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ProteinChat: Towards Achieving ChatGPT-Like Functionalities on Protein 3D Structures

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Abstract

The study of proteins is critical in various scientific disciplines, but understanding their complex structure-function relationships remains challenging. Recent advancements in large language models (LLMs) have demonstrated their ability to comprehend task-specific knowledge, suggesting the potential for specially trained ChatGPT-like systems to accelerate protein research. In this work, we introduce ProteinGPT, a prototype model aimed at learning and understanding protein 3D structures. ProteinGPT enables users to upload proteins, ask questions, and engage in interactive conversations to gain insights. The ProteinChat system consists of three main components: a composite encoder block, a projection layer, and an LLM. The protein undergoes encoding to form a protein embedding, which is then projected to conform with the LLM. The LLM combines user questions with the embedding to generate informative answers. To train ProteinChat, we curated the RCSB-PDB Protein Description Dataset, comprising 143,508 protein-description pairs from publicly available sources. By leveraging the capabilities of ProteinGPT, researchers can potentially expedite their investigations into protein functionalities and structures, benefiting areas such as drug development and therapeutics, food science and nutrition, and various aspects of our lives. This initial step lays the foundation for further exploration and utilization of the ChatGPT-like system in protein research. The code is available at <https://github.com/UCSD-AI4H/proteinchat> and the dataset can be downloaded from https://drive.google.com/file/d/1AeJW5BY5C-d8mKJjAULTax6WA4hzWSON/view?usp=share_link.

1 Introduction

Proteins play a critical role in biological processes, and understanding the structure, function, and interactions of proteins is crucial to the advancement of biological and biomedical research. However, traditional protein engineering involves manual and often laborious processes of studying proteins through laboratory experiments and extensive literature reviews. This can be time-consuming and requires specialized knowledge and resources. The field is progressively adopting computational methods, such as those used in protein structure prediction [5], but there is still a significant and urgent need for tools that can intuitively process and extract valuable insights from protein structures.

This technical report introduces the concept of applying ChatGPT-like capabilities to protein 3D structures, which could be a powerful tool that could greatly advance our understanding of biology and accelerate the development of new treatments for diseases. This AI-based protein query system is capable of understanding protein 3D structures and answering various questions about these proteins, and can be beneficial in several ways:

- **Accelerating Research.** Such a system would make it easier for researchers to find relevant information about specific proteins, their functions, structures, interactions, mutations, and related diseases. This could significantly speed up research in fields such as drug discovery, molecular biology, and genetics.

- **Improving Understanding of Protein Function.** Proteins are the workhorses of the cell, and understanding their function is crucial for understanding how life works at a molecular level. A system that can provide accurate, detailed information about protein function would be a valuable tool for educators and students.
- **Personalized Medicine.** In the field of personalized medicine, understanding the patient’s unique protein structures can guide the development of personalized treatments. A system that can quickly and accurately provide this information could revolutionize the way we approach healthcare.
- **Drug Discovery.** The process of drug discovery involves understanding how potential drug molecules interact with target proteins in the body. An AI system for protein queries can help identify potential drug targets and predict the effects of drug candidates.
- **Disease Diagnosis and Treatment.** Many diseases are associated with changes in protein structure or function. Understanding these changes can help in the diagnosis and treatment of diseases. For example, a system like this could potentially provide insights into the protein-related mechanisms behind cancer, neurodegenerative diseases, and other conditions.
- **Data Analysis.** The number of known proteins and the amount of data related to each of them is immense. Manual analysis of this data would be time-consuming and challenging. An AI system could quickly analyze this data and provide useful insights.

Developing a ChatGPT-like system for proteins poses significant challenges that need to be addressed. Firstly, a major hurdle is the encoding of proteins. Unlike sequential and well-structured text data, proteins are complex molecules with diverse structures and functions. Consequently, developing a methodology to represent proteins in a format compatible with GPT models becomes crucial. Secondly, a substantial amount of protein-related information exists in unstructured formats, such as scientific literature. Extracting meaningful insights from such data necessitates sophisticated natural language processing capabilities to effectively handle the complexities and nuances of scientific texts. Thirdly, training such a system requires large datasets encompassing protein structures and their associated literature. However, generating or compiling such datasets is a challenging task due to the proprietary nature of much of this information and the vast diversity within the biological space. Addressing these challenges will be crucial in the development of a successful ChatGPT-like system tailored for proteins. Overcoming the encoding, natural language processing, and dataset limitations will pave the way for an intuitive and comprehensive platform for protein-related research and analysis.

