Small, Open-Source Text-Embedding Models as Substitutes to OpenAI Models for Gene Analysis

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Abstract

While foundation transformer-based models developed for gene expression data analysis
can be costly to train and operate, a recent approach known as GenePT offers a low-cost
and highly efficient alternative. GenePT utilizes OpenAl's text-embedding function to encode background information, which is in textual form, about genes. However, the closedsource, online nature of OpenAl's text-embedding service raises concerns regarding data
privacy, among other issues. In this paper, we explore the possibility of replacing OpenAl's models with open-source transformer-based text-embedding models. We identified
ten models from Hugging Face that are small in size, easy to install, and light in computation. Across all four gene classification tasks we considered, some of these models have
outperformed OpenAl's, demonstrating their potential as viable, or even superior, alternatives. Additionally, we find that fine-tuning these models often does not lead to significant
improvements in performance.

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Introduction

The integration of large language models (LLMs), particularly transformer models [1], into gene-expression data analysis has generated substantial interest due to their improved predictive capabilities across various applications (see, e.g., [2, 3, 4, 5, 6, 7, 8] for a review). Foundation models like scBERT [9], Geneformer [10], scGPT [11], and scFoundation [12] are trained on extensive collections of single-cell RNA-seq data that include thousands of datasets and millions of cells. This training process is designed to capture intricate information about genes and their interactions. Subsequently, these models are fine-tuned on much smaller, user-specific datasets tailored to specific applications. However, the development of foundation models from scratch necessitates significant resources. The extensive data collection and computational demands often make this process prohibitively expensive for most research groups. Additionally, deploying and fine-tuning these models for personalized applications presents challenges related to hardware requirements, software compatibility, and programming expertise [13].

The recently developed GenePT [14] introduces an innovative approach that eliminates the
necessity of training foundation models from scratch. Utilizing OpenAI's text-embedding
function, this method transforms standard NCBI gene descriptions [15] into embeddings—dense
numeric vectors that effectively encapsulate the textual content [16]. These embeddings
comprehensively capture gene functions and their interactions as detailed in NCBI descriptions, offering a novel way to summarize and utilize existing knowledge about genes. These
embeddings are directly employed as inputs for various machine learning methods, such as
logistic regression and random forests, across diverse applications, such as classifying genes
into drug-sensitive or drug-insensitive categories. The GenePT approach has been shown
to achieve accuracy comparable to, or even surpassing, that of gene-expression foundation
models in various gene-classification tasks [14].

The advantages of the GenePT approach are significant. It leverages OpenAI's publicly ac-

cessible text-embedding function, eliminating the need for resource-intensive training of

gene-expression foundation models. Additionally, this method is highly generalizable and can be extended to numerous other applications; OpenAI's tool is capable of embedding descriptions of various biological entities, not limited to genes. Consequently, this approach is poised for broad adoption in the near future. Indeed, text-embedding plays a crucial role in natural language processing, where it is widely used in key applications such as text retrieval and translation, among others (see, e.g., [17] for a review).

However, relying on OpenAI's text-embedding can also impose limitations on GenePT's applicability. OpenAI's embedding is an online service that requires users to send text to the OpenAI server and retrieve the embeddings from it. This reliance not only raises concerns about internet connectivity and security but also, and more critically, about the privacy of the uploaded text. While privacy might not be a significant concern for NCBI's descriptions of genes, it becomes crucial if researchers wish to include their own insights, research results, or descriptions of other entities that are intended to remain confidential. The privacy issues associated with online LLMs have gained significant attention (see, e.g., [18, 19]); a recent study [20] reports that "all the methods leak query data," and concludes that "to achieve truly privacy-preserving LLM adaptations that yield high performance and more privacy at lower costs, taking into account current methods and models, one should use 62 open LLMs." Additionally, using an online service raises other potential concerns, such as 63 the reproducibility of results [21]. Furthermore, OpenAI charges a per-token fee for text embedding. 65

In this paper, we aim to address these limitations by replacing OpenAl's service with opensource, transformer-based text-embedding models that can be installed and run locally. To
ensure manageability for regular users with limited computational resources, we limit the
size of these models to less than 100 million parameters. We refer to these as "small LLMs,"
or S-LLMs for short. It is important to note that S-LLMs are text-embedding models designed
to convert natural-language text into embeddings, and they are not the gene-expression
foundation models discussed earlier. We will test these S-LLMs across the four gene-level
applications discussed in the GenePT paper to determine if they perform comparably to

GenePT's approach, which relies on OpenAI's embedding model. Specifically, we will employ

logistic regression or random forest on the embeddings generated by S-LLMs or OpenAI's

model, and compare the accuracy of the predictions.

