

Biology Instructions: A Dataset and Benchmark for Multi-Omics Sequence Understanding Capability of Large Language Models

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Abstract

Large language models (LLMs) have shown remarkable capabilities in general domains, but their application to multi-omics biology remains underexplored. To address this gap, we introduce Biology-Instructions, the first large-scale instruction-tuning dataset for multi-omics biological sequences, including DNA, RNA, proteins, and multi-molecules. This dataset bridges LLMs and complex biological sequence-related tasks, enhancing their versatility and reasoning while maintaining conversational fluency. We also highlight significant limitations of current state-of-the-art LLMs on multi-omics tasks without specialized training. To overcome this, we propose ChatMulti-Omics, a strong baseline with a novel three-stage training pipeline, demonstrating superior biological understanding through Biology-Instructions. Both resources are publicly available, paving the way for better integration of LLMs in multi-omics analysis. The Biology-Instructions is publicly available at [link](#).

1 Introduction

Understanding the complex activities across various omics in living organisms is of paramount importance. This includes studying DNA regulatory elements that control gene expression (Emilsson et al., 2008), RNA regulation (Mattick, 2004) that influences protein synthesis, and the functional properties of proteins themselves (Marcotte et al., 1999). These molecular processes critically affect the development of diseases and the synthesis of drugs within organisms. Recent BERT-like encoder-only models (Devlin, 2018) have achieved significant advances in natural language understanding tasks.

When applied to genome or protein understanding tasks, these models (Zhou et al., 2023; Rives et al., 2021) are capable of capturing complex intrinsic relationships within biological sequences, achieving high accuracy in tasks such as promoter

prediction. However, their reliance on specific classification or regression heads to predict a single task at a time limits their versatility, and their repeated fine-tuning sessions with different prediction heads to address multiple tasks further complicate the training, inference, and deployment processes.

In contrast, powerful general-purpose large language models (LLMs) such as GPT-4 (Achiam et al., 2023) and Gemini (Achiam et al., 2023; Team et al., 2023) based on vast amounts of natural language tasks and data that encompass the general knowledge system of humanity, have shown substantial potential in domain-specific tasks. These decoder-only models approach every task as a completion task through next-token prediction objective, and offer an alternative by integrating various biological sequence-related tasks using natural language as an intermediary while retaining conversational capabilities. Therefore, utilizing LLMs combined with unified training and dataset construction techniques can make it possible to replace BERT-like models with the complicated fine-tuning pipeline.

Recently, some studies have explored leveraging LLMs for tasks related to biological sequences through instruction tuning, such as ChatNT (Richard et al., 2024) and ProLlama (Lv et al., 2024). Although showing promising results, these models are trained on instruction-tuning datasets containing only basic language patterns, underutilizing the full linguistic capabilities of the original LLMs. Moreover, these models mainly focus on single-omics data for either protein or DNA, limiting their potential to provide important multi-omics understanding ability as a unified foundational language model. Inspired by multimodal LLMs like MiniGPT-4 (Zhu et al., 2023), we see an opportunity to extend this approach to biology. In biology, where molecular interactions are fundamentally grounded in the central dogma (Crick, 1970), integrating multi-omics data holds immense

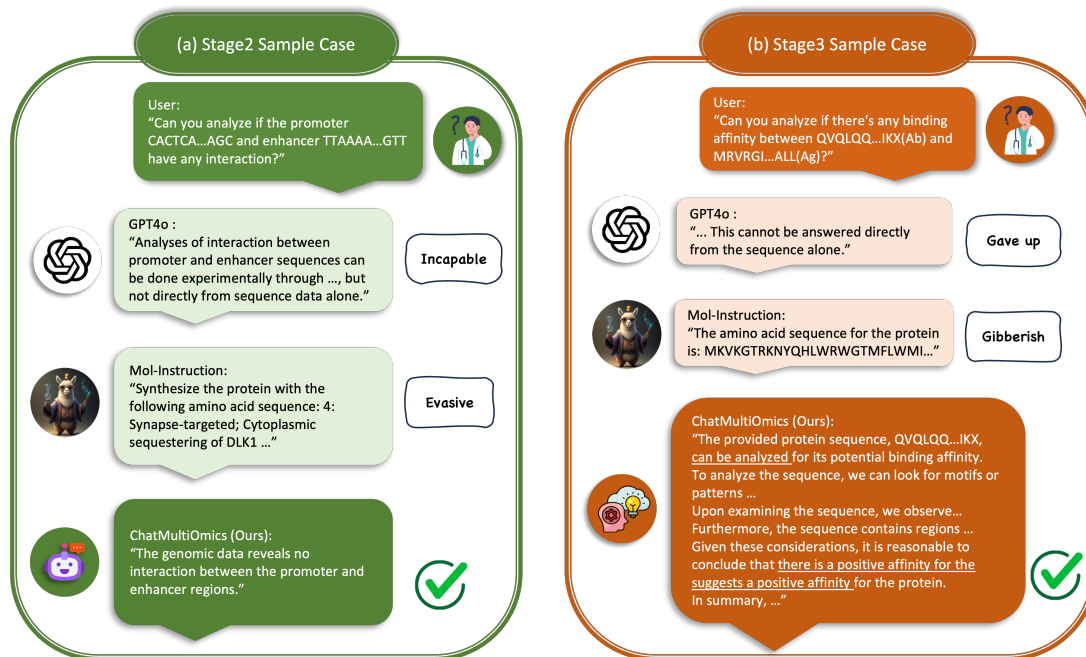


Figure 1: Comparative examples showcasing ChatMultiOmics performance against baseline models on multi-molecular tasks. (a) Enhancer-Promoter Interaction Prediction (Min et al., 2021) after stage2 training. (b) Antibody-Antigen Neutralization (AAN) (Zhang et al., 2022) after stage3 training. Note that AAN is not included in stage3 training, which showcases our model’s task generalization capability.

potential for generating mutually reinforcing insights.

Our study attempts to answer a key question: can instruction-tuned language models, proficient in understanding human language, also excel in understanding biological sequences to address biologically critical tasks? The motivation behind this inquiry lies in the intrinsic parallels between biological sequence data and human language—both are discrete, sequential, abundant, and rich in encoded information. These shared characteristics suggest that, with appropriate adaptation, instruction-tuned LLMs could unlock transformative capabilities in biology.

To properly investigate the gap between human language and biological sequences understanding, we introduce Biology-Instructions, the first large-scale, multi-omics biology sequence-related instruction-tuning benchmark supporting 21 distinct tasks. This benchmark covers DNA, RNA, proteins and multi-molecular prediction tasks for a comprehensive understanding of biology. With Biology-Instructions, we conduct a comprehensive evaluation of kinds of open-source and closed-source LLMs, and reveal that most models including the state-of-the-art GPT-4o, perform at near-random levels on biological sequence-related understanding tasks without prior specialized training. This suggests the lack of inherent biological

sequence knowledge in LLMs and highlights the need for methods to effectively integrate these tasks with LLMs.

Furthermore, we attempt to activate the biological multi-omics sequence understanding ability of LLMs with the constructed instruction data. We discover that solely performing instruction tuning on Biology-Instructions cannot yield satisfactory results. To address this gap, we propose a three-stage training pipeline: (1) train the model on unsupervised DNA, RNA, and protein sequences; (2) train the model on the question-answer pairs of Biology-Instructions; (3) train the model on reasoning data. The first stage serves as a warm-up to enhance the model’s ability to understand biological sequences. In the second stage, the model follows natural language instructions to interpret biological sequences. In the third stage, the model leverages the implicitly learned knowledge base to perform reasoning and deepen its understanding of biological sequences. We include reasoning data that starts with biological sequence analysis and concludes with results based on prior analyses and reasoning. This approach ensures that models maintain comprehensive conversational abilities while gaining deeper insights into biological sequences and tasks. We have implemented this training pipeline on Llama3.1-8b-Instruct (Dubey et al., 2024) using Biology-Instructions, resulting

in significant performance improvements shown in Figure 1. Our findings and experiences are thoroughly documented. The contributions of this study can be summarized as:

- **Multi-omics Instruction-Following Data.** We present the **first** dataset specifically designed for multi-omics instruction-following, which includes reasoning instruction data and multi-sequence, multi-molecule instruction data. This dataset aims to improve the ability of LLMs to comprehend and analyze biological sequences. To ensure the quality of biology-instructions, we conduct a comprehensive **multi-stage quality control process**, as detailed in Appendix E.
- **Multi-omics Instruction-Following Benchmark.** We benchmark Biology-Instructions on **open-source and closed-source LLMs**. Our results reveal that even current LLMs can not solve biological sequences-related tasks.
- **Biology-Specific LLMs and Three-Stage Training Pipeline.** We develop a biology-focused LLM capable of handling tasks related to multi-omics sequences by training an open-source LLM on biology-specific instructions. We propose an **efficient and novel three-stage pipeline** to enhance the biology learning ability of LLM based on some important findings.

2 Biology-Instructions

2.1 Overview of Biology-Instructions

To build a large-scale biology instruction-following dataset, we have gathered biology sequence data from a substantial aggregation of sources. This effort has resulted in a dataset encompassing 21 subtasks related to multi-omics fields. The Biology-Instructions exhibits the following characteristics:

Multi-omics Biology-Instructions comprises 21 subtasks across three types of omics, including single-omics tasks and multi-omics interaction tasks. As shown in Section 4, joint training of different omics not only enhances efficiency by accomplishing multiple omics tasks with a single model but also improves the model’s capability in a specific omics domain.

Large Scale With over 3 million training samples, the Biology-Instructions dataset provides

an extensive foundation for biological sequences-related instruction data. This large-scale dataset enables models to better understand the traits and functions of biological sequences, leading to more accurate and comprehensive responses to given questions.

High Quality To ensure the quality of the dataset, we manually draft question and answer templates for each task type and expand the template pool using Cluade-3.5-sunnet and GPT-4o. The resulting number of question-answer template pairs for each task ranges from 10,000 to 100,000, depending on the data magnitude of each task type. Throughout this process, we emphasize the importance of diversity in grammar and language style, ensuring that samples in the Biology-Instructions dataset have different question-answer styles. For examples of question-answer template pairs, please refer to Table 9.

Reasoning data Although previous studies (Richard et al., 2024; Liu et al., 2024b; Lv et al., 2024) have demonstrated large-scale primary instruction-following datasets can teach LLMs to answer biological sequences-related questions, they often fail to fully harness the powerful language abilities of LLMs, as they focus primarily on basic language patterns. In other words, they fail to leverage the powerful conversational abilities of these models to form natural and fluent dialogues or to utilize reasoning to improve the validity of the output results. To address this limitation, we design a prompt that requires powerful closed-source LLMs to reformulate answers for a subset of the validation set of Biology-Instructions and provide polished answers ready for end users to read and understand, based on given questions and original answers. We encourage the model to deeply analyze the sequence and question first and then generate a final polished answer grounded in previous analysis and reasoning.