This technical report presents our initial endeavor to empower ChatGPT-like capabilities for three-dimensional protein structures through the development of a prototype system called ProteinChat. Inspired by ChatGPT, ProteinChat operates on the same principles. Users can upload protein 3D structures (e.g., PDB format, widely used for files containing atomic coordinates) and pose diverse questions regarding them. ProteinChat adeptly engages in multi-turn, interactive conversations to provide comprehensive answers to these inquiries. By leveraging ProteinChat, users can gain valuable insights and explore the intricacies of protein structures in an interactive and intuitive manner.

The ProteinChat system comprises three key components: a GVP-Transformer block [4], a projection layer, and a large language model. To begin, the GVP-Transformer block receives the 3D structure of a protein as input and effectively learns a representation that captures translation-invariant and rotation-equivalent features. This enables the system to extract crucial information from the protein structure. The projection layer further encodes the protein embeddings generated by the GVP-Transformer block, aligning them with the requirements of the LLM. Finally, the LLM leverages the composite representation of the encoded protein, along with the users’ prompt related to the current protein, to generate insightful and contextually relevant answers. Through the collaborative functioning of these components, ProteinChat enables seamless interactions and facilitates accurate responses based on the protein’s structural information and user queries. For our project, we specifically utilize the Vicuna-13b LLM [2] and a pre-trained GVP-Transformer from ESM-IF1 [4] as the protein encoder block. During the training phase, we freeze the protein encoder block and the LLM, solely focusing on training the projection layer. To train the ProteinChat model, we construct the RCSB-PDB Protein Description Dataset, which pairs protein structures with corresponding textual descriptions, from the publicly available RCSB-PDB database.

The major contributions of this technical report are as follows:

- We propose the ProteinChat, a prototype ChatGPT-like model that is capable of engaging Q&A with users and generating text descriptions for proteins based on their 3D structures.
- We introduce the RCSB-PDB Protein Description Dataset. This dataset contains 143,508 protein entries. Each entry consists of a protein 3D structure represented in backbone atomic coordinates and an abstract that describes this protein.
- To the best of our knowledge, ProteinChat is the first work that aims to harness the power of LLM to study proteins. Our work can be easily generated to other domains by changing the encoder and input data.

2 Related Works

Protein Science and Engineering is increasingly being influenced by computational approaches, especially with artificial intelligence. Large-scale protein structure prediction, as demonstrated by DeepMind’s AlphaFold [5], is a prime example of how AI is revolutionizing protein research. Meta proposed Evolutionary Scale Modeling (ESM) [7], including inverse folding (ESM-IF1) [4], as Transformer-based protein language models for structure prediction. The main goal of ESM-IF1 is to predict a protein sequence from its backbone atom coordinates, and in ProteinChat, we leverage the GVP-Transformer of ESM-IF1 to encode proteins from their 3D structures. However, generating or predicting protein properties based on protein 3D structures using LLMs is still a missing area, and our research made preliminary efforts towards bridging this gap by training both on the protein 3D structures and texts.

Large Language Models (LLMs) have shown impressive accomplishments in natural language processing tasks [3, 1]. Such models are typically trained on an extensive, diverse corpus, which includes resources like Wikipedia, web texts, and books. Two strategies often adopted to tailor LLMs for a specific task involve either training a new language model on a domain-specific database or adapting general LLMs for a specific task, the latter being our focus. For instance, scientific language models have been created based on a corpus of scientific knowledge. An example is Galactica by Meta AI [8], which explicitly modeled the sequences and SMILES (instead of the 3D structure in our work) of proteins with scientific literature, and make the model explain properties of the sequences. Further, the development of publicly accessible LLMs, including multi-modal variants, has allowed for the understanding of information in other modalities beyond text. We introduce three of them in the following, and our model is built upon these open-source projects.