In the broader context of natural language processing, the performance of various embed-

ding tools has been systematically assessed through the Massive Text Embedding Benchmark

(MTEB) [22], which includes 58 datasets across 112 languages from eight embedding tasks,

such as document classification, clustering, and retrieval. On average across these datasets,

OpenAI's embedding tool outperforms most open-source alternatives. However, some open-

source models can perform just as well, or even better than, OpenAI's tools in specific tasks.

Therefore, it will be interesting to see whether the S-LLMs we have selected can match the

performance of OpenAI's embeddings in gene analysis.

If the S-LLMs cannot compete, there is a potential remedy: fine-tuning the S-LLMs. Specifically, instead of using the static text embeddings provided by the S-LLM as inputs for a separate classifier such as logistic regression or random forest, we could integrate an additional layer into the S-LLM, transforming it into a combined embedding and classification system. This integrated system would then be fine-tuned as a whole, allowing the embeddings to evolve during training. It is important to note that this fine-tuning process involves only minor adjustments to the weights in the pre-trained transformer model, resulting in a computational burden significantly lower than that of training an LLM from scratch. It is also worth noting that the capability to fine-tune is not available with OpenAI's embedding function, which is closed-source online service.

Results

Settings of the comparisons

Our comparisons focus on the four gene-level tasks considered in the GenePT paper [23]. For the remainder of this paper, we will refer to these tasks as Task 1 through Task 4, respectively.

Each of these tasks is a two-class classification problem, classifying genes into categories such as dosage-sensitive or dosage-insensitive transcription factors. Table 1 details the two classes and the sample size for each class. These datasets were curated, pre-processed, and made available by [10].

For the gene descriptions, we utilized all human genes from the genome assembly version GRCh38.111, obtained from the Ensembl database [24]. Following the procedures outlined in the GenePT paper [23], we extracted descriptions from the summary section of the NCBI Gene database, after removing hyperlinks and date information. These cleaned descriptions were then used as input to generate text embeddings.

Hugging Face [25] offers a wide range of publicly available transformer-based text embedding models. These models vary greatly in size, measured by the number of parameters,
and are categorized into five groups: fewer than 100 million, 100 million to 250 million,
billion to 500 million, 500 million to 1 billion, and over 1 billion. Models on Hugging
Face are systematically evaluated using the MTEB.

We selected ten models with fewer than 100 million parameters that ranked highest on the
Hugging Face Leaderboard (https://huggingface.co/spaces/mteb/leaderboard_legacy,
as of December 9th, 2024) for the "classification" embedding task in English. The models chosen include GIST-small-Embedding-v0 [26], NoInstruct-small-Embedding-v0 [27],
stella-base-en-v2 [28], bge-small-en-v1.5 [29], e5-small-v2 [30], GIST-all-MiniLM-L6-v2
[26], gte-small [31], MedEmbed-small-v0.1 [32], e5-small [30], and gte-tiny [33]. A summary of these ten models is presented in Table 2, which includes the number of parameters,

memory usage, average performance on MTEB classification datasets, and the embedding dimension each model produces. Notably, all of these S-LLMs contain no more than 55 million parameters. For context, OpenAI's GPT-3 model contains 175 billion parameters—over a thousand times larger than our S-LLMs—and GPT-4 has 1.76 trillion parameters. These S-LLMs require a minimal amount of memory and can be easily installed and operated on a regular laptop computer. Except for stella-base-en-v2, which produces 768-dimensional embeddings, all other S-LLMs generate 384-dimensional embeddings.

For GenePT, we downloaded the gene text embeddings from its Zenodo repository. These embeddings were generated using OpenAI's text-embedding-ada-002 model [34], with each embedding having a dimension of 1536. This dimensionality is significantly higher than that of the embeddings produced by the S-LLMs.

Logistic regression and random forests on S-LLM embeddings

For each of the four two-class classification tasks, we supplied gene embeddings generated by the ten S-LLMs, as well as those from OpenAI, to a classifier. We measured performance using the area under the ROC curve (AUC), which ranges from 0 to 1. Higher AUC values indicate better performance.

Following the GenePT paper, we chose logistic regression and random forest as our classifiers. These are implemented using the LogisticRegression() function from the sklearn.linear_model Python package and the RandomForestClassifier() function from the sklearn.ensemble Python package, respectively. We used the default hyperparameter settings for both functions without any further tuning.

For each task, we randomly split the data into training and testing sets, comprising 90% and 10% of the total data, respectively. The classifier—either logistic regression or random forest—is trained on the training data and then tested on the test data. To minimize the randomness in the evaluation, this entire procedure (random splitting, training, and testing)

is repeated 10 times. Tables 3 and 4 present the mean AUC scores from these 10 repetitions, as well as the overall mean AUC scores across the four tasks. To aid in comparison, the tables also include the ranking (from highest to lowest AUC) of the embedding methods for each task and a final column that ranks the methods based on the overall mean AUC scores across all tasks, where a lower rank number indicates better performance.