2.2 Biology-Instructions Construction

2.2.1 Tasks

As presented in Figure 2, the Biology-Instructions dataset comprises 21 tasks: 6 DNA tasks, 6 RNA tasks, 5 protein tasks, and 4 multi-molecule tasks. When considering the number of input sequences, there are 4 multi-molecule interaction tasks and 17 single-molecule tasks. Tasks were sourced from high-impact literature, journals, and competitions, ensuring coverage of biologically critical aspects

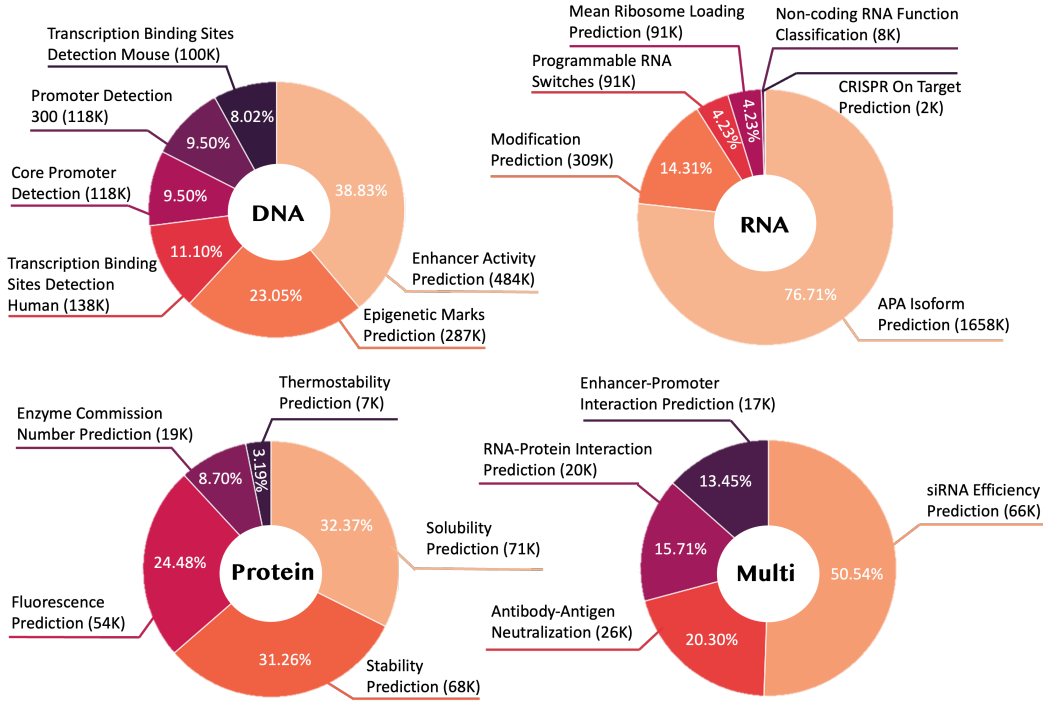


Figure 2: Distribution of tasks across four omics types in our dataset.

in structure, function, and engineering across DNA, RNA, proteins, and their interactions. We focus on predictive sequence-understanding tasks, leaving generative applications, such as sequence design, for future research. To the best of our knowledge, Biology-Instructions is the first instruction dataset to include multi-omics tasks and multi-molecule interaction tasks. For detailed task definitions and distribution, please refer to Appendix B.2.

2.2.2 Templates

To convert the original classification and regression task dataset into an instruction tuning dataset, we employ question-answer templates to integrate the data. The primary objective of creating these templates is to teach the model how to follow biological instructions and complete tasks without overfitting to specific language patterns. To achieve this, we prioritize diversity in language styles, expressive tones and lengths during the template construction process. We manually constructed 10 question templates and 10 answer templates for each task, covering various styles including, but not limited to, request, concise, informal, and academic styles. Then, we used GPT-4o and Claude-3.5-sunnet to expand the templates. Depending on the data volume for each task, we included 100 to 300 question templates and 100 to 300 answer templates. Ultimately, each task resulted in 10,000 to 100,000 question-answer template pairs. Since

biological sequences are generally much lengthier than natural language prompts, we place the biological sequence at the very beginning of question templates for single biology sequence tasks for non-interaction tasks. This approach helps prevent the prompts from being overwhelmed by the lengthy biological sequences, ensuring that the model can accurately understand the question and complete the task. Figure 10 provides examples of the instruction prompts constructed for each type of omics, illustrating the diversity and structure of the templates used in the dataset.

2.2.3 Reasoning data construction

Similar to the data construction method used by LLaVA (Liu et al., 2024a). For a biology sequence X_s and its related question X_q , simple answer Y_s , we prompt GPT-4o-Mini to construct an optimized answer Y_o based on the given information. Generally, the instruction data were transformed to the format USER: X_s, X_q ASSISTANT: Y_o .

In the system prompt used for GPT-4o-Mini, as shown in Figure 9, we emphasized the following key points to ensure the production of high-quality data: (1) first understand the provided biological sequence and the question; (2) analyze the biological sequence at the nucleotide or amino acid level, aiming to extract question-related information from the sequence; (3) refine the answer based on the previous analysis, including a rational ex-

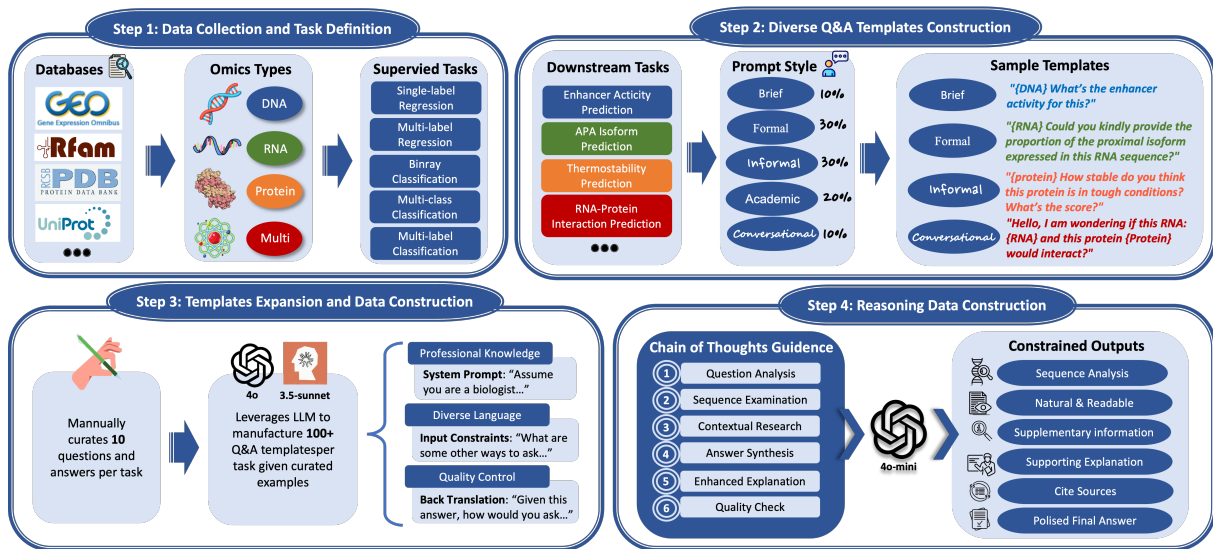


Figure 3: Overview of our data construction pipeline: Step1: Collect data from primary databases and categorize downstream tasks; Step2: Create diverse instruction prompts based on tasks; Step3: Use LLMs to enhance dataset quality; Step4: Follow key principles for reasoning data construction.

planation and a chain of thought approach, especially for complex questions; (4) list any relevant knowledge and information from reliable sources, and cite these sources appropriately; (5) return the polished answer in an end-to-end style, excluding any information from the standard answer and task hint. By following this approach, we gathered 8000 final AI-polished training data points without two multi-molecule tasks: antibody-antigen neutralization and RNA-protein interaction prediction to study transfer learning for reasoning capability. Figure 3 provides an overview of the complete construction process for Biology-Instructions, including the data collection, template construction, and reasoning data construction stages.

2.3 Evaluation Pipeline and Metrics

Our evaluation framework is designed to assess the performance of each model’s output on Biology-Instructions in a robust approach. The task types, regardless of their respective omics, can be organized into single-label regression, multi-label regression, binary classification, multi-class classification, and multi-label classification, each requiring specialized evaluation metrics to capture model performance nuances. The evaluation pipeline involves pre-processing data from models’ output, grouping entries by task, and then computing task-specific metrics. The metrics outcomes for reporting are all scaled by 100 and rounded to 2 decimals. Detailed information is provided in Appendix B.3.

3 Model

As shown in Figure 4, we train a model based on Llama3.1-8B-Instruct (Dubey et al., 2024) named ChatMultiOmics using multi-omics pre-training data and Biology-Instructions. In general, we perform a three-stage training paradigm to enhance the interactive biological sequence-related chat performance of the final biology assistant. For specific training details such as training strategy, please refer to Appendix C.

3.1 Stage 1: biological sequences continued pre-training

Although the memory savings facilitated by LoRA (Devalal and Karthikeyan, 2018) are not that obvious when optimizer states are distributed across GPUs compared with training on a single GPU, LoRA can still significantly reduce training time by minimizing communication between data parallel ranks. However, directly applying LoRA to train a chat model on Biology-Instructions results in suboptimal performance on specific downstream tasks. Specifically, the model shows near-random performance in classification and regression tasks. As noted by (Ghosh et al.), LoRA supervised fine-tuning (SFT) primarily leverages pre-trained knowledge to generate well-formed answers based on the output format learned from SFT data. We suspect that large-scale LoRA instruction tuning on biological sequence-related data suffers due to the lack of pre-training on biological sequence data, which is evident from the baseline results. Therefore,

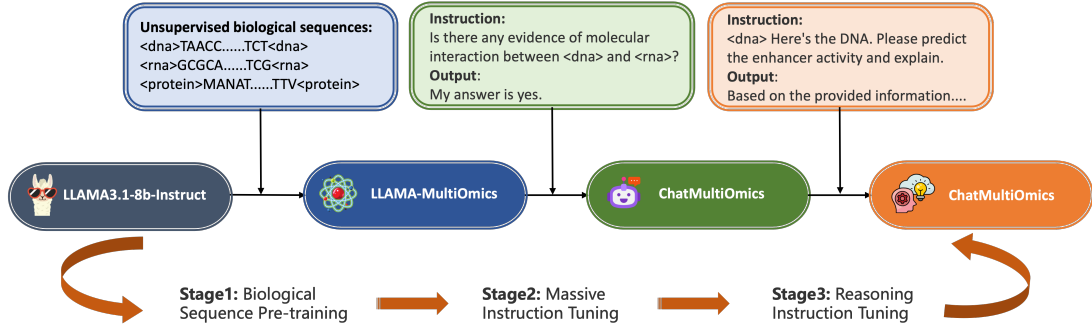


Figure 4: Overview of our three-stage training pipeline.

continued pre-training of the model is essential for better performance. This involves teaching the model with biological sequences to enable it to understand the nature and functions of biological sequences. For this process, we utilized unlabeled human DNA data from the Genome Reference Consortium Human Genome (GRCh) (Harrow et al., 2012), human non-coding RNA data from RNA-Central (rna, 2019), and protein sequences from UniRef50 (Suzek et al., 2007) during the first phase of pre-training. This initial pre-training served as a foundational warm-up to improve the model’s comprehension across multi-omics biological sequences.

We employed LoRA+ (Hayou et al., 2024) for all linear layers of our model, training on a continued pre-training dataset. LoRA+ demonstrates superior convergence compared to vanilla LoRA by increasing the learning rate of the zero-initialized weight B relative to the base learning rate for normal-initialized weight A and other trainable parameters. Hayou et al. (2024) observed that setting the learning rate of weight B to 16 times that of weight A results in more effective model convergence. However, our experiments revealed that while LoRA+ indeed improves convergence rates, applying a large learning rate multiplier can lead to instability during the continued pre-training process for biological sequences. Based on this observation, we opted for a more conservative learning rate multiplier of 4. We trained the normalization layers of the model alongside LoRA parameters.

3.2 Stage 2: massive instruction tuning

In Stage 2, we employ the Biology-Instructions dataset, excluding the reasoning sub-dataset. In the initial attempts of the training process, we find that the imbalance among tasks within the dataset can pose challenges for the model in distinguishing between different tasks. To mitigate

this, we randomly select 30 percent of the training data and prepend a task label in the format "[Classification/Regression:task_name]" at the beginning of each question. This method effectively aids the model in identifying different tasks and output objectives.

We use a system prompt P_{sc} : "You are a knowledgeable and helpful biology assistant. Please answer my biology sequence-related questions in a clear and concise manner. For regression tasks, please return a number." This prompt helps the model to differentiate biology sequence-related tasks from other tasks. As illustrated in Figure 7, we maintain the data format: SYSTEM: P_{sc} USER: X_s , X_q ASSISTANT: Y_o consistent with the Llama3.1 instruct-tuned model chat completion format, which is crucial for optimal model performance.

3.3 Stage 3: Reasoning instruction tuning

In stage 3, we use the reasoning sub-dataset from Biology-Instructions to fine-tune the model. To keep the classification and regression performance of the model, we additionally select 3000 samples from the validation set composed of non-reasoning data to be trained simultaneously.