LLaMA [9] is a general LLM model with 65 billion parameters developed by Meta AI. This model is trained on publicly accessible datasets including English CommonCrawl, C4, Github, Wikipedia, Gutenberg Project, ArXiv and Stack Exchange. With a size smaller than GPT-3, LLaMA achieves competitive performance on many tasks, including commonsense reasoning, question answering, reading comprehension and code generation. **Vicuna** [2] is an open-source chatbot trained by fine-tuning LLaMA on around 70,000 user-shared conversations with ChatGPT, with training costs as low as around \$300.

MiniGPT-4 [11] is a vision-language model that can process images and generate text interactively. It is built upon Vicuna and Lavis [6] for language and vision tasks. Users can upload their own images and then chat with the model based on those images. The architecture of MiniGPT-4 integrates a single linear projection layer, designed to capture the visual information from a pretrained vision encoder. Vicuna serves as the language decoder in this setup, while a ViT backbone operates as the visual encoder.

3 Method

3.1 Data Collection

The three-dimensional structures of proteins were sourced from the Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB) ¹, which includes 204,826 experimentally determined 3D structures. We utilized the data version last updated on May 17, 2023. Of these proteins, 163,635 have a primary publication linked with a PubMed ID. Among those, the PDB

¹<https://www.rcsb.org/>

format of 143,508 proteins can be extracted with a valid chain using Biotite, a Python library for computational molecular biology ², and these constituted the main focus of our study. For every protein taken into account, we compiled its 3D atomic coordinates, representing the molecular structure, along with the abstract of corresponding scientific literature to train our model. Table 3 shows some examples of the abstract data.

We also obtained various protein properties in multiple levels from Protein Data Bank. Entry level properties contain molecular weight and count of atoms. Entity level properties include the number of entities and their classification as polymer, non-polymer, branched molecular, or solvent entities. We also collected the statistics in assembly and instance level. Additionally, we collected protein-specific experimental details, such as whether the structure was determined using experimental or AlphaFold, and the methods of experiments. This information is directly requested from Protein Data Bank using its web service APIs. Based on these properties, we manually designed 30 question-answer pairs, asking about numbers, true/false questions, categories, and explanations. An example of Q&A for a specific protein is displayed in Table 2. Note that there are some missing values in the original data corpus, so the designed questions would be slightly different for each protein.

Table 1: Dataset statistics.

Data Format	Number of Entries	Total Size
Protein PDB files	143,508	121GB
Encoded PT files		83GB
Abstract TXT files		182MB

Table 2: An example of designed Q&A for a specific protein from the Protein Data Bank.

Protein PDB	1KIT.pdb
QA Pair 1	Q: How many assemblies does this protein have? A: 1.
QA Pair 2	Q: How many entities does this protein have? A: 3.
QA Pair 3	Q: Does this protein contain non-polymer entities? A: Yes.
QA Pair 4	Q: Does this protein contain polymer entities? A: Yes.
QA Pair 5	Q: Does this protein contain DNA polymer entities? A: No.
QA Pair 6	Q: Does this protein contain RNA polymer entities? A: No.
QA Pair 7	Q: Does this protein contain solvent entities? A: Yes.
QA Pair 8	Q: Does this protein contain branched entities? A: No.
QA Pair 9	Q: What is the polymer entity composition for this protein? Please choose from DNA, DNA/RNA, NA-hybrid, NA/oligosaccharide, RNA, heteromeric protein, homomeric protein, oligosaccharide, other type composition, other type pair, protein/NA, protein/NA/oligosaccharide, protein/oligosaccharide and other. A: Homomeric protein.
QA Pair 10	Q: What is the nucleic acid polymer entity type for this protein? Please choose from DNA (only), DNA/RNA (only), NA-hybrid (only), RNA (only) and others. A: Other.