Surprisingly, OpenAI's embedding does not emerge as the top performer on any of the four tasks, regardless of whether logistic regression or random forest is employed. With logistic regression, OpenAI's embedding ranks 3rd, 11th, 6th, and 11th, with an overall ranking of 7th. Moreover, two of the S-LLMs we evaluated, NoInstruct-small-Embedding-v0 and e5-small, consistently outperformed OpenAI's embedding across all four tasks. Similar results are observed with random forest: OpenAI's embedding ranks 10th, 11th, 5th, and 9th, with an overall ranking of 10th. Additionally, three S-LLMs, NoInstruct-small-Embedding-v0, e5-small, and stella-base-en-v2, consistently performed better across all tasks.

Logistic regression and random forests on S-LLM embeddings, with hyperparameter tuning

In the aforementioned analysis, we employed logistic regression and random forest classifiers without tuning their hyperparameters. For logistic regression, this involved using an ℓ_2 penalty with a strength of 1, specified by setting penalty = '12' and C = 1.0 in the LogisticRegression() function. For random forest, we used a default configuration of 100 unpruned trees, set by n_estimators = 100 and max_depth = None in the RandomForestClassifier() function.

The sub-par performance of OpenAI's embedding observed in the previous section may be attributed to the lack of hyperparameter tuning. Therefore, in this section, we will tune these hyperparameters to see if the conclusions change. For logistic regression, we explored all combinations of penalty = ['11', '12'] and C = [0.01, 0.1, 1, 10, 100]. For random forest, we considered all combinations of n_estimators = [25, 50, 100, 200, 400]and max_depth = [None, 10, 20, 30].

Once again, we randomly divided the data for each task into training and test datasets, consisting of 90% and 10% of all samples, respectively. We employed five-fold cross-validation on the training data to determine the optimal hyperparameters. These selected hyperparameters were then used to train a classifier on the entire training dataset. The classifier was subsequently tested on the test data, which had been set aside during the hyperparameter selection and training phases. This entire process was repeated ten times to minimize variability, and the mean AUC values were calculated and reported. The results for logistic regression and random forest are presented in Tables 5 and 6, respectively.

Despite the adjustments, OpenAI's embedding still does not outperform those from the S-LLMs, as detailed in the tables. It fails to achieve the highest AUC value in any of the four tasks, and on average across these tasks, it is ranked 10th and 8th out of 11 embeddings when using logistic regression and random forest, respectively. This means that for each task, at least one S-LLM embedding performs better than OpenAI's. On average, nine out of ten S-LLMs outperform OpenAI when using logistic regression, and seven do so when using random forest.

Comparing Table 5 with Table 3, we observe that hyperparameter tuning enhances the AUC 187 values for nine out of ten S-LLMs using logistic regression, with an average improvement 188 of 0.011. In contrast, when using random forest, as shown by comparing Table 6 with 189 Table 4, tuning improves AUC values for only four S-LLMs, with an average decrease of 190 0.003. This suggests that tuning the hyperparameters of the classifiers does not consistently 191 enhance performance. This phenomenon is likely due to the small sample sizes of our tasks, 192 coupled with high-dimensional input (the embeddings). For instance, in tasks 1 and 4, 193 there are fewer than 50 samples in the minor class. This limited sample size, along with the 194 high dimensionality of the input embeddings, contributes to significant randomness in the 195 selection of optimal hyperparameters and high variance in the test AUC, especially for more

complicated methods like random forest.

S-LLM embeddings with fine-tuning

So far, we have demonstrated that the embeddings produced by S-LLMs often perform as well as, or even better than, those generated by OpenAI in our four tasks. These unexpected results render our initial plan to fine-tune S-LLMs to catch up with OpenAI's performance unnecessary. However, we still wish to explore the fine-tuning of these S-LLMs in this section, with the aim of determining whether fine-tuning can further enhance their performance and thereby extend their advantage over OpenAI.

This fine-tuning approach differs significantly from the methods considered in previous ses-205 sions. Previously, all methods involved two independent steps. Initially, an LLM (either 206 OpenAI's or an S-LLM) would generate an embedding from text. Subsequently, a classifier 207 (logistic regression or random forest) would use this embedding to predict the class label. 208 These two steps were independent, meaning the embeddings generated in the first step did 209 not change during the classifier's training. Conversely, the fine-tuning approach employs a 210 single integrated model. It involves adding a fully connected layer to the LLM, effectively 211 transforming the LLM from an embedding generator into a classification model. This sin-212 gle deep-neural-network-based model is trained by taking NCBI gene descriptions as input 213 and outputting the predicted class labels directly. During training, both the weights in the 214 LLM and in the final layer are adjusted. Thus, the embeddings from the LLM are tuned specifically for the classification task, potentially enhancing classification accuracy. 216

For fine-tuning, we randomly divided the data for each task into training, evaluation, and test sets in proportions of 80%, 10%, and 10%, respectively. The fine-tuning process consisted of two stages. In the first stage, the model was trained on the training data and evaluated on the evaluation data to determine the optimal training hyperparameters. In the second stage, the model, configured with the best hyperparameters, was further trained

on a combined set of the training and evaluation datasets, which accounted for 90% of all data, for several additional epochs to maximize the use of available information. Finally, this model was applied to the test data, which had been isolated from all fine-tuning and training activities, to compute the AUC score. This entire procedure was repeated ten times, and the mean AUC values were reported.