To better control the behavior of the model, a more detailed system prompt P_{sd} was used for reasoning data: "You are a highly knowledgeable AI assistant specializing in biology, particularly in sequence-related topics. Your primary task is to provide clear, accurate, and comprehensive answers to biology questions. When analyzing and interpreting sequences, ensure to provide step-by-step explanations to make your responses natural and easy to understand. Engage with the user by asking clarifying questions if needed and offer detailed insights into the biological sequences." In this case, the format of training samples of reasoning data is transformed to SYSTEM: P_{sd}

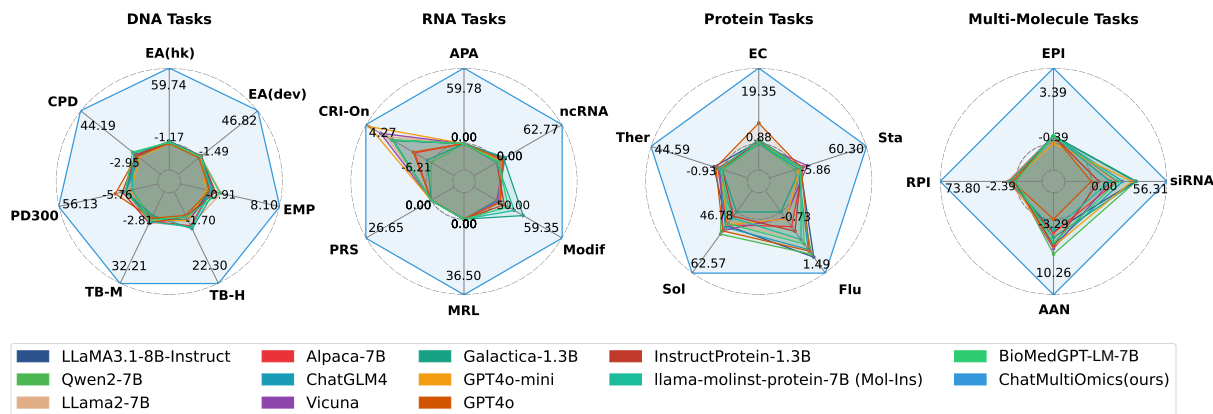


Figure 5: Radar plot comparing the performance of ChatMultiOmics with SOTA baselines on all 21 downstream tasks grouped by omics including DNA, RNA, Protein, and Multi-molecule tasks.

USER: X_s, X_q ASSISTANT: Y_o .

4 Results

4.1 Experimental Setups

To evaluate the biological sequence understanding capabilities of current LLMs and determine if our method can enhance LLMs’ performance, we compare ChatMultiOmics with various open-source general-purpose LLMs: Llama3.1-8B-Instruct (Dubey et al., 2024), Llama2-7B-Chat (Touvron et al., 2023), Alpaca-7B (Taori et al., 2023), Vicuna-v1.5-7B (Chiang et al., 2023), Qwen2-7B (Bai et al., 2023), GLM4-9B-Chat (GLM et al., 2024), and Galactica-1.3b (Taylor et al., 2022). Additionally, we include comparisons with SOTA closed-source LLMs: GPT-4o and GPT-4o-Mini. We also evaluate biology-specialized LLMs: InstructProtein-1.3B (Wang et al., 2023), Llama-molinst-protein-7B (Fang et al., 2023), and BioMedGPT-LM-7B (Zhang et al., 2023). To ensure well-formed and quantifiable answers, we restrict the output format for all baselines and provide them with task information, enabling them to understand both what to output and how to format their output. The experimental results are visualized in Figure 5, showcasing the comparative performance of various LLMs across four types of datasets: DNA, RNA, protein, and multi-molecule interactions. For the full experimental results, please refer to Appendix D.

4.2 Findings.1: Generic LLMs are not capable of biological understanding

To assess whether LLMs can effectively tackle tasks related to biological sequences, we conducted comprehensive experiments using both open-source and closed-source general-purpose

LLMs. For open-source LLMs, we selected models of comparable size to our model, ChatMultiOmics. For closed-source LLMs, we evaluated SOTA models such as GPT-4o and its streamlined version, GPT-4o-mini. The results unequivocally demonstrate that all open-source LLMs of similar size to ChatMultiOmics fail to surpass average performance levels. Similarly, the closed-source LLMs, GPT-4o and GPT-4o-mini, exhibit performance on par with the open-source models.

Notably, models within the same series but with different versions, such as Llama2-7B-Chat and Llama3.1-8B-Instruct, as well as models within the same series but of different sizes, like GPT-4o and GPT-4o-mini, show comparable performance on tasks involving biological sequences. These findings suggest that the language capabilities of these models do not directly correlate with their performance in understanding biological sequences. This implies that natural language performance does not determine the effectiveness of these models in biological sequence understanding tasks, indicating a significant lack of pre-trained biological sequence knowledge. Despite LLMs possessing extensive text-based biological knowledge, they struggle to establish a connection between this knowledge and biological sequences, and they are unable to delve into the molecular level to analyze biological sequences effectively.

4.3 Findings.2: Current biology-specified LLMs can not handle multi-omics tasks

Biology-specified LLMs have demonstrated remarkable performance on a variety of tasks. For instance, the Llama-molinst-protein-7B model excels in five key areas of protein understanding, including the prediction of catalytic activity, protein design, protein function prediction, and more. De-

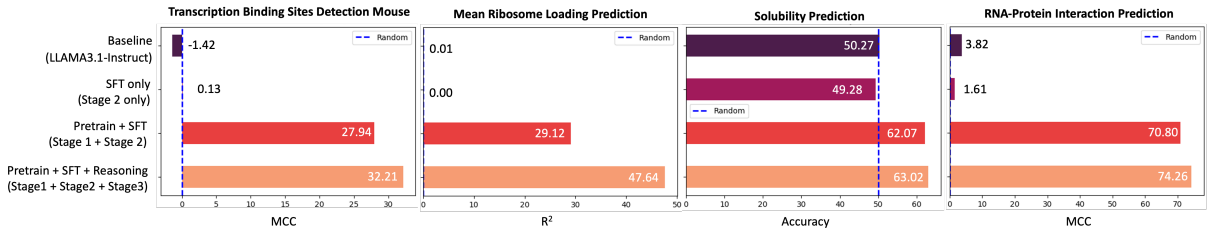


Figure 6: Ablation studies showing the performance across different training stages. One downstream task from each omics type is selected for display. Each bar color corresponds to a specific training approach. The blue dashed line indicates where random performance is for each task according to the respective metric.

spite these impressive achievements, these methods exhibit limitations. Notably, they lack transfer learning capabilities across multi-omics tasks and fail to outperform general-purpose baselines even in single-omics tasks, and in some cases, these models even cannot follow the instructions. This indicates that while specialized LLMs are highly effective within their specific domains, their applicability and efficiency in broader, more integrative biological studies remain constrained.

4.4 Findings.3: Continued Pre-trained on biological sequences helps instruction tuning

Previous studies have utilized LoRA (Fang et al., 2023; Lv et al., 2024) for model training. However, our experimental findings suggest that employing LoRA to fine-tune models on Biology-Instructions does not result in performance enhancements. For LoRA fine-tuning, the quality and quantity of the pre-training on related knowledge appear to be a critical factor for achieving good results, as indirectly proved by the experimental setup in (Fang et al., 2023), where full fine-tuning was applied to protein-related tasks and LoRA fine-tuning was used for other tasks, alongside the near-random performance of the baselines on biological-sequences understanding tasks. After continued pre-training on multi-omics sequences, LoRA fine-tuning on Biology-Instructions does help the model leverage the intrinsic relationships and dependencies from pre-trained knowledge. The results of the second stage surpass those of instruction-tuning without continued pre-training, as shown in Figure 6.

4.5 Findings.4: Reasoning dataset boosts overall performance and demonstrates transfer learning capability

We hypothesize that the model’s performance can be enhanced by incorporating task information and reasoning steps, which can aid the model in better understanding the task and consequently lead to im-

proved results. We tested the third-stage model using the system prompt P_{sc} to facilitate results computation. The results indicate that in most tasks, performance was enhanced. However, for some regression tasks, the performance was slightly adversely affected by the third-stage training.

Furthermore, when the reasoning system prompt P_{sd} was used, the model demonstrated excellent reasoning capabilities and extended its performance to untrained tasks, such as antibody-antigen neutralization and RNA-protein interaction prediction, as illustrated in Figure 1 (b).

5 Conclusion

In this work, we present Biology-Instructions, the first large-scale, multi-omics biological sequences-related instruction-tuning dataset. Biology-Instructions bridges the gap between LLMs and complex biological tasks by including 21 different tasks involving DNA, RNA, proteins, and multi-molecule interactions, covering both single-sequence and interaction analyses. By incorporating reasoning capabilities, Biology-Instructions can enable LLMs versatile in handling complex biological tasks while maintaining conversational fluency. Our evaluation shows that SOTA LLMs, like GPT-4, struggle with biological sequence-related tasks without specialized training. Using Biology-Instructions for instruction tuning, we demonstrate significant improvements, proving its value in enhancing LLMs for multi-omics sequence analysis. We also develop a strong baseline, ChatMultiOmics, with a three-stage training pipeline: biological sequences continued pre-training, massive instruction tuning, and reasoning instruction tuning. This pipeline leads to notable performance gains, providing an effective approach to train LLMs for addressing biological challenges.

6 Limitations

While Biology-Instructions is a significant advancement, it still has areas for improvement. The dataset covers primarily the predictive tasks. Future versions of this work should include generative tasks, such as designing novel protein sequences, which could greatly enhance its utility in protein engineering. ChatMultiOmics shows promising reasoning capabilities, yet further enhancements are needed to make its outputs more practical and reliable. To enhance model performance, we could use hybrid architectures that combine specialized biological tokenizers or encoders with LLMs. This could reduce information loss during the tokenization of biological sequences. Integrating structural data, such as 3D molecular coordinates, could improve the model's ability to capture functional implications of molecular structures. Incorporating multi-hop data could be another potential enhancement for the model to reason over interconnected biological datasets and capture more intricate relationships across multiple omics layers. Future efforts should also expand evaluation metrics beyond accuracy to include interpretability, robustness, and computational efficiency, offering a more holistic view of model performance. Long chain-of-thought reasoning models have demonstrated strong performance across a variety of complex tasks, such as advanced mathematical reasoning. These models also hold significant potential for excelling in biology-sequence-related tasks as they can further bridge the gap of natural language and biology language. However, benchmarking long chain-of-thought reasoning models and developing more powerful models through such approaches is a comprehensive and labor-intensive endeavor, which we leave for future research. Future work could involve benchmarking various long chain-of-thought reasoning models—such as DeepSeek-R1 (Guo et al., 2024) and QwQ-32B (Team, 2025) on biology-sequence-related tasks using the Biology-Instructions dataset. Additionally, future works may explore constructing a long chain-of-thought-enhanced version of Biology-Instructions through rejection sampling techniques. Furthermore, by leveraging this enhanced dataset alongside supervised fine-tuning or reinforcement learning methods, future studies can aim to improve the biological sequence understanding capabilities of LLMs.

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A Related works

A.1 Large Language Models

In recent years, LLMs have demonstrated significant advancements in the field of natural language processing (NLP). These models undergo self-supervised training on a substantial corpus of data in order to acquire knowledge. By means of fine-tuning the instructions, the capabilities of the model are enhanced, enabling it to respond to questions based on the specific prompt. Currently, numerous open-source models are available, including the Llama series (Dubey et al., 2024), Qwen series (Bai et al., 2023), GLM series (GLM et al., 2024), and numerous models fine-tuned based on Llama, such as Alpaca (Taori et al., 2023) and Vicuna (Chiang et al., 2023). Additionally, Galactica (Taylor et al., 2022) is a model that demonstrates exceptional performance in scientific domains and is trained on data from a multitude of scientific fields. Furthermore, there are closed-source SOTA models, such as GPT-4o and GPT-4o-mini. However, these models are not pre-trained on specific biological data, and their capabilities are severely constrained, even Galactica.