²<https://github.com/biotite-dev/biotite>

QA Pair 11	Q: What are the bound nonpolymer components for this protein? A: CA.
QA Pair 12	Q: What experimental methods were used to determine the structure of this protein? Please choose from EM, Multiple methods, NMR, Neutron, X-ray and other. A: X-ray.
QA Pair 13	Q: What is the molecular mass (KDa) of polymer and non-polymer entities (exclusive of solvent) for this protein? A: 83.12.
QA Pair 14	Q: What's the polymer entity type for this protein? Choose from nucleic acid (only), oligosaccharide (only), protein (only), protein/NA, protein/oligosaccharide and other. A: Protein (only).
QA Pair 15	Q: What are the software programs reported in connection with this protein? A: DENZO, TNT.
QA Pair 16	Q: Is this protein determined by experimental or computational methods? A: Experimental methods.
QA Pair 17	Q: How many heavy atom coordinates records does this protein have? A: 6560.
QA Pair 18	Q: How many hydrogen atom coordinates records does this protein have? A: 0.
QA Pair 19	Q: How many model structures deposited for this protein? A: 1.
QA Pair 20	Q: How many polymer monomers does this protein have? A: 757.
QA Pair 21	Q: How many heavy solvent atom coordinates records does this protein have? A: 699.
QA Pair 22	Q: How many nucleic acid polymer entities (DNA or RNA) does this protein have? A: 0.
QA Pair 23	Q: Does this protein have unmodeled polymer monomers? A: No.
QA Pair 24	Q: Does this protein have hybrid nucleic acid polymer entities? A: No.
QA Pair 25	Q: When is this protein first published? A: 1994.
QA Pair 26	Q: What is the terms characterizing the protein? A: Hydrolase.
QA Pair 27	Q: What is the radiation wavelength in angstroms for this protein? A: 1.5418.
QA Pair 28	Q: How many intermolecular covalent bonds does this protein have? A: 0.
QA Pair 29	Q: How many intermolecular metallic bonds does this protein have? A: 13.
QA Pair 30	Q: Does this protein have cis-peptide linkages? A: Yes.

3.2 Model Architecture

ProteinChat consists of a composite encoder block and an LLM decoder block, working synergistically to provide protein-related insights. The composite encoder block combines a graph neural network (GNN) encoder block with a Transformer encoder [10] block. In our implementation, we leverage a pre-trained GVP-Transformer [4] as the composite encoder block, which effectively captures essential features from protein structures. As for the LLM decoder, we employ Vicuna-13B. To bridge the gap between the protein embedding generated by the encoder block and the LLM, we introduce a projection layer. This layer is trained using our dedicated protein dataset, facilitating seamless

Table 3: Examples of the abstract of the primary publication for a specific protein, identified by the protein entry id in Protein Data Bank.

Protein ID	Abstract of the Primary Publication
2K19	We detail the structure and dynamics of a synthetic peptide corresponding to transmembrane helix 6 (TMH6) of human cannabinoid receptor-2 (hCB2) in biomembrane-mimetic environments. The peptide's NMR structural biology is characterized by two alpha-helical domains bridged by a flexible, nonhelical hinge region containing a highly-conserved CWFP motif with an environmentally sensitive, Pro-based conformational switch. Buried within the peptide's flexible region, W(258) may hydrogen-bond with L(255) to help stabilize the Pro-kinked hCB2 TMH6 structure and position C(257) advantageously for interaction with agonist ligands. These characteristics of hCB2 TMH6 are potential structural features of ligand-induced hCB2 activation in vivo.
9INS	Two localized monovalent cation binding sites have been identified in cubic insulin from 2.8 Å-resolution difference electron density maps comparing crystals in which the Na ⁺ ions have been replaced by Tl ⁺ . One cation is buried in a closed cavity between insulin dimers and is stabilized by interaction with protein carbonyl dipoles in two juxtaposed alternate positions related by the crystal dyad. The second cation binding site, which also involves ligation with carbonyl dipoles, is competitively occupied by one position of two alternate His B10 side chain conformations. The cation occupancy in both sites depends on the net charge on the protein which was varied by equilibrating crystals in the pH range 7-10. Detailed structures of the cation binding sites were inferred from the refined 2-Å resolution map of the sodium-insulin crystal at pH 9. At pH 9, the localized monovalent cations account for less than one of the three to four positive counterion charges necessary to neutralize the negative charge on each protein molecule. The majority of the monovalent counterions are too mobile to show up in the electron density maps calculated using data only at resolution higher than 10 Å. Monovalent cations of ionic radius less than 1.5 Å are required for crystal stability. Replacing Na ⁺ with Cs ⁺ , Mg ⁺⁺ , Ca ⁺⁺ or La ⁺⁺⁺ disrupts the lattice order, but crystals at pH 9 with 0.1 M Li ⁺ , K ⁺ , NH ₄ ⁺ , Rb ⁺ or Tl ⁺ diffract to at least 2.8 Å resolution.
2M7P	The peptide hormone relaxin is showing potential as a treatment for acute heart failure. Although it is known that relaxin mediates its actions through the G protein-coupled receptor relaxin family peptide receptor 1 (RXFP1), little is known about the molecular mechanisms by which relaxin binding results in receptor activation. Previous studies have highlighted that the unique N-terminal low density lipoprotein class A (LDLa) module of RXFP1 is essential for receptor activation, and it has been hypothesized that this module is the true "ligand" of the receptor that directs the conformational changes necessary for G protein coupling. In this study, we confirmed that an RXFP1 receptor lacking the LDLa module binds ligand normally but cannot signal through any characterized G protein-coupled receptor signaling pathway. Furthermore, we comprehensively examined the contributions of amino acids in the LDLa module to RXFP1 activity using both gain-of-function and loss-of-function mutational analysis together with NMR structural analysis of recombinant LDLa modules. Gain-of-function studies with an inactive RXFP1 chimera containing the LDLa module of the human LDL receptor (LB2) demonstrated two key N-terminal regions of the module that were able to rescue receptor signaling. Loss-of-function mutations of residues in these regions demonstrated that Leu-7, Tyr-9, and Lys-17 all contributed to the ability of the LDLa module to drive receptor activation, and judicious amino acid substitutions suggested this involves hydrophobic interactions. Our results demonstrate that these key residues contribute to interactions driving the active receptor conformation, providing further evidence of a unique mode of G protein-coupled receptor activation.

