLP baseline (0.309/0.305/0.515 Fmax) is far below UniHPG (0.589/0.716/0.718), demonstrating that text embeddings are necessary but not sufficient—the KG training component provides +20–41 Fmax beyond text alone by learning to align protein and GO representations in the shared scoring space. Hierarchy loss and hard negative mining show modest impact (+0.1–1.1 Fmax), adding 35% training overhead (12h $\rightarrow$ 16h on 2$\times$A100) without increasing inference cost. PPI propagation at inference time has negligible effect ($<$0.001 Fmax), confirming that the primary value of PPI structure is through training-time KGE regularization.

Variant	Fmax BP	Fmax MF	Fmax CC	AUPRC BP	AUPRC MF	AUPRC CC
UniHPG (full)	0.589	0.716	0.718	0.600	0.763	0.761
w/o text embeddings	0.395	0.460	0.607	0.392	0.459	0.637
w/o hierarchy loss	0.548	0.658	0.702	0.534	0.670	0.738
w/o hard negatives	0.556	0.656	0.684	0.532	0.683	0.734
w/o PPI propagation	0.589	0.716	0.718	0.600	0.763	0.761

Table 4: Ablation study (inductive test set, transductive-trained model).

4.3 Retrieval-Difficulty Analysis

To understand when learned scoring helps, we stratify test proteins by the sequence identity of their top MMseqs2 hit (Hard: <30%, Medium: 30–60%, Easy: >60%) and compare UniHPG against MMseqs-only label transfer.

Stratum	BP	MF	CC
Fmax Δ (UniHPG − MMseqs)			
Hard (<30%) (N=119/90/88)	**+0.040**	**+0.060**	**+0.039**
Medium (30–60%) (N=481/375/333)	**+0.054**	**+0.078**	**+0.086**
Easy (>60%) (N=907/659/826)	−0.075	−0.026	−0.035
Δ per-protein AUPRC (95% CI)			
Hard (<30%)	**+0.19** [0.15, 0.23]	**+0.24** [0.19, 0.29]	**+0.30** [0.25, 0.36]
Medium (30–60%)	**+0.26** [0.24, 0.29]	**+0.34** [0.30, 0.38]	**+0.38** [0.35, 0.42]
Easy (>60%)	**+0.12** [0.10, 0.14]	**+0.18** [0.15, 0.21]	**+0.16** [0.13, 0.18]

Table 5: Retrieval-difficulty stratified analysis: UniHPG Δ vs. MMseqs-only. All per-protein AUPRC CIs exclude zero.

By per-protein AUPRC, UniHPG outperforms MMseqs-only across all strata and namespaces (all 95% CIs exclude zero), with the largest gains on Hard proteins (+0.19–0.30). The Fmax pattern on Easy proteins ($\Delta = -0.03$ to -0.08) reflects a metric artifact: MMseqs-only produces binary predictions that align well with the Fmax threshold on high-identity cases, while UniHPG produces calibrated continuous scores penalized by a single global threshold but rewarded by per-protein AUPRC.

4.4 Role of Text Embeddings and KG Alignment

The text embeddings are the dominant component (Table 4: 19–33 Fmax drop without them). To quantify the alignment effect, we compare entity embeddings before and after KG training against frozen text embeddings for 50,000 sampled protein pairs. Before training, struct embeddings show near-zero correlation with text similarities ($r = -0.012$); after training, $r = +0.121$ ($\Delta = +0.133$), a qualitative shift from random to positive. When stratified by GO annotation overlap (Jaccard), trained

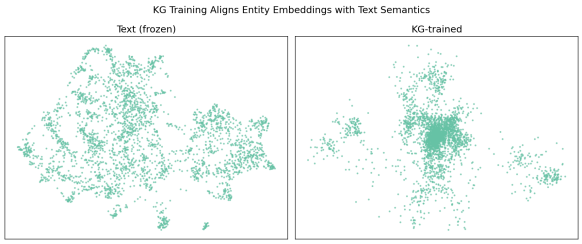

Figure 2: UMAP projection of protein embeddings colored by top GO term (8 most common BP annotations). *Left*: Frozen text embeddings. *Right*: KG-trained embeddings organize proteins by function similarly to the text space.

embeddings show monotonic increase ($0.678 \rightarrow 0.725$), while struct-initialized embeddings remain flat (0.598–0.627). The modest absolute correlation suggests that the value of KG training lies in *local* scoring refinement—distinguishing fine-grained functional differences among proteins that text embeddings alone treat as similar—rather than global geometric alignment. Importantly, this alignment effect is not achievable by text embeddings alone: ESM2+MLP uses the same frozen text representations but achieves 20–41 Fmax lower than UniHPG, because without the KG training signal, the model cannot learn to project proteins and GO terms into a shared scoring space where link prediction is effective.