In the first stage of fine-tuning, we initialized the model with the following parameters:

learning_rate = 1e-5, num_train_epochs = 20, max_grad_norm = 0.7, warmup_ratio

= 0.1, and weight_decay = 0.2, with other parameters set to their default values. To pre
vent overfitting, we set up the early stopping (EarlyStoppingCallback(early_stopping_patience

= 5)) and the ReduceLROnPlateau scheduler (factor = 0.8, patience = 2) to gradually

decrease the learning rate. In the second stage, the parameters were adjusted to learning_rate

= 1e-6, num_train_epochs = 10, max_grad_norm = 0.7, and weight_decay = 0.2, with

other settings remaining as default.

The computation was conducted on a single NVIDIA TITAN Xp GPU, an older model released in April 2017. The total time spent on the entire fine-tuning process, including data loading, model loading, and both stages of fine-tuning, is detailed in Table 7. For the two models with 23 million parameters, fine-tuning all four tasks takes about 20 minutes. Models with 33 million parameters take no more than 40 minutes, while the largest model, stella-base-en-v2, which has 55 million parameters, requires approximately one and a half hours. This demonstrates that the computational load is generally quite manageable, even on dated hardware.

Table 8 presents the results from fine-tuning the ten S-LLMs. Unexpectedly, compared to the results in previous tables, whether using logistic regression or random forest, with or without hyperparameter tuning, fine-tuning generally does not yield noticeable improvements in classification accuracy, if any. It is worth noting that we have tried more settings of training parameters than what we have described above. Specifically, we have tried learning_rate = [1e-6, 5e-6, 1e-5, 5e-5, 1e-4], weight_decay = [0.0, 0.1,

0.2, 0.3, 0.4], warmup_ratio = [0.00, 0.05, 0.10, 0.15, 0.20], max_grad_norm = [0.6, 0.7, 0.8, 0.9, 1.0], and num_train_epochs = [5, 10, 15, 20, 25], and have not obtained results that are significantly better than those presented in Table 8.

Conclusions and Discussion

Recently, LLMs have been developed and utilized for describing and analyzing gene-expression data. While training a gene-expression foundation model can be labor-intensive and compu-254 tationally prohibitive for most labs, GenePT's approach of using gene embeddings generated 255 by OpenAI's text-embedding tools offers an affordable and efficient alternative. However, 256 privacy concerns and other potential issues associated with the closed-source, online service 257 nature of OpenAI's embeddings may hinder the widespread adoption of GenePT's approach. 258 In this paper, we have explored the possibility of using open-source S-LLMs, which can be 259 readily installed and run locally, as alternatives to OpenAI's text-embedding. Our evaluation 260 has focused on the four gene-level tasks considered in the GenePT paper. 261

While the expectation was that the embeddings from these S-LLMs could not compete with those from OpenAI, and that fine-tuning these S-LLMs might be necessary, the observations have been surprisingly different. We have found that even without fine-tuning, there are S-LLMs that outperform OpenAI on every task. Some S-LLMs even surpass OpenAI across all four tasks. This holds true regardless of whether logistic regression or random forest is used, and irrespective of whether the hyperparameters in the classifier are carefully tuned. This suggests that S-LLMs can be a legitimate alternative to OpenAI's embedding tool for applications similar to those we have considered.

Second, we have found that although fine-tuning S-LLMs can be readily performed, it did not result in enhanced performance. This outcome is not entirely surprising. In fact, previous literature in more general settings of large language models, unrelated to genetics, has reported that fine-tuning pretrained LLMs is often brittle [35] and prone to degraded performance under small training sample sizes [36]. While our research does not preclude the
possibility that fine-tuning might improve the performance of S-LLMs for gene analysis, and
further investigation into this matter is certainly valuable, our findings suggest that simple,
straightforward fine-tuning of S-LLMs may not consistently enhance their performance for
gene analysis with small sample sizes.