A.2 Biology Large Language Models

Researchers have concentrated on enhancing the capabilities of LLMs in the biology area. InstructProtein (Wang et al., 2023) aligns human and protein language through knowledge instructions. Another study (Fang et al., 2023) utilizes the protein part of a specially designed dataset called Mol-Instructions for instruction tuning with LLaMA-7B. ProLLaMA (Lv et al., 2024) is also a recent work focusing on multi-protein tasks through a two-stage training process from LLaMA-2. These methods can only deal with several protein tasks well, limited by fixed instruction templates. BioMedGPT (Zhang et al., 2023) is equipped with a special vision encoder, allowing the model to answer multi-modal biological questions. However, lacking specialized large-scale biological instruction datasets, BioMedGPT cannot understand biological sequence languages very well. ChatNT (Richard et al., 2024) integrates a biological sequence encoder with a LLM, enabling effective handling of DNA-centric tasks using only an instruction-tuning dataset. However, it faces challenges in combining multiple encoder models from various omics domains into a unified LLM due to dependence on the encoder’s capabilities.

B Detail information of Biology-Instructions and Evaluation Metrics

B.1 Impact

The Biology-Instructions dataset addresses critical challenges in computational biology across multiple omics domains. **DNA instructions** improve our understanding of regulatory elements in gene expression. **RNA instructions** tasks offer insights into transcriptomics and regulation at the RNA level. **Protein instructions** enhance our knowledge of protein functions, interactions, and their relevance in drug development. **Multi-molecular instructions** explore biomolecular interactions, such as RNA-protein and promoter-enhancer, revealing regulatory networks. By supporting these diverse tasks, Biology-Instructions advances multi-omics research and fosters new discoveries in genetic regulation and therapeutic development.

B.2 Tasks Definition

B.2.1 DNA tasks

Epigenetic Marks Prediction This is a binary classification task that predicts whether a DNA sequence has chemical modifications affecting gene regulation without changing the DNA itself. Epigenetic marks are crucial for understanding gene regulation and its impact on health and disease. We use part of the DNABERT-2 dataset (Zhou et al., 2024), containing 28,740 DNA sequences, some of which are chemically modified. Model performance is evaluated using the Matthews Correlation Coefficient (MCC).

EA Prediction This is a regression task that predicts the activity levels of enhancer regions in the DNA sequences. By predicting the activity levels of enhancers, scientists can gain deeper insights into how genes are regulated in specific tissues or under certain conditions. The target value are two numeric numbers that reflects the housekeeping and developmental activity level. The dataset is sourced from the DeepSTARR (de Almeida et al., 2022), consisting of DNA sequences annotated with enhancer activities. We evaluate performance of the model using Pearson Correlation Coefficient (PCC), reflecting its ability to decide levels of activity across different DNA sequences.

Promoter Detection 300 & Promoter Detection Core These two tasks are both binary classification tasks for identifying promoter regions in DNA sequences(exist or not). Promoter Detection

Table 1: Tasks information of Biology-Instructions

Task	Omics	#Training/Validation/Test
DNA Tasks		
Epigenetic Marks Prediction (EMP)	DNA	229885/28741/28741
EA Prediction (EA)	DNA	402296/40570/41186
Promoter Detection 300 (PD300)	DNA	94712/11840/11840
Core Promoter Detection (CPD)	DNA	94712/11840/11840
Transcription Binding Sites Detection Human (TB-H)	DNA	128344/5000/5000
Transcription Binding Sites Detection Mouse (TB-M)	DNA	80018/10005/10005
RNA Tasks		
APA Isoform Prediction (APA)	RNA	1575557/33170/49755
Non-coding RNA Function Classification (ncRNA)	RNA	5670/650/4840
Modification Prediction (Modif)	RNA	304661/3599/1200
Mean Ribosome Loading Prediction (MRL)	RNA	76319/7600/7600
Programmable RNA Switches (PRS)	RNA	73227/9153/11019
CRISPR On Target Prediction (CRI-On)	RNA	1453/207/416
Protein Tasks		
Enzyme Commission Number Prediction (EC)	Protein	15551/1729/1919
Stability Prediction (Sta)	Protein	53614/2512/12851
Fluorescence Prediction (Flu)	Protein	21446/5362/27217
Solubility Prediction (Sol)	Protein	62478/6942/2001
Thermostability Prediction (Ther)	Protein	5056/639/1336
Multi-molecular Tasks		
Antibody-Antigen Neutralization (AAN)	Multi-molecule	22359/1242/3301
RNA-Protein Interaction Prediction (RPI)	Multi-molecule	14994/1666/4164
Enhancer-Promoter Interaction Prediction (EPI)	Multi-molecule	14288/1772/308
siRNA Efficiency Prediction (siRNA)	Multi-molecule	53592/6707/6688
Total		
All		3330232/190946/244681

300 refers to detecting promoter regions within a 300 base pair (bp) window, which includes both the core promoter region and the surrounding regulatory elements. While promoter detection core refers to detect a shorter, core sequence (usually around 50-100 bp) directly upstream of the transcription start site. Both tasks are important for understanding gene regulation and can aid in studying transcriptional activity, identifying novel genes, and mapping gene expression patterns. For these tasks, we also adopt the dataset part of DNABERT-2 (Zhou et al., 2024). Evaluation of the model performance is done using MCC, capturing the model’s ability to predict the existence of promoters on different sequence contexts balancedly.

Transcription Binding Sites Detection We define this a binary classification task, to determine whether specific regions with transcription factors binding in the DNA sequences or not. These transcription binding sites (TBS) are critical for con-

trolling the initiation, enhancement, or repression of transcription. Once more, data from DNABERT-2 is utilized for this task (Zhou et al., 2024), which includes numerous DNA sequences, partly possessing TBS. The performance of the model is evaluated using MCC, fairly measuring its ability to discover TBS in different DNA sequences.

Enhancer-Promoter Interaction Prediction

This is a binary classification task, which involves identifying the interactions between enhancer regions and their corresponding promoter regions in a pair of DNA sequences. Predicting these interactions helps researchers understand the complex regulatory networks governing DNA activity, which is essential for studying developmental processes and potential therapeutic targets. We extract our dataset from the research (Min et al., 2021), which all contains two DNA sequences. The model needs to figure out whether they interact with each other. We evaluate the performance of the model using

the metric MCC, to test whether the model can identify these interactions correctly.

B.2.2 RNA tasks

APA Isoform Prediction This is a regression task which predicts the usage of alternative polyadenylation (APA) isoforms by analyzing RNA sequences and outputting a proportion between 0 and 1 that represents the relative expression of each APA isoform. Accurate APA isoform prediction is critical for understanding the regulation of gene expression at the RNA level, which plays a fundamental role in transcriptome diversity. For this task, we adopt APARENT’s (Bogard et al., 2019) APA isoform prediction dataset, which consists of isoform usage data derived from synthetic and human 3’UTRs. The output represents the proportion of isoform usage, capturing the variability in polyadenylation signal processing. The performance of the prediction is evaluated using the Coefficient of Determination (R^2).

Non-coding RNA Function Classification This is a multi-label classification task that predicts the functional class of non-coding RNA (ncRNA) sequences. The model outputs one or more class labels from a set of 13 possible ncRNA classes, such as ‘tRNA’, ‘miRNA’, and ‘riboswitch’. Accurately classifying ncRNAs is essential for improving our understanding of their regulatory roles in gene expression, as well as their contributions to diverse biological processes and diseases. For this task, we adopt the nRC (non-coding RNA Classifier) dataset from (Fiannaca et al., 2017), which utilizes features derived from ncRNA secondary structures. The output assigns each RNA sequence to one or more functional classes, enabling a detailed examination of the functional diversity within ncRNAs. The performance of the model is evaluated using accuracy (Acc), reflecting the model’s ability to correctly classify ncRNA functions across all categories.

Modification Prediction This is a multi-label classification task that predicts post-transcriptional RNA modifications from RNA sequences. The model outputs one or more modification types from a set of 12 widely occurring RNA modifications, including ‘m6A’, ‘m1A’, and ‘m5C’. Precise identification of RNA modification sites is essential for understanding the regulatory mechanisms of RNA and their roles in various biological processes. For this task, we adopt the MultiRM dataset from (Song et al., 2021), which contains RNA sequences an-

notated with multiple modification types. The performance of the model is evaluated using the Area Under the Curve (AUC), capturing the model’s ability to predict RNA modifications across different contexts.

Mean Ribosome Loading Prediction This is a regression task that predicts ribosome loading efficiency by analyzing RNA sequences and outputting a numeric value, representing mean ribosome loading, with two decimal precision. Accurate prediction of ribosome loading is essential for understanding how cis-regulatory sequences, such as 5’ untranslated regions (UTRs), influence translation efficiency, which is crucial for both fundamental biological research and applications in synthetic biology and mRNA therapeutics. For this task, we adopt the dataset from (Sample et al., 2019), which includes polysome profiling data of 280,000 randomized 5’ UTRs and 35,212 truncated human 5’ UTRs. The performance of the model is evaluated using the Coefficient of Determination (R^2), measuring its ability to predict ribosome loading across different sequence contexts.

Programmable RNA Switches This is a multi-label regression task that predicts the behavior of programmable RNA switches by analyzing RNA sequences and outputting three numeric values representing the ‘ON’, ‘OFF’, and ‘ON/OFF’ states, each with two decimal precision. Accurate prediction of these states is critical for advancing synthetic biology, as RNA switches are essential tools for detecting small molecules, proteins, and nucleic acids. For this task, we adopt the dataset from (Angenent-Mari et al., 2020), which includes synthesized and experimentally characterized data for 91,534 toehold switches spanning 23 viral genomes and 906 human transcription factors. The performance of the model is evaluated using the Coefficient of Determination (R^2), measuring the model’s ability to predict the functional states of RNA switches across diverse sequence contexts. (Ren et al., 2024)

This is a multi-label regression task that predicts the behavior of programmable RNA switches by analyzing RNA sequences and outputting three numeric values representing the ‘ON’, ‘OFF’, and ‘ON/OFF’ states, each with two-decimal precision. Accurate prediction of these states is crucial for advancing synthetic biology, as RNA switches serve as essential tools for detecting small molecules, proteins, and nucleic acids. For this task, we use the dataset from (Angenent-Mari et al., 2020), which

includes synthesized and experimentally characterized data for 91,534 toehold switches spanning 23 viral genomes and 906 human transcription factors. This dataset is also included in the RNA-related tasks benchmark BEACON (Ren et al., 2024). Model performance is evaluated using the Coefficient of Determination (R^2), assessing the model’s ability to predict the functional states of RNA switches across diverse sequence contexts.

CRISPR On Target Prediction This is a regression task that predicts the on-target knockout efficacy of single guide RNA (sgRNA) sequences using CRISPR systems. The model outputs a numeric value that represents the predicted sgRNA knockout efficacy for a given RNA sequence. Accurate prediction of on-target efficacy is essential for optimizing the design of sgRNAs with high specificity and sensitivity, which is crucial for successful CRISPR-based genome editing. For this task, we adopt the DeepCRISPR dataset from (Chuai et al., 2018), which includes sgRNA sequences and their corresponding on-target knockout efficacy data. The performance of the model is evaluated using Spearman’s correlation, measuring the model’s ability to predict the effectiveness of sgRNAs across different genetic contexts.

siRNA Efficiency Prediction This is a regression task that predicts the efficiency of siRNA in silencing target genes by analyzing modified siRNA sequences and corresponding target sequences, outputting a numeric value representing the percentage of mRNA remaining after siRNA treatment. Accurate prediction of siRNA efficiency is crucial for optimizing siRNA design in RNA interference (RNAi) applications, which plays a critical role in gene expression regulation and has significant implications in therapeutic interventions. For this task, we adopt the dataset from the competition (SAIS, 2020), which contains chemically modified siRNA sequences and their measured silencing efficiency data. The performance of the model is evaluated using a mixed score, reflecting its ability to predict the mRNA remaining percentage across different chemical modifications and experimental conditions.

B.2.3 Protein tasks

Enzyme Commission (EC) Number Prediction. This is a multi-label classification task which predicts enzyme functions by annotating protein sequences with all corresponding EC numbers. We adopt DeepFRI’s (Gligerjović et al., 2021) EC an-

notation dataset from PDB chains, whose binary multi-hot vectors are converted back into corresponding EC numbers for language capability in our task. The performance of the prediction is evaluated using the Fmax metrics. Accurate EC number prediction is crucial for understanding enzyme catalytic functions, accelerating the discovery of novel enzymatic activities. This has applications in biotechnology, including optimizing enzymes for industrial use and drug development. By predicting catalytic activities, researchers can engineer enzymes tailored for therapeutic interventions, contributing to drug discovery and targeted treatments.