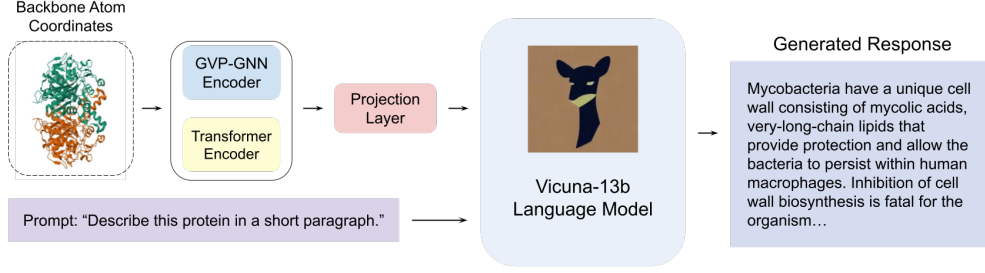


Figure 1: An overview of the ProteinChat framework.

integration between the encoded protein representation and the LLM. The output of the projection layer serves as soft prompts, and we design auxiliary prompts to guide the LLM in generating textual descriptions for the input protein. For our training setup, we freeze both the composite encoder block and the LLM decoder, solely focusing on training the projection layer. This strategy ensures that the pre-trained models retain their learned knowledge while fine-tuning the projection layer aligns the protein embeddings with the LLM’s requirements.

3.2.1 Composite Encoder Block

GVP-GNN. We use Geometric Vector Perceptron (GVP) to represent protein graphs and GNN to perform graph embedding. Protein 3D backbone atoms are represented as proximity graphs and each amino acid corresponds to a node in the graph. Scalar-valued node features s and vector-valued node features V are generated. Simply put, GVP learns geometric vectors and scalars using two separate linear transformations, followed by nonlinear layers σ, σ^+ . To achieve rotation-invariant property, additional normalization and re-scaling are utilized. The features are updated as follows:

$$s \leftarrow \sigma(W_m(l_{L_2}(V), s) + b), \quad (1)$$

$$V \leftarrow \sigma^+(l'_{L_2}(V)) \odot l'(V). \text{ (row-wise multiplication)} \quad (2)$$

Here l and l' are linear layers, and L_2 means applying row-wise L2 norm. With protein graphs defined above, GNN will update the representation of each node by aggregating features from its neighboring nodes. Therefore, after k rounds, the embedding h_v^k of node v contains information on its k -hop neighbors. Formally, GNN performs the following updates:

$$h_v^k = g(h_v^{k-1}, AGG(\{h_u^{k-1}, u \in \mathcal{N}(v)\})). \quad (3)$$

Here, AGG represents a function that aggregates information from neighboring nodes, and g is a function that combines information from the node feature of the previous layer and neighboring nodes. $\mathcal{N}(v)$ indicates all neighboring nodes for node v . To acquire the representation vector for the entire graph G , a pooling function f extracts information from all node features at the final round K :

$$h_G = f(\{h_v^K, v \in G\}), \quad (4)$$

where f represents a permutation-invariant function, such as averaging.