Third, we have discovered that hyperparameter tuning slightly improves the performance 279 of logistic regression but does not enhance the performance of random forest. Thus, using 280 the default settings of these classifiers in Python functions can be a practical and reliable 281 choice. Additionally, when comparing the AUC values generated by logistic regression with 282 those produced by random forest, we observe that random forest often does not outperform 283 logistic regression, despite its higher complexity and capability to capture non-linear relationships between features. These somewhat counterintuitive findings may be attributed to a couple of factors. First, the datasets we analyzed are characterized by high dimensions 286 and small sample sizes, which makes reliable model selection very challenging. Second, 287 the correlations or associations between the dimensions of the embeddings remain an open area of research, and it is still unclear whether random forest can effectively capture such 289 relationships. Overall, using gene-description embeddings for gene analysis is a recent de-290 velopment. Further advancements in this field may hinge on a deeper understanding of 291 these high-dimensional embeddings and how to utilize them most effectively. Additionally, 292 exploring effective dimensionality reduction of these high-dimensional embeddings could 293 also be a meaningful direction for future research. 294

Our current work has a limited scope, focusing primarily on gene-level analysis. GenePT also has potential applications at the cell level, such as cell-type clustering. As highlighted by [37], the question of how to efficiently combine gene embeddings with gene expression data to enhance the performance of gene-level tasks remains largely unanswered. Extending our analysis to cell-level tasks represents a challenging but potentially valuable future direction.

Data availability

All datasets used in the study have been published and cited in the main body.

Code availability

The source code is available at https://github.com/RavenGan/FinetuneEmbed.

Conflicts on Interests

None.

6 Acknowledgment

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References

- [1] Ashish Vaswani, Noam Shazeer, Niki Parmar, Jakob Uszkoreit, Llion Jones, Aidan N
 Gomez, Łukasz Kaiser, and Illia Polosukhin. Attention is all you need. *Advances in*neural information processing systems, 30, 2017.
- [2] Artur Szałata, Karin Hrovatin, Sören Becker, Alejandro Tejada-Lapuerta, Haotian Cui,
 Bo Wang, and Fabian J Theis. Transformers in single-cell omics: a review and new
 perspectives. *Nature methods*, 21(8):1430–1443, 2024.

- [3] Mohammad Lotfollahi. Toward learning a foundational representation of cells and genes. *nature methods*, 21(8):1416–1417, 2024.
- ³¹⁸ [4] Ziyu Chen, Lin Wei, and Ge Gao. Foundation models for bioinformatics. *Quantitative*³¹⁹ *Biology*, 12(4):339–344, 2024.
- [5] Tianyu Liu, Kexing Li, Yuge Wang, Hongyu Li, and Hongyu Zhao. Evaluating the utilities of foundation models in single-cell data analysis. *bioRxiv*, pages 2023–09, 2024.
- [6] Elana Simon, Kyle Swanson, and James Zou. Language models for biological research:
 a primer. *Nature Methods*, 21(8):1422–1429, 2024.
- Wasif Khan, Seowung Leem, Kyle B See, Joshua K Wong, Shaoting Zhang, and Ruogu Fang. A comprehensive survey of foundation models in medicine. *IEEE Reviews in Biomedical Engineering*, 2025.
- ³²⁸ [8] Wei Ruan, Yanjun Lyu, Jing Zhang, Jiazhang Cai, Peng Shu, Yang Ge, Yao Lu, Shang Gao, Yue Wang, Peilong Wang, et al. Large language models for bioinformatics. *arXiv* preprint arXiv:2501.06271, 2025.
- [9] Fan Yang, Wenchuan Wang, Fang Wang, Yuan Fang, Duyu Tang, Junzhou Huang, Hui
 Lu, and Jianhua Yao. scbert as a large-scale pretrained deep language model for cell
 type annotation of single-cell rna-seq data. *Nature Machine Intelligence*, 4(10):852–
 866, 2022.
- In Christina V Theodoris, Ling Xiao, Anant Chopra, Mark D Chaffin, Zeina R Al Sayed,
 Matthew C Hill, Helene Mantineo, Elizabeth M Brydon, Zexian Zeng, X Shirley
 Liu, et al. Transfer learning enables predictions in network biology. *Nature*,
 618(7965):616–624, 2023.
- Haotian Cui, Chloe Wang, Hassaan Maan, Kuan Pang, Fengning Luo, Nan Duan, and
 Bo Wang. scgpt: toward building a foundation model for single-cell multi-omics using
 generative ai. *Nature Methods*, pages 1–11, 2024.