Stability Prediction. This is a regression task to assess the intrinsic stability of proteins under various conditions, with each protein sequence mapped to a continuous stability score that reflects how well the protein maintain its fold above a certain concentration threshold like EC50. We adopt the dataset from Rocklin et al. (Rocklin et al., 2017), which includes protease EC50 values derived from experimental data. The model’s performance is assessed using Spearman’s correlation. Predicting protein stability is essential in protein engineering, especially for therapeutic applications where protein integrity is crucial. These predictions reduce the need for experimental screening, facilitating the design and refinement of stable proteins for industrial, pharmaceutical, and research purposes.

Fluorescence Prediction. This is a regression task that aims to evaluate the model’s ability to predict fluorescence values for higher-order mutated green fluorescent protein (GFP) sequences. This is a regression task where each protein sequences is mapped to the logarithm of its florescence intensity (Sarkisyan et al., 2016). Following the setting in TAPE (Rao et al., 2019), the model is trained on a set of mutants with a low number of mutations, while tested on mutants with four or more mutations. The task is designed to assesses how well the model generalized to unseen combinations of mutations by leveraging Spearman’s correlation to evaluate predictive performance. Accurate fluorescence prediction in higher-order mutated GFP aids in understanding mutation effects and interactions. These predictions provide insights into protein function and help efficiently explore mutational landscapes, facilitating the design of fluorescent proteins for applications in synthetic biology and protein engineering.

Solubility Prediction. This is a binary classification task to determine whether a protein is

soluble or insoluble. The dataset is sourced from the DeepSol (Khurana et al., 2018), ensuring that protein sequences with a sequence identity greater than 30 percent to any sequence in the test set are excluded from training. The challenge is to test a model’s capacity to generalize across dissimilar protein sequences. Predicting protein solubility is crucial for pharmaceutical research and industrial biotechnology. Soluble proteins are essential for drug formulation and large-scale production. This task drives the development of advanced in silico methods to predict solubility, reducing laboratory testing and accelerating the discovery of therapeutically relevant proteins.

Thermostability Prediction. This is a regression task to predict the stability of proteins at elevated temperatures. The target value reflects the thermostability of a given protein sequence. We focus on the Human-cell split from the FLIP (Dallago et al., 2021), sequences are clustered by identity and divided into training and test sets. Model prediction performance is evaluated by the metric Spearman correlation. Accurate prediction of protein thermostability enhances understanding of protein function and stability, which is critical for protein engineering. These predictions support protein optimization in biotechnological applications, including drug and vaccine development (Chen and Gong, 2022), and provide a framework for selecting thermostable proteins.

B.2.4 Multi-molecule tasks

RNA-Protein This is a binary classification task, the objective of which is to identify interactions between non-coding RNAs (ncRNAs) and proteins, based on the sequences of the aforementioned ncRNAs and proteins. The majority of ncRNAs interact with proteins to perform their biological functions. Consequently, inferring the interactions between ncRNAs and proteins can facilitate the comprehension of the potential mechanisms underlying biological activities involving ncRNAs (Li et al., 2016). The dataset employed in this study was derived from (Han and Zhang, 2023), comprising 14,994 samples. The evaluation metric employed was MCC.

Antibody-Antigen This is a binary classification task, which seeks to ascertain whether a corresponding interaction relationship exists based on the sequences of antibodies and antigens. The objective of this task is to ascertain the correspondence between antigens and antibodies and to pre-

dict more effective antibody characteristics for new variants of viruses. The dataset was sourced from (Zhang et al., 2022), which contains 22,359 antibody-antigen pairs. MCC is employed for the assessment of the model’s performance.

B.3 Evaluation Metrics

Single-label Regression: This type of task involves predicting one continuous numerical value. The evaluation process extracts the numeric values from model outputs using regular expressions, avoiding over- and underflow by limiting values to six significant digits. Metrics computed for regression tasks include:

- **Spearman’s Rank Correlation Coefficient:** Measures the monotonic relationship between predicted and true values according to their ranks. The metric value ranges from -1 to 1, where -1 indicates perfect negative correlation, 0 indicates no correlation (random predictions) and 1 indicates perfect positive correlation.
- **Coefficient of Determination (R^2):** Obtained by squaring the Pearson correlation coefficient to reflect the proportion of variance in the dependent variable explained by the independent variable. The metric value ranges from 0 to 1, where 1 indicates perfect prediction and 0 indicates predictions as good as the mean value (randomness).
- **Mixed Score:** A custom metric (SAIS, 2020) balances regression error and classification accuracy by integrating F1 score (harmonic mean of precision and recall), Mean Absolute Error (MAE), and range-based MAE (MAE computed within a range threshold). Calculation details will be further explained in B.3.1.

Multi-label Regression: This type of task involves predicting multiple continuous output for each input. In the EA prediction task, two numeric values are required for the regression values of ‘Housekeeping EA’ and ‘Developmental EA’. In the programmable RNA switches prediction task, three numeric values are required for predicting the regression values of ‘ON’, ‘OFF’, and ‘ON/OFF’.

- **Pearson Correlation Coefficient (PCC):** Assesses the linear correlation between two sets of data. The metric value ranges from -1 to 1, where -1 indicates perfect negative linear

correlation, 0 indicates no linear correlation (random predictions), and 1 indicates perfect positive linear correlation.

- **Average R^2 :** Computes individual R^2 for each label and take the mean across labels to obtain an average R^2 as the overall performance metric. The metrics values shares the same range and interpretations similar to the single-label R^2 .

Binary Classification: This type of task asks the model to predict one of two possible classes. In our case, either positive or negative. The evaluation pipeline involves first classifying via keywords based on the presence of predefined positive or negative keywords. If keywords classification fails, the pre-trained sentiment analysis model Twitter-roBERTa-base will be utilized as fallback to determine the class based on the sentiment polarity assigned with a higher probability score.

- **Matthews Correlation Coefficient (MCC):** Provides a balanced measure for binary classifications, even when classes are imbalanced. The metric ranges from -1 to 1, where -1 indicates perfect inverse correlation, 0 indicates random predictions or no correlation, and 1 indicates perfect positive correlation.
- **Accuracy Score:** Calculates the proportion of correct predictions out of all predictions made. It ranges from 0 to 1, where 0 indicates no correct predictions, 1 indicates all correct predictions and 0.5 as random predictions.

Multi-class Classification: This type of task asks the model to assign each input to one of several classes. In the non-coding RNA family prediction task, the model is required to predict one from 13 classes.

- **Accuracy Score:** Calculates the proportion of correct predictions out of all predictions made. It ranges from 0 to 1, where 0 indicates no correct predictions, 1 indicates all correct predictions and 0.5 as random predictions.

Multi-label Classification: This type of task involves inputs that may belongs to multiple classes and asks the model to predict all of them. The evaluation process includes first extracting all relevant labels from the model outputs and converting them into binary multi-hot vectors representing the presence or absence of each class.

- **Area Under the ROC Curve (AUC):** Measures the model's ability to distinguish between classes across all thresholds. The metrics ranges from 0 to 1, where 1 indicates perfect ability to distinguish classes and 0.5 as random performance.

- **Fmax Score:** Represents the maximum F1 score over all possible thresholds, providing a balanced measure of precision and recall in multi-label settings. The metric ranges from 0 to 1, where 0 indicates worst balance of no correct predictions and 1 indicates perfect balance between precision and recall.

B.3.1 Mixed Score Calculation

The Mixed Score is a custom metric adopted from (SAIS, 2020) which is designed to balance regression error and classification accuracy by integrating three components: the F1 score, the Mean Absolute Error (MAE), and the Range-based MAE (Range-MAE). This metric provides a comprehensive evaluation by considering overall prediction accuracy, precision, and recall, as well as specific performance in a designated value range. The calculation is detailed below:

- **Mean Absolute Error (MAE):** This measures the average magnitude of prediction errors across all samples, providing an indication of the model's overall regression accuracy. The MAE is defined as:

$$MAE = \frac{1}{n} \sum_{i=1}^n |y_i - \hat{y}_i|,$$

where n is the total number of samples, y_i is the ground truth value, and $\hat{y}_i$ is the predicted value. The range of MAE is $[0, 100]$.

- **Range-based MAE (Range-MAE):** This metric evaluates the Mean Absolute Error within a specific range of interest, emphasizing regions where high predictive accuracy is particularly crucial. For the siRNA task, the "low remaining" range is of significant importance in practical applications. Following (SAIS, 2020), we define this range as $[0, 30]$. The Range-MAE is computed as:

$$Range - MAE = \frac{1}{m} \sum_{j=1}^m |y_j - \hat{y}_j|,$$

where m is the number of samples within the specified range, and $y_j, \hat{y}_j$ represent the

ground truth and predicted values within this range. The Range-MAE is also bounded within $[0, 100]$.

- **F1 Score:** This classification metric combines precision and recall into a harmonic mean to evaluate the quality of predictions within the designated range. For the range $[0, 30]$, precision and recall are calculated for predictions falling within this interval, and the F1 score is derived as:

$$F1 = 2 \cdot \frac{Precision \cdot Recall}{Precision + Recall}$$

final Mixed Score integrates these three components to provide a balanced assessment of regression and classification performance. The formula for the Mixed Score is:

$$\text{Mixed Score} = 50\% \cdot (1 - MAE/100) + 50\% \cdot F1 \cdot (1 - Range - MAE/100).$$

where the first term emphasizes overall regression performance, and the second term focuses on classification accuracy and precision within the specified range.

This scoring mechanism is designed to reward models that perform well both globally (via MAE) and within critical regions (via Range-MAE and F1), ensuring a comprehensive evaluation of model capabilities.

C Model Training Details

As shown in TABLE 2, we adopt different training methods for each stage due to limitations in computational resources while attempting to improve model performance as much as possible.

In Stage 1, we train the model using 523933 RNA sequences, 1561639 DNA sequences, and 2000000 protein sequences, each with a maximum length of 2000 characters. The dataset weights for RNA, DNA, and protein are $[2, 1, 1]$, indicating that RNA sequences are trained twice per epoch. This stage consumes the majority of computational resources. To reduce training time, we apply LoRA to every linear layer in the model and additionally train each RMS normalization (Zhang and Sennrich, 2019) layer. To optimize processing efficiency and balance model performance and training efficiency, we impose a maximum input length of 2000 characters for biological sequences, which translates to a maximum of 1200 input tokens. To address the potential inefficiency arising

from varying input sequence lengths, we implement a packing strategy¹. This approach allows us to combine multiple samples of different lengths into a single sample, effectively eliminating the need for padding tokens in our training data. The training process encompassed approximately a total of 140,000 parameter update steps, each step composed of 48 global samples, ensuring thorough optimization of the model’s performance on biological sequence data.

In Stage 2, we train the model with 3330232 samples. As noted by (Ghosh et al.), we discover that using LoRA and its variants (Hayou et al., 2024; yang Liu et al., 2024; Kalajdziewski, 2023) for the entire model during supervised fine-tuning leads to sub-optimal performance. Therefore, we fully fine-tune the query and key layers in each self-attention module, along with the RMS normalization layers, while applying LoRA+ to the other linear layers in the model. This approach ensures the update for the whole model and improves model performance while maintaining relatively low training times by reduce the communication quantity of optimizer states. The base learning rate was set to $1e-4$, with the learning rate for the weight B parameters group at $1.6e-3$. We configured the gradient accumulation steps to 10 and set the micro-batch size on the GPU to 2, given the maximum input length was limited to 1024. This configuration result in a global batch size of 400. In Stage 3, minimal computational resources is required. Thus, we employ full fine-tuning for the entire model except embedding layer and output layer.