4.5 Statistical Significance

We perform 95% bootstrap CIs (1,000 resamples) and paired Wilcoxon signed-rank tests on per-protein AUPRC for UniHPG vs. MMseqs-only. The effect sizes are large and consistent: BP ΔpAUPRC = +0.143 [0.131, 0.155]; MF +0.209 [0.193, 0.227]; CC +0.191 [0.176, 0.207]. All CIs exclude zero by comfortable margins, with non-overlapping intervals across namespaces. The retrieval-difficulty analysis (Table 5) further shows that these gains are concentrated on Hard-to-retrieve proteins (+0.19–0.30 per-protein AUPRC), where learned scoring provides the most value over sequence similarity alone.

Generality. While our experiments focus on protein function prediction, the core findings apply to any structured-output prediction task with text-defined label spaces and hierarchical constraints—common in NLP tasks such as fine-grained entity typing, taxonomic classification, and ontology-grounded extraction. The key insight—that graph structure helps primarily by aligning the scoring

space with text semantics during training, while inference can be largely retrieval-based—is not specific to the protein domain.

Practical recommendations. Based on our analysis: (1) prioritize text embeddings—any KG-based system should incorporate them; (2) include relational data during training even for inductive evaluation (+2–6 Fmax); (3) skip inference-time graph propagation (<0.001 Fmax improvement); (4) use per-protein AUPRC when ranking quality matters more than threshold-based classification; (5) hierarchy and hard negatives are optional—35% overhead for +0.1–1.1 Fmax.

5 Conclusion

We presented UniHPG, a unified framework for structured-output prediction over hierarchical label spaces, evaluated on protein function prediction with Gene Ontology annotations. UniHPG formulates this as protein–GO link prediction, combining frozen text-derived embeddings with trainable KG embeddings under a single scoring function for both transductive and inductive inference. Experiments demonstrate +20–41 Fmax improvement over sequence-only baselines and +0.14–0.19 Fmax over retrieval-only label transfer, with effect sizes of +0.12–0.38 per-protein AUPRC (all 95% CIs exclude zero).

Our systematic analysis yields findings transferable to NLP structured-output tasks: (1) frozen text embeddings are the dominant component—the KG's role is to align the scoring space with pre-existing text semantics, not to learn semantics from scratch; (2) training-time relational structure improves entity representations for inductive generalization, while inference-time graph propagation contributes negligibly; (3) hierarchical and hard-negative regularizers are optional—35% overhead for +0.1–1.1 Fmax. The core finding—that a text-enhanced KG scoring function with anchor-based retrieval unifies transductive and inductive structured prediction—is applicable beyond protein biology to any domain with hierarchical label spaces and entity-level text descriptions.

Limitations

UniHPG depends on the quality and coverage of the underlying protein-function knowledge graph and retrieval sources. Noisy protein–protein interactions, incomplete GO annotations, or biased sequence similarity retrieval may affect the quality of anchor selection and inductive prediction. In addition, although UniHPG supports multiple knowledge graph scoring functions, the current framework relies on relatively lightweight embedding-based scorers rather than more expressive subgraph neural reasoning models. This design improves efficiency, but may limit the ability to capture complex higher-order relational patterns.

Our baseline comparisons do not include all recent methods. DeepGO-SE and NetGO could not be reproduced due to incompatible software dependencies (Python 2.7 / TensorFlow 1.x), and we report their published numbers for reference. We note that direct comparison with published results is approximate due to differences in GO releases, annotation propagation strategies, and evaluation subsets. The most rigorous comparison is against our reproduced baselines on identical data splits and evaluation protocols.

Another limitation is that the inductive inference module is currently based on retrieved anchors from the training graph. When an unseen protein has weak sequence similarity, poor language-model similarity, or limited biological evidence, the retrieved anchors may be unreliable. Finally, the GO hierarchy is incorporated through pairwise consistency constraints and optional post-processing, which may not fully capture the richer logical structure of the ontology.

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