- [12] Minsheng Hao, Jing Gong, Xin Zeng, Chiming Liu, Yucheng Guo, Xingyi Cheng,
 Taifeng Wang, Jianzhu Ma, Xuegong Zhang, and Le Song. Large-scale foundation
 model on single-cell transcriptomics. *Nature Methods*, pages 1–11, 2024.
- Rishi Bommasani, Sayash Kapoor, Kevin Klyman, Shayne Longpre, Ashwin Ramaswami, Daniel Zhang, Marietje Schaake, Daniel E Ho, Arvind Narayanan, and Percy Liang. Considerations for governing open foundation models. *Science*, 386(6718):151–153, 2024.
- yiqun Chen and James Zou. Genept: A simple but effective foundation model for genes and cells built from chatgpt. *bioRxiv*, 2023.
- [15] Garth R Brown, Vichet Hem, Kenneth S Katz, Michael Ovetsky, Craig Wallin, Olga
 Ermolaeva, Igor Tolstoy, Tatiana Tatusova, Kim D Pruitt, Donna R Maglott, et al. Gene:
 a gene-centered information resource at ncbi. *Nucleic acids research*, 43(D1):D36–D42,
 2015.
- openAI. New embedding models and api updates. https://openai.com/blog/new-embedding-models-and-api-updates, 2024. Accessed: 2024-08-08.
- Deepak Suresh Asudani, Naresh Kumar Nagwani, and Pradeep Singh. Impact of word embedding models on text analytics in deep learning environment: a review. *Artificial intelligence review*, 56(9):10345–10425, 2023.
- [18] Yifan Yao, Jinhao Duan, Kaidi Xu, Yuanfang Cai, Zhibo Sun, and Yue Zhang. A survey
 on large language model (llm) security and privacy: The good, the bad, and the ugly.
 High-Confidence Computing, page 100211, 2024.
- Fangzhou Wu, Ning Zhang, Somesh Jha, Patrick McDaniel, and Chaowei Xiao. A new era in llm security: Exploring security concerns in real-world llm-based systems. *arXiv* preprint arXiv:2402.18649, 2024.
- [20] Vincent Hanke, Tom Blanchard, Franziska Boenisch, Iyiola Emmanuel Olatunji,
 Michael Backes, and Adam Dziedzic. Open llms are necessary for current private adap-

- tations and outperform their closed alternatives. *arXiv preprint arXiv:2411.05818*, 2024.
- Matthew Hutson. Forget chatgpt: why researchers now run small ais on their laptops.

 Nature, 633(8030):728–729, 2024.
- ³⁷² [22] Niklas Muennighoff, Nouamane Tazi, Loïc Magne, and Nils Reimers. Mteb: Massive text embedding benchmark. *arXiv preprint arXiv:2210.07316*, 2022.
- ³⁷⁴ [23] Yiqun Chen and James Zou. Simple and effective embedding model for single-cell biology built from chatgpt. *Nature Biomedical Engineering*, pages 1–11, 2024.
- Peter W Harrison, M Ridwan Amode, Olanrewaju Austine-Orimoloye, Andrey G Azov,
 Matthieu Barba, If Barnes, Arne Becker, Ruth Bennett, Andrew Berry, Jyothish Bhai,
 et al. Ensembl 2024. *Nucleic acids research*, 52(D1):D891–D899, 2024.
- ₃₇₉ [25] Hugging Face. Hugging face the ai community building the future.
- ³⁸⁰ [26] Aivin V. Solatorio. Gistembed: Guided in-sample selection of training negatives for text embedding fine-tuning. *arXiv preprint arXiv:2402.16829*, 2024.
- ³⁸² [27] Aivin V. Solatorio. Noinstruct-small-embedding-v0, 2023. Accessed: 2025-01-07.
- ³⁸³ [28] Infgrad. stella-base-en-v2, 2023. Accessed: 2025-01-07.
- ³⁸⁴ [29] Shitao Xiao, Zheng Liu, Peitian Zhang, and Niklas Muennighoff. C-pack: Packaged resources to advance general chinese embedding, 2023.
- [30] Liang Wang, Nan Yang, Xiaolong Huang, Binxing Jiao, Linjun Yang, Daxin Jiang, Rangan Majumder, and Furu Wei. Text embeddings by weakly-supervised contrastive pretraining. arXiv preprint arXiv:2212.03533, 2022.
- ³⁸⁹ [31] Zehan Li, Xin Zhang, Yanzhao Zhang, Dingkun Long, Pengjun Xie, and Meishan Zhang. Towards general text embeddings with multi-stage contrastive learning. *arXiv* preprint arXiv:2308.03281, 2023.

- [32] Abhinand Balachandran. Medembed: Medical-focused embedding models, 2024.
- ³⁹³ [33] TaylorAI. gte-tiny, 2023. Accessed: 2025-01-07.
- ³⁹⁴ [34] OpenAI. text-embedding-ada-002, 2022. Accessed: 2025-01-07.
- Jesse Dodge, Gabriel Ilharco, Roy Schwartz, Ali Farhadi, Hannaneh Hajishirzi, and Noah Smith. Fine-tuning pretrained language models: Weight initializations, data orders, and early stopping. *arXiv preprint arXiv:2002.06305*, 2020.
- ³⁹⁸ [36] Cheolhyoung Lee, Kyunghyun Cho, and Wanmo Kang. Mixout: Effective reg³⁹⁹ ularization to finetune large-scale pretrained language models. *arXiv* preprint
 ⁴⁰⁰ *arXiv*:1909.11299, 2019.
- Fangfang Guo, Dailin Gan, and Jun Li. Cell-to-cell distance that combines gene expression and gene embeddings. *Computational and structural biotechnology journal*, 23:3929–3937, 2024.