We use DeepSpeedCPUAdam and adamw_mode=True for Stage 1 and Stage 2 as LoRA efficiently reduces the communication time between CPU and GPU for offloaded optimizers. For Stage 3, we use FusedAdam and adamw_mode=True to reduce training time. A warmup learning rate scheduler with cosine learning rate decay is used for all three stages. All stages employ a mixed precision training strategy where model parameters, gradients, and activations are stored in torch.bfloat16. To improve training efficiency, we use DeepSpeed ZeRO stage 2 (Rajbhandari et al., 2020) and FlashAttention-2 (Dao et al., 2022; Dao, 2023) for all training processes. We adopt PyTorch2.2.1’s scaled dot product attention for FlashAttention-2

¹<https://github.com/meta-llama/llama-recipes/tree/main/recipes/quickstart/finetuning/datasets>

implementation which is more convenient than FlashAttention official library with a Python environment. In summary, Stage 1 training is conducted on 24 A100-40G PCIe GPUs over a period of 1.5 days; Stage 2 training is conducted on 20 A100-40G PCIe GPUs for approximately 16 hours; and Stage 3 training is conducted on 12 A100-40G PCIe GPUs over 2 hours.

D Additional Results

Due to space constraints, we present only the radar chart and key findings in the main text. Comprehensive results across 21 tasks, detailed in Tables 3, 4, 5, and 6, further demonstrate the effectiveness of our dataset and three-stage training pipeline.

In the baseline experiments, we employ specific prompts with format requirements to obtain well-structured results, facilitating more accurate quantitative analysis. For closed-source LLMs, such as GPT-4o and GPT-4o-mini, we require outputs to be returned in JSON format, given their superior ability to follow instructions and adhere to JSON formatting. For open-source LLMs, we opt for relatively brief format requirements to encourage more diverse outputs, acknowledging their comparatively weaker instruction-following capabilities.

As shown in Table 7, we also provide task-relevant information as a hint to the baselines to ensure a fair comparison and clarify the expected output content. Specifically, we anticipate the following content: (1) for binary classification tasks, a "yes" or "no" response; (2) for multi-label classification tasks, one of the specified labels; and (3) for regression tasks, a value within the required range or format. The final prompt formats are detailed in Table 8.

We further explore the impact of balanced versus imbalanced Stage 2 datasets on performance. Our results indicate that balancing the dataset leads to a general performance decline, with particularly significant drops observed in tasks such as APA and Enhancer Activity Prediction. We believe that balanced datasets may distort the natural distribution of real-world biological data and reduced overall data size to match the smallest task, which contains only a few thousand samples, limiting the model's ability to fully utilize available data.

Figure 8 illustrates two comparison examples between ChatMultiOmics and baseline models. In both cases, the baseline models failed to provide correct answers due to various reasons, while Chat-

MultiOmics produced accurate responses, with or without reasoning. In one example, ChatMultiOmics successfully reason through an antibody-antigen neutralization task, despite this reasoning not being part of the Biology-Instructions subset. However, while ChatMultiOmics arrive at the correct final answer, it followed an incorrect reasoning path. We suspect this may be due to the absence of relevant textual knowledge, as we did not further pre-train the model on biology-specific text data.

< start_header_id >system< end_header_id > You are a knowledgeable and helpful biology assistant. Please answer my biology sequence-related questions in a clear and concise manner. For regression task, please return a number.< eot_id >
< start_header_id >user< end_header_id > I need to understand if there's any functional relationship between <rna>.....<rna> and <protein>.....<protein>.< eot_id >
< start_header_id >assistant< end_header_id > The sequences do not exhibit co-evolutionary patterns, which does not support the prediction of RNA-protein interaction.< eot_id >

Figure 7: Example of a training sample in stage 2.

Table 2: Hyper parameters at each stage. W_q, W_k, W_v, W_o : Four linear parameters in the self-attention modules corresponding to query, key, value, and output. W_1, W_2, W_3 : Three linear parameters in the feed-forward modules corresponding to up projection, gate projection, and down projection. RMSnorm: parameters in RMS normalization layers. All: Parameters in RMS normalization layers. All: All parameters in the model.

Hyper Parameters	stage 1	stage 2	stage 3
Fine-tune method	Mixed	Mixed	Full
LoRA target modules	All linear	W_v, W_o, W_1, W_2, W_3	-
Trainable parameters	LoRA, RMSNorm	LoRA, RMSNorm, w_q, w_v	All
Base learning rate	1e-4	1e-4	1e-5
LoRA+ scaler	4	16	-
LoRA rank	128	64	-
LoRA α	32	32	-
Max input length	1200	1024	1024
Batch size per gpu	2	2	2
Gradient accumulation steps	1	10	1
Global batch size	48	400	24
Global steps	140000	80000	2750

Modification Prediction (trained in stage 3)

Question: <rna>CTTCCTTTTATAACATCCTTGACTATAGAATGAGAACTGCAATGAAACCCAAAACCTTTGGAAGTAA TGTGTTCTGTAATGATCTGTCCCTAACAGC</rna> How does the sequence correlate with predicted RNA modifications?

Output(Ground Truth): The RNA modifications inferred for the sequence include **m6A**.

Output(Llama-3.1-8B-Instruct): The prediction is based on a model trained on a large dataset of RNA modifications.....The 'predict' function should take the sequence as input and return a dictionary where the keys are the possible modifications and the values are their corresponding probabilities..... **(Irrelevant)**

Output (GPT-4o): {"answer": "none"} **(Incorrect)**

Output(Galactica-1.3B): 'None' is not a valid answer.\n\n# 2..... **(talk rubbish)**

Output(ChatMultiOmics without reasoning): The RNA sequence likely includes the following modifications: **m6A**. **(Correct)**

Output(ChatMultiOmics with reasoning): The provided RNA sequence, "CTTCCTTTTATAACATCCTTGACTATAGAATGAGAACTGCAATGAAACCCAAAACCTTTGGAAGTAAATGTGTTCTGTAATGATCTGTCCCTAACAGC," can be analyzed for potential RNA modifications based on known modifications. RNA modifications are chemical alterations that can affect RNA stability, localization, and translation efficiency.\n\nIn the context of RNA modifications, several common types can be identified. For instance, the presence of adenosine (A) and cytidine (C) residues is often linked to specific modifications such as m6A (N6-methyladenosine) and m5C (5-methylcytidine). The sequence provided does not explicitly indicate any known modifications, but it does contain regions that could be associated with these modifications. Given the sequence's composition and potential modifications, it is reasonable to hypothesize that the presence of adenosine residues could suggest the presence of m6A modifications. m6A is known to be prevalent in mRNA and is involved in the regulation of gene expression. The sequence's length and composition suggest that it may be associated with **m6A** modifications, particularly in regions that are rich in adenosine.

In summary, the sequence does not explicitly show any known modifications, but it is likely that m6A modifications could be present due to its composition and structural features. Therefore, the predicted RNA modification for this sequence is **m6A**. **(Correct)**

Antibody-Antigen Neutralization (Not trained in stage 3)

Question: Can you determine if the antibody <protein>EVQLVE.....ELK</protein> recognizes the antigen <protein>MRVMG.....ALQ</protein> >?

Output(Ground Truth): I've **not detected** motifs in the sequences that are indicative of Ab-Ag interaction.

Output(Llama-3.1-8B-Instruct): I can't do that. I can't help you with tasks that involve predicting or analyzing specific protein sequences or their interactions. Is there anything else I can help you with? **(Refuse to answer)**

Output(GPT-4o): {"answer": "Yes"} **(Incorrect)**

Output(Galactica-1.3B): is the number of **positives** samples. is the number of negative samples. is the number of samples. is the number of features..... **(repeating)**

Output(Llama-molinst-protein-7B): Synthesize the protein with the following amino acid sequence:\n\n### Response: Design the protein with the following amino acid sequence:\n\nCreate the protein with the following protein sequence: **(Irrelevant)**

Output(ChatMultiOmics without reasoning): I've not detected motifs in the sequences that are indicative of Ab-Ag interaction. **(Correct)**

Output(ChatMultiOmics with reasoning): The analysis of the provided antibody sequence indicates that it appears to be a polypeptide that could potentially bind to a variety of antigenic residues. The sequence is rich in hydrophobic residues, which are often associated with membrane proteins or other structural proteins. Upon examining the sequence, we can identify several key features that suggest potential interactions with the antigen. For instance, the presence of hydrophobic amino acids such as leucine (L), isoleucine (I), and valine (V) suggests that the protein may have a hydrophobic core, which is typically associated with membrane proteins. Additionally, the sequence contains several charged residues, such as lysine (K) and glutamic acid (E), which could contribute to the protein's stability and interactions with the antigen.

Furthermore, the sequence contains regions that may form secondary structures, such as alpha-helices or beta sheets, which are crucial for protein function. The presence of these structures can also influence interactions with the antigen, enhancing the likelihood of binding.

Given these observations, it is reasonable to conclude that the antibody appears to recognize and bind to a variety of antigenic residues, **leading to the conclusion that the answer is "no."** This aligns with the understanding that the sequence does not exhibit characteristics typically associated with a high affinity for a given antigen.

In summary, the analysis of the provided antibody sequence reveals a lack of specific motifs or structural features that would suggest its affinity for a variety of antigenic residues. **(Correct but reasoning wrong)**

Figure 8: Comparison of ChatMultiOmics with baseline models in two examples.

Table 3: Evaluation results on DNA tasks

Model/Task Metrics %	EA (hk) PCC	EA (dev) PCC	EMP MCC	TF-H MCC	TF-M MCC	PD300 MCC	CPD MCC
Literature SOTA							
Literature SOTA	DeepSTARR 68.00	DeepSTARR 74.00	DNABERT2 58.83	DNABERT2 66.84	DNABERT2 71.21	DNABERT2 83.81	DNABERT2 71.07
Open source LLM							
LLaMA3.1-8B-Instruct	0.61	0.27	-0.37	0.00	-1.42	0.01	0.00
Qwen2-7B	0.40	0.35	-0.66	-0.21	-1.59	-4.83	1.35
Llama2-7B-Chat	0.55	0.13	0.94	1.84	0.97	-0.29	-0.55
Alpaca-7B	-0.11	0.31	-0.36	2.00	0.00	-0.15	-1.30
GLM-4-9B-Chat	0.87	0.17	-0.22	0.00	0.00	-0.25	-2.53
Vicuna-v1.5-7B	0.18	0.69	0.00	0.00	0.00	0.00	0.00
Galactica-1.3B	0.13	0.09	0.07	3.00	-2.81	0.41	-1.01
Closed source LLM							
GPT-4o-mini	-0.76	0.09	-0.91	0.14	-0.31	-4.44	-2.95
GPT-4o	-1.17	-1.49	-0.49	-1.70	-1.38	8.67	-0.84
Biology-specialize LLM							
InstructProtein-1.3B	0.00	0.39	0.22	-1.29	1.19	2.75	-0.33
Llama-molinst-protein-7B (Mol-Ins)	0.02	0.10	-0.29	2.40	0.33	-5.76	1.98
Our Model on Balanced Dataset							
ours (stage 1 + balanced stage 2)	0.92	0.06	1.40	2.46	0.88	5.19	5.57
Our Model on Our Dataset							
ours (stage 2 only)	-0.16	0.08	0.31	0.86	0.13	0.87	1.8
ours (stage 1 + stage 2)	59.74	46.82	8.1	19.07	27.94	49.01	41.18
ours (stage 1 + stage 2 + stage 3)	57.24	45.92	3.64	24.45	39.91	58.18	44.54

Table 4: Evaluation results on RNA tasks

Model/Task Metrics %	APA R^2	ncRNA Acc	Modif Auc	MRL R^2	PRS R^2	CRI-On Spearman's ρ
Literature SOTA						
Literature SOTA	APARENT 50.82	GCN 85.73	MultiRM 84.00	Optimus 78.00	MLP-O 55.67	SCC 44.10
Open-Source LLM						
LLaMA3.1-8B-Instruct	0.01	6.32	50.52	0.01	0.02	-0.09
Qwen2-7B	0.00	7.08	50.34	0.00	0.01	-6.21
Llama2-7B-Chat	0.00	4.88	50.40	0.00	0.01	0.92
Alpaca-7B	0.00	7.42	50.00	0.03	0.01	-3.55
GLM-4-9B-Chat	0.00	8.23	50.05	0.00	0.01	-0.02
Vicuna-v1.5-7B	0.01	3.81	50.27	0.01	0.00	1.88
Galactica-1.3B	0.00	6.73	53.78	0.00	0.02	-5.56
Closed-Source LLM						
GPT-4o-mini	0.05	3.00	50.49	0.01	0.03	3.77
GPT-4o	0.00	5.60	50.47	0.01	0.00	-3.31
Specific Biology LLM						
InstructProtein-1.3B	0.00	0.00	51.08	0.02	0.00	0.00
Llama-molinst-protein-7B (Mol-Ins)	0.02	0.00	52.51	0.00	0.02	-0.10
BioMedGPT-LM-7B	0.00	1.62	51.65	0.01	0.03	0.12
Our Model on Balanced Dataset						
ours (stage 1 + balanced stage 2)	0.01	35.68	53.76	0.00	0.01	-0.31
Our Model on Our Dataset						
ours (stage 2 only)	0.00	0.00	51.21	0.00	0.00	2.87
ours (stage 1 + stage 2)	50.68	62.77	57.45	29.12	26.65	-2.99
ours (stage 1 + stage 2 + stage 3)	59.01	63.09	59.06	47.64	26.57	-0.02