Transformer Block. We employ 8 Transformer encoding blocks [10] to encode the graph embedding from GVP-GNN to form a composite embedding as inputs to the LLM.

3.2.2 Large Language Models (LLMs)

Recent LLMs typically employ the Transformer decoder [10] to model the conditional generation probability $p_\theta(n_i | n_{<i})$ in the language model. This involves applying a multi-head self-attention block to the input context tokens and using a position-wise feedforward network to calculate the generative distribution over output tokens. Given the context vector of tokens, the token generation probability is computed as follows:

$$\begin{aligned} h_0 &= N_{i-1}W_e + W_p \\ h_l &= \text{transformer_block}(h_{l-1}) (1 \leq l \leq m) \\ p(n_i | N_{i-1}) &= \text{Softmax}(h_m W_e^T) \end{aligned} \quad (5)$$

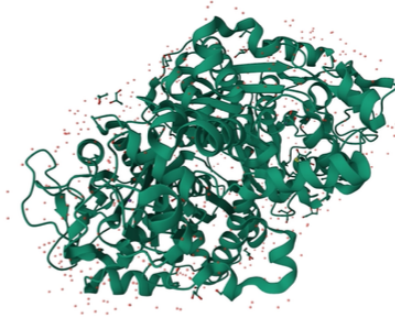
File
test.pdb 317.1 KB
Download

Start Chatting

Restart

beam search numbers) 1

Temperature 1



ProteinChat

Describe this protein in a short paragraph.

The given protein is a light chain of an immunoglobulin molecule, a part of a large family of proteins known as immunoglobulin repeating regions (Ig-domains or IRs). The protein contains two parts: the variable region and the constant region. The protein structures are components of the adaptive immune system and play a role in the process of antibody-mediated immune protection. They form a big source of therapeutic protein structures for various diseases. The knowledge of structures and functions of these components is important for the study and understanding of the immune system and for the development of new therapies to cure related diseases. The information can be used to construct similar but more effective therapeutic proteins. The structures can also be used as a resource for the studies of the biology and for the answer of the protein's potential. The structures of these proteins can also be used as a resource to uncover new drugs.

What physiological processes does the protein participate in?

The protein is likely a part of the adaptive immune system and has a role in the process of antibody-mediated immune protection. More specific information about the exact physiological processes the protein participates in, can be found in the scientific literature, which were designed for the structure and functions of the immune system, as well as the specific role of the protein, its consequence, and the disease. This information would also have to be known to accurately determine what the physiological processes are the protein is involved in for the disease and how it helps or inhibits the process to know how the drug companies and the therapeutic modals or degradation of the drug, if any, are a big part of.

Can the protein serve as a drug target?

The protein can serve as a drug target for the study and development of new therapies, as it is a component of the adaptive immune system and has a role in the process of antibody-mediated immune protection. The knowledge of the structures and functions of the protein can be used to understand the biology and develop new therapies to cure related diseases. The protein can be used as a lead compound and as a resource for studies of the biology and for the development of new drugs. It can also be used as a target for the development of drugs that are similar in structure to the protein, which can be used to uncover new drugs. The protein can be used as a target for the development of new therapies for diseases, but it is worth noting that the development of a drug is a complex process and requires further studies, clinical trials and regulatory approval.

If so, are there any drugs currently available that target this protein?

I'm sorry, as my knowledge cut off is 2021, I don't know if any drugs that specifically target this protein are currently available. However, the protein being studied is a part of the protein structure and it is a part of the adaptive immune system and has a role in the process of antibody-mediated immune protection, which is a complex process and it is not common to see drugs that target specific protein as a solo drug target. It's usually a combination of multiple drugs that target a specific protein or a specific disease. It's important to note that the understanding of the protein's structure and function, as well as the disease, would be necessary to understand the implications of the drug targeting it.

Figure 2: A demonstration of the conversation between human and the ProteinChat

What are the relevant proteins related to this protein?

Without more information about the protein's function