Tables

	Class 1	Sample Size in Class 1	Class 2	Sample Size in Class 2
Task 1	Long-range transcription factors	46	Short-range transcription factors	130
Task 2	Dosage-sensitive transcription factors	122	Dosage-insensitive transcription factors	368
Task 3	Bivalent genes	107	Lys4-only-methylated genes	80
Task 4	Bivalent genes	107	Non-methylated genes	42

Table 1: Datasets and the number of samples in each class.

Models	Model parameters (million)	Memory Usage (GB)	MTEB Average Performance	Embedding dimensions
GIST-small-Embedding-v0	33	0.12	76.1	384
NoInstruct-small-Embedding-v0	33	0.12	76.0	384
stella-base-en-v2	55	0.20	75.3	768
e5-small-v2	33	0.12	72.9	384
GIST-all-MiniLM-L6-v2	23	0.08	72.7	384
gte-small	33	0.12	72.3	384
bge-small-en-v1.5	33	0.12	72.2	384
MedEmbed-small-v0	33	0.12	71.8	384
gte-tiny	23	0.08	70.4	384
e5-small	33	0.12	68.1	384

Table 2: Information about the ten S-LLMs we use; more detailed information for each model can be found on the MTEB Hugging Face Leaderboard (https://huggingface.co/spaces/mteb/leaderboard_legacy).

Embedding	AUC Rank on Task 1	AUC Rank on Task 2	AUC Rank on Task 3	AUC Rank on Task 4	Mean AUC	Rank of Mean AUC
OpenAI	0.712 3	0.863 11	0.931 6	0.875 11	0.845	7
GIST-small-Embedding-v0	0.641 7	0.887 6	0.940 1.5	0.917 3	0.846	6
NoInstruct-small-Embedding-v0	0.728 2	0.908 1	0.935 3	0.907 8	0.870	1
stella-base-en-v2	0.702 5	0.885 8	0.934 4	0.927 1	0.862	4
e5-small-v2	0.692 6	0.879 9	0.915 10	0.922 2	0.852	5
GIST-all-MiniLM-L6-v2	0.608 11	0.887 5	0.940 1.5	0.912 5.5	0.837	8
gte-small	0.629 8.5	0.866 10	0.914 11	0.915 4	0.831	11
bge-small-en-v1.5	0.629 8.5	0.886 7	0.924 9	0.905 9	0.836	9
MedEmbed-small-v0	0.612 10	0.892 4	0.925 8	0.910 7	0.835	10
gte-tiny	0.706 4	0.904 2	0.930 7	0.912 5.5	0.863	3
e5-small	0.732 1	0.898 3	0.932 5	0.892 10	0.864	2

Table 3: Performance of logistic regression with default hyperparameter settings on different embeddings.

Embedding	AUC Rank on Task 1	AUC Rank on Task 2	AUC Rank on Task 3	AUC Rank on Task 4	Mean AUC	Rank of Mean AUC
OpenAI	0.625 10	0.883 11	0.924 5	0.882 9	0.829	10
GIST-small-Embedding-v0	0.653 6	0.903 6	0.903 9	0.894 5	0.838	8
NoInstruct-small-Embedding-v0	0.666 4	0.906 4.5	0.941 3	0.897 3	0.853	3
stella-base-en-v2	0.784 1	0.902 8	0.954 1	0.905 2	0.886	1
e5-small-v2	0.736 2	0.894 10	0.900 10	0.858 11	0.847	4
GIST-all-MiniLM-L6-v2	0.607 11	0.895 9	0.942 2	0.864 10	0.827	11
gte-small	0.652 8	0.906 4.5	0.891 11	0.892 6	0.835	9
bge-small-en-v1.5	0.652 7	0.903 7	0.911 8	0.910 1	0.844	7
MedEmbed-small-v0	0.664 5	0.910 2	0.916 6.5	0.890 7	0.845	6
gte-tiny	0.730 3	0.907 3	0.916 6.5	0.887 8	0.860	2
e5-small	0.638 9	0.920 1	0.928 4	0.895 4	0.845	5

Table 4: Performance of random forest with default hyperparameter settings on different embeddings.