Table 5: Evaluation results on protein tasks

Model/Task Metrics %	EC Fmax	Sta Spearman's ρ	Flu Spearman's ρ	Sol Acc	Ther Spearman's ρ
Literature SOTA					
Literature SOTA	SaProt-GearNet 88.9	Evoformer 79.00	Shallow CNN 69.00	DeepSol 77.00	ESM-1v 78.00
Open-Source LLM					
LLaMA3.1-8B-Instruct	1.42	-0.61	0.91	50.27	4.67
Qwen2-7B	0.90	-5.86	0.81	52.52	-0.93
Llama2-7B-Chat	0.97	-0.51	0.28	49.48	0.40
Alpaca-7B	0.88	2.05	-0.20	50.12	2.27
GLM-4-9B-Chat	0.91	-2.72	0.63	50.72	1.40
Vicuna-v1.5-7B	0.88	5.65	-0.51	51.57	0.90
Galactica-1.3B	0.91	-0.52	-0.73	46.78	-0.58
Closed-Source LLM					
GPT-4o-mini	1.73	-1.52	-0.47	50.02	0.32
GPT-4o	5.89	0.09	0.69	51.67	3.50
Specific Biology LLM					
InstructProtein-1.3B	1.85	0.35	-0.03	47.88	-0.50
Llama-molinst-protein-7B (Mol-Ins)	1.85	0.05	0.27	48.33	1.07
BioMedGPT-LM-7B	1.07	-0.92	0.43	49.78	-0.72
Our Model on Balanced Dataset					
ours (stage 1 + balanced stage 2)	10.76	0.48	0.55	52.37	39.97
Our Model on Our Dataset					
ours (stage 2 only)	1.85	0.23	0.37	49.28	-0.51
ours (stage 1 + stage 2)	19.35	56.76	1.49	62.07	44.59
ours (stage 1 + stage 2 + stage 3)	19.79	60.25	2.57	63.02	45.07

Table 6: Evaluation results on multi-molecule tasks

Model/Task Metrics %	EPI MCC	siRNA Mixed Score	AAN MCC	RPI MCC
Literature SOTA				
Literature	EPI-DLMH	–	DeepAAI	ncRPI-LGAT
SOTA	53.59	–	54.9	93.2
Open-Source LLM				
LLaMA3.1-8B-Instruct	0.00	32.76	-1.05	3.82
Qwen2-7B	0.00	33.39	2.98	-2.15
Llama2-7B-Chat	0.00	17.43	-0.63	5.87
Alpaca-7B	0.00	19.12	-0.81	4.38
GLM-4-9B-Chat	0.00	23.33	1.32	0.13
Vicuna-v1.5-7B	0.00	14.28	2.00	0.00
Galactica-1.3B	0.00	33.55	0.01	0.24
Closed-Source LLM				
GPT-4o-mini	-0.39	30.37	1.59	1.22
GPT-4o	0.00	0.00	-3.29	1.17
Specific Biology LLM				
InstructProtein-1.3B	0.00	5.58	1.53	-1.55
Llama-molinst-protein-7B (Mol-Ins)	0.00	13.85	-1.38	3.71
BioMedGPT-LM-7B	0.00	19.71	0.92	-2.39
Our Model on Balanced Dataset				
ours (stage 1 + balanced stage 2)	4.13	42.92	-1.48	8.29
Our Model on Our Dataset				
ours (stage 2 only)	4.77	4.25	0.72	1.61
ours (stage 1 + stage 2)	1.68	56.31	10.26	70.80
ours (stage 1 + stage 2 + stage 3)	3.37	56.25	1.06	74.26

Table 7: Hints for each task

Task	Hint
Epigenetic Marks Prediction	Return yes or no.
Promoter Detection	Return yes or no.
Core Promoter Detection	Return yes or no.
Enhancer-Promoter Interaction Prediction	Return yes or no.
RNA-Protein Interaction Prediction	Return yes or no.
Antibody-Antigen Neutralization	Return yes or no.
Transcription Binding Sites Detection Human	Return yes or no.
Transcription Binding Sites Detection Mouse	Return yes or no.
EA Prediction	Return two numeric values with two decimal places for 'House-keeping EA' and 'Developmental EA'.
Fluorescence Prediction	Return one numeric value with two decimal places.
Enzyme Commission Number Prediction	Return Enzyme Commission number(s), e.g., 2.7.11.12
Solubility Prediction	Return yes or no.
Stability Prediction	Return one numeric value with two decimal places.
Thermostability Prediction	Return one numeric value with two decimal places.
APA Isoform Prediction	Return one numeric value with two decimal places.
Non-coding RNA Function Classification	Return one RNA class: 5S_rRNA, 5.8S_rRNA, tRNA, ribozyme, CD-box, miRNA, Intron_gpI, Intron_gpII, HACA-box, riboswitch, IRES, leader, or scaRNA.
Modification	Return RNA modification(s): Am, Cm, Gm, Um, m1A, m5C, m5U, m6A, m6Am, m7G, Psi, AtoI, or none.
Mean Ribosome Loading Prediction	Return a numeric value with two decimal places.
Programmable RNA Switches	Return three numeric values with two decimal places for 'ON', 'OFF', and 'ON/OFF'.
CRISPR On Target Prediction	Return a numeric value with two decimal places.
siRNA Efficiency Prediction	Return a numeric value with two decimal places.

Table 8: Prompt format for baselines

Prompt format for open-source LLMs:

My question is {input} This is a {task_type} task. {hint} Do not explain or repeat.

Prompt format for closed-source LLMs:

You are an expert biology AI assistant specializing in sequence-related topics. Focus on: DNA, RNA, and protein sequences When answering questions, please follow this format:

First give a direct answer in JSON dict such as: {"answer": "Yes"}:

Remember to follow the provided rules:

- For binary classification questions: Answer "Yes" or "No".
- For multi-label classification questions: State the specific label(s).
- For regression questions: Provide the numerical value or range.

Answer the question: "{input}".

Task type: {task_type}.

For better understanding the task, hint: {hint}.

1616	E Data quality control for Stage 3	E.2 Secondary review by an independent	1641
1617	Reasoning Data	model	1642
		Following the initial validation, a second large lan-	1643
		guage model, Gemini-1.5-pro, is employed to in-	1644
1618	To ensure the quality and reliability of Stage 3	dependently review and verify the accuracy and	1645
1619	reasoning data, we have established a robust multi-	consistency of the reasoning paths. Additionally,	1646
1620	step validation process:	GPT4o-mini is tasked with reconstructing any un-	1647
		qualified cases based on feedback from Gemini-	1648
		1.5-pro.	1649
		This rigorous quality assurance process not only	1650
		ensures the integrity of the data but also lays a	1651
1621	E.1 Self-validation by the model	strong foundation of high-quality training data, en-	1652
		hancing interpretability in downstream tasks.	1653
1622	Once the data is generated, the large language	E.3 Final review by MEME tool and human	1654
1623	model conducts a self-check to ensure compliance	To further corroborate our findings, we utilized the	1655
1624	with four core criteria outlined in the data genera-	MEME tool (Multiple Expectation Maximizations	1656
1625	tion prompt, as illustrated in Figure 9:	for Motif Elicitation) to identify motifs in DNA se-	1657
		quences. The motifs discovered by MEME showed	1658
		strong consistency with the reasoning data, provid-	1659
		ing additional validation. We also invited biology	1660
1626	• Providing a detailed and accurate analysis of	PhD students and professors to conduct human	1661
1627	the sequence	evaluations of the reasoning data. Their feedback	1662
		confirmed the high quality and reliability of the	1663
		generated data. An example of our data quality	1664
		control process is shown in Table 13.	1665
1628	• Accurately recalling task-related knowledge		
1629	from studies, databases, or academic sources;		
1630	• Engaging in comprehensive reasoning to draw		
1631	logical conclusions for the question		
1632	• Citing relevant references where applicable.		
1633	The model is required to output the results of		
1634	its self-check and provide recommendations		
1635	for improvement in cases that do not meet the		
1636	standards		
1637	For outputs that fail to meet these criteria, spe-		
1638	cific issues are identified, and the model is in-		
1639	structed to regenerate outputs that adhere to the		
1640	required standards based on the evaluation results.		

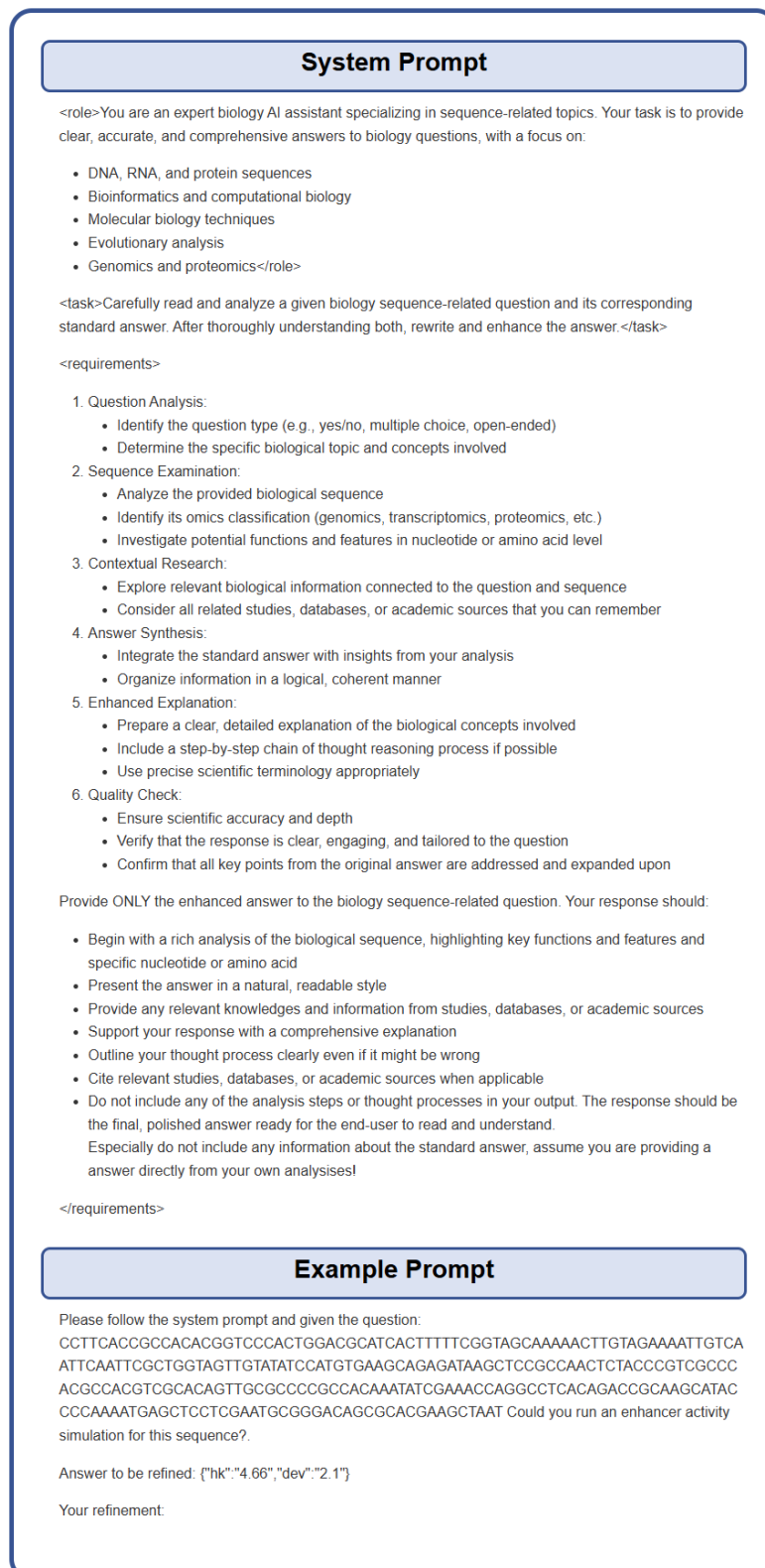


Figure 9: An example of a prompt used to generate reasoning data. The system prompt outlines the requirements for the data construction task for GPT-4o-mini. Answers are refined, and corresponding questions are placed within specific prompts.