Embedding	AUC Rank on Task 1	AUC Rank on Task 2	AUC Rank on Task 3	AUC Rank on Task 4	Mean AUC	Rank of Mean AUC
OpenAI	0.674 10	0.891 11	0.934 3	0.875 11	0.843	10
GIST-small-Embedding-v0	0.731 3	0.897 10	0.934 3	0.903 6	0.866	4
NoInstruct-small-Embedding-v0	0.739 2	0.905 5	0.934 3	0.910 2	0.872	2
stella-base-en-v2	0.723 5	0.919 2	0.915 9	0.908 3.5	0.866	3
e5-small-v2	0.689 9	0.912 4	0.921 6	0.918 1	0.860	6
GIST-all-MiniLM-L6-v2	0.622 11	0.917 3	0.943 1	0.888 8	0.842	11
gte-small	0.703 7	0.903 7	0.905 11	0.908 3.5	0.855	8
bge-small-en-v1.5	0.700 8	0.900 9	0.911 10	0.885 9	0.849	9
MedEmbed-small-v0	0.708 6	0.901 8	0.921 6	0.893 7	0.856	7
gte-tiny	0.725 4	0.904 6	0.919 8	0.905 5	0.863	5
e5-small	0.772 1	0.928 1	0.921 6	0.883 10	0.876	1

Table 5: Performance of logistic regression with hyperparameter tuning on different embeddings.

Embedding	AUC Rank on Task 1	AUC Rank on Task 2	AUC Rank on Task 3	AUC Rank on Task 4	Mean AUC	Rank of Mean AUC
OpenAI	0.640 7.5	0.883 11	0.932 4	0.880 9	0.834	8
GIST-small-Embedding-v0	0.682 5	0.894 10	0.934 2.5	0.893 7.5	0.851	5
NoInstruct-small-Embedding-v0	0.657 6	0.911 2	0.914 7	0.894 6	0.844	7
stella-base-en-v2	0.685 4	0.908 4	0.938 1	0.900 5	0.858	3
e5-small-v2	0.740 1	0.909 3	0.908 8.5	0.876 10	0.858	2
GIST-all-MiniLM-L6-v2	0.534 11	0.900 9	0.926 6	0.871 11	0.808	11
gte-small	0.602 9	0.904 8	0.906 10	0.906 2.5	0.829	10
bge-small-en-v1.5	0.600 10	0.908 5	0.908 8.5	0.919 1	0.834	9
MedEmbed-small-v0	0.640 7.5	0.906 7	0.931 5	0.906 2.5	0.846	6
gte-tiny	0.719 2	0.908 6	0.904 11	0.893 7.5	0.856	4
e5-small	0.715 3	0.923 1	0.934 2.5	0.903 4	0.869	1

Table 6: Performance of random forest with hyperparameter tuning on different embeddings.

Models	Time on Task 1	Time on Task 2	Time on Task 3	Time on Task 4	Mean Time	Rank of Mean Time
GIST-small-Embedding-v0	33	36	32	30	32.8	6
NoInstruct-small-Embedding-v0	26	33	26	24	27.3	3
stella-base-en-v2	87	94	82	79	85.5	10
e5-small-v2	32	35	31	32	32.5	5
GIST-all-MiniLM-L6-v2	18	23	19	18	19.5	1
gte-small	36	43	37	32	37.0	8
bge-small-en-v1.5	30	38	34	31	33.3	7
MedEmbed-small-v0	37	44	37	39	39.3	9
gte-tiny	19	24	21	17	20.3	2
e5-small	26	31	29	25	27.8	4

Table 7: Computational time (in minutes) spent on fine-tuning S-LLMs under each task.

Embedding	AUC Rank on Task 1	AUC Rank on Task 2	AUC Rank on Task 3	AUC Rank on Task 4	Mean AUC	Rank of Mean AUC
GIST-small-Embedding-v0	0.602 4.5	0.880 6	0.924 1.5	0.905 3	0.828	3
NoInstruct-small-Embedding-v0	0.591 8	0.891 1	0.909 4	0.927 1	0.830	2
stella-base-en-v2	0.692 1	0.881 4.5	0.889 7	0.897 5	0.840	1
e5-small-v2	0.620 2.5	0.868 8.5	0.881 8.5	0.873 9.5	0.810	9.5
GIST-all-MiniLM-L6-v2	0.602 4.5	0.885 2	0.873 10	0.895 7	0.813	7
gte-small	0.600 6	0.882 3	0.906 5	0.897 5	0.821	4
bge-small-en-v1.5	0.577 9	0.871 7	0.924 1.5	0.885 8	0.814	6
MedEmbed-small-v0	0.561 10	0.881 4.5	0.920 3	0.912 2	0.819	5
gte-tiny	0.592 7	0.868 10	0.892 6	0.897 5	0.813	8
e5-small	0.620 2.5	0.868 8.5	0.881 8.5	0.873 9.5	0.810	9.5

Table 8: Performance of S-LLMs with fine tuning on different embeddings.