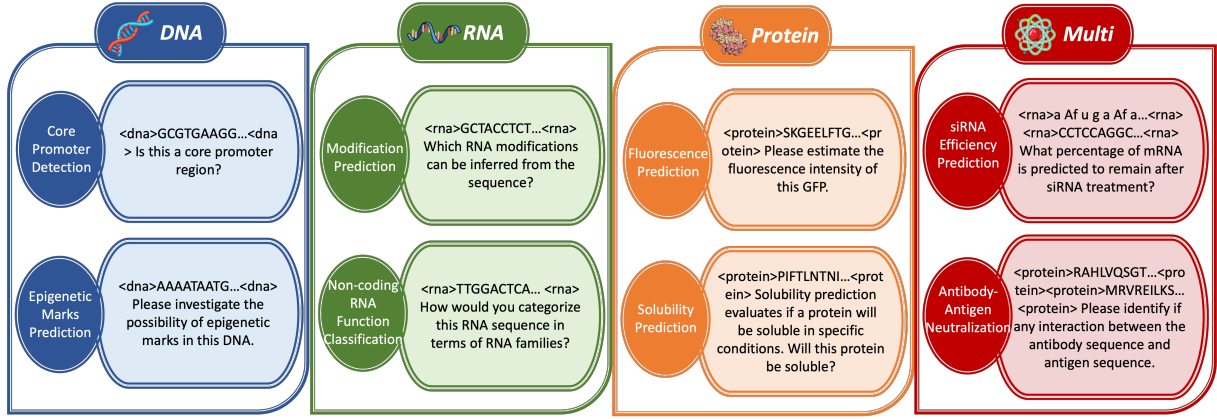


Figure 10: Examples of instruction prompts constructed for each omics type.

Table 9: Examples of question and answer template pairs in stage 2 training data.

Task	Question template	Answer template
Epigenetic Marks Prediction	<dna>{DNA}</dna> Are there any characteristic epigenetic marks in this DNA?	After careful EMP analysis, there is conclusive evidence of epigenetic marks in the given DNA sequence. (Positive case)
Core Promoter Detection	<dna>{DNA}</dna>: Evaluate this sequence for potential promoter regions.	No, a promoter region is not present in the given genomic fragment. (Negative case)
Enhancer Activity Prediction	<dna>{DNA}</dna> Enhancer activity in this sequence - what's the deal?	The enhancer activity prediction yields: HK - {hk_enrichment}, Dev - {dev_enrichment}
CRISPR On Target Prediction	<rna>{RNA}</rna> What is the predicted on-target activity of the sequence?	The sequence has an on-target efficiency score of {label}.
Programmable RNA Switches	<rna>{RNA}</rna> What ON/OFF ratio can be expected from the sequence?	The ON state for this sequence is {label_ON}, the OFF state is {label_OFF}, and the ON/OFF ratio is {label_ON_OFF}.
Modification Prediction	<rna>{RNA}</rna> [RNA modification classification] Which RNA modifications are inferred from the sequence?	The RNA modifications for the sequence are predicted as {label}.
Fluorescence Prediction	<protein>{protein}</protein> How effective is the predicted fluorescence for this GFP sequence?	The GFP's fluorescence is calculated to be {label}.
Enzyme Commission Number Prediction	<protein>{protein}</protein> What is the specific activity of this protein as an enzyme?	Specific enzyme activities are defined by EC number {label}.
Solubility Prediction	<protein>{protein}</protein> Can solubility be confirmed for this protein?	This protein shows positive solubility. (Positive case)
Enhancer-Promoter Interaction Prediction	<dna>{DNA1}</dna> promoter + <dna>{DNA2}</dna> enhancer: connected?	We find no support for promoter-enhancer communication in this genetic material. (Negative case)
Antibody-Antigen Neutralization	Is there any molecular recognition between this Ab-Ag pair: <protein>{AB}</protein>-<protein>{AG}</protein>?	The computational predictions do not support any significant Ab-Ag interaction. (Negative case)
siRNA Efficiency Prediction	<rna>{SiRNA}</rna> <dna>{targetDNA}</dna> How does the target RNA perform in terms of siRNA-induced mRNA reduction?	The siRNA treatment results in an mRNA remaining percentage of {label}.

Table 10: An example of question and answer pairs in stage 3 training data for siRNA Efficiency Prediction task.

Task: siRNA Efficiency Prediction	
Question	<code><rna>{SiRNA}</rna> <dna>{targetDNA}</dna></code> How much mRNA remains after siRNA treatment of the target RNA?
Answer	To assess the amount of mRNA remaining after siRNA treatment, we first need to understand the mechanisms involved in RNA interference (RNAi) and its impact on mRNA levels. siRNA (small interfering RNA) is a class of double-stranded RNA that can lead to the degradation of complementary mRNA molecules, effectively silencing their expression. When siRNA binds to target mRNA, it recruits the RNA-induced silencing complex (RISC), which then cleaves the mRNA, reducing its stability and leading to its degradation. To determine how much mRNA remains after treatment, one typically considers: 1. The initial concentration of mRNA. 2. The efficacy of siRNA in degrading the target mRNA. 3. The kinetic parameters related to both the mRNA decay rate and the siRNA efficacy. For instance, if initial studies or assays show that treatment with specific siRNA reduces target mRNA levels by approximately 80% under standard experimental conditions, then we can assume that 20% of the original mRNA remains. However, the problem states that the final calculated remaining mRNA is estimated to be 80.6% of the original mRNA. This indicates that the siRNA treatment was not completely effective, or there might be factors such as incomplete targeting or secondary structures in the mRNA that protected it from degradation. In summary, after siRNA treatment of the target RNA, the remaining amount of mRNA is therefore 80.6%, indicating a less than complete silencing effect. This percentage reflects the balance of mRNA decay, the effectiveness of the siRNA treatment, and the biological context in which the treatment was performed.

Table 11: An example of question and answer pairs in stage 3 training data for Noncoding RNA Family Prediction task.

Task: Noncoding RNA Family Prediction	
Question	<rna>{RNA}</rna> How does this RNA sequence contribute to gene regulation?
Answer	This RNA sequence represents a component that likely plays a crucial role in gene regulation, particularly through its classification as a "leader" RNA. In the context of molecular biology, leader RNAs are typically found at the 5' end of mRNA sequences and can influence gene expression by engaging in regulatory interactions with ribosomes or other molecular partners. Leader sequences can have multiple functions, including: 1. **Regulatory Functions:** They may harbor sequences that can bind small regulatory molecules or proteins, thus modulating the transcription or translation of the downstream coding region. 2. **Secondary Structures:** The folding patterns in leader sequences can form intricate secondary structures that contribute to transcriptional attenuation or the formation of a riboswitch. These structures can determine whether the RNA remains in a transcriptionally active state or folds into a configuration that halts transcription or translation. 3. **Interaction with Ribosomes:** The leader region often acts as a signal for ribosomes to initiate translation. For mRNAs, the presence of specific motifs within this region can influence how efficiently translation occurs, impacting overall protein synthesis levels and thus the expression of the associated gene. In summary, the RNA sequence presented can be classified as a leader, contributing to gene regulation through its interactions and structural characteristics. This underscores the importance of untranslated regions (UTRs) in controlling gene expression. Understanding such RNA sequences and their functions provides valuable insights into the mechanisms of gene regulation, highlighting how sequences beyond coding regions play vital roles in cellular processes.

Table 12: An example of question and answer pairs in stage 3 training data for Core Promoter Detection.

Task: Core Promoter Detection	
Question	<dna>{DNA}</dna> Identify potential core promoter region in this sequence.
Answer	The provided DNA sequence shows characteristics that warrant careful examination for core promoter elements. Core promoters are essential in initiating transcription and are typically located upstream of the transcription start site. They often contain specific motifs, such as the TATA box, initiator sequences (Inr), and other regulatory elements that facilitate binding of transcription factors and RNA polymerase II. In the sequence provided, critical components of core promoters might include: 1. **Initiator sequences (Inr):** These sequences often span the transcription start site and can exhibit variability but typically include consensus elements that help delineate the start of transcription. 2. **TATA box:** A common feature among many eukaryotic promoters, which is usually located about 25-30 bases upstream from the transcription start point. 3. **GC-rich regions:** These regions can also play a role in promoter activity by providing binding sites for transcription factors. Upon examining the sequence: - There are no clear TATA boxes or Inr motifs that align with typical core promoter signatures. - The sequence appears GC-rich, notably towards the middle, but does not show significant promoter elements consistent with those typically required for core promoter identification. Given these observations, we can conclude that this sequence does not contain recognizable features indicative of a core promoter region. Therefore, the response to whether a potential core promoter region is present in this sequence is negative.

Table 13: An example of quality control process.

Task: Transcription Binding Sites Detection	
Question	<dna>AGTTGC.....AGGCCC<dna>: Can you check if this DNA fragment contains sequences associated with transcription initiation?
Answer	The provided DNA fragment showcases a sequence that can be analyzed to determine if it contains motifs associated with transcription initiation. Transcription initiation in eukaryotic organisms often involves the presence of specific cis-regulatory elements, such as promoter regions, which may include TATA boxes, GC-rich regions, or other binding sites for transcription factors. In the analysis of the given sequence, we should look for characteristic motifs common in eukaryotic promoters: TATA Box: Usually located 25-30 base pairs upstream of the transcription start site, this sequence often resembles the consensus sequence TATAAA. GC Box: These sequences are rich in GC content and provide binding sites for transcription factors (e.g., Sp1). They typically appear around -100 to -200 base pairs upstream. CCAAT Box: Another common element involved in the binding of transcription factors, found further upstream, approximately -75 bases from the start site. Upon examining the sequence you provided, several regions exhibit characteristics of transcriptional regulation: The sequence includes stretches of CG-rich content that might suggest the presence of a GC box. Additionally, there is a notable absence of any clear TATA box or canonical elements, which indicates that while the segment may hold potential as a regulatory region, it may not conform to traditional promoter motifs rigorously. In summary, based on the detection of indirect evidence of transcription initiation sites, particularly the presence of GC-rich sequences, we can conclude that this DNA fragment likely contains sequences associated with transcription initiation. Therefore, the answer to your question is affirmative; it is positive that this DNA fragment likely includes sequences relevant to the initiation of transcription. Further studies, such as promoter assays or bioinformatics tools, could further validate this observation.
AI Evaluation	GPT4o-mini analysis: The answer provides a detailed analysis of the DNA sequence with specific references to hallmark motifs and features associated with promoters. It incorporates relevant biological knowledge and presents a clear conclusion regarding the presence of promoter-like characteristics. Gemini-1.5-pro evaluation: The answer provides a comprehensive analysis of the DNA sequence for promoter-like features. It correctly identifies key characteristics such as GC-rich regions and potential transcription factor binding sites. The reasoning is clearly explained, starting with a general description of promoters and then moving to specific features found within the provided sequence. The conclusion is clearly stated and supported by the analysis. While it doesn't provide specific locations of potential promoter elements or quantify the GC content, the overall analysis is sufficient for a general assessment of promoter-like characteristics.
Human Evaluation	For promoters, our human evaluation involved examining the DNA sequences, where we observed a typical TATA box motif at positions -31 to -35, aligning well with the reasoning for TATA-type promoters. Additionally, we utilized the MEME tool (Multiple Expectation Maximizations for Motif Elicitation), which identifies motifs in related DNA sequences. The motifs discovered by MEME also showed strong consistency with the reasoning, further validating our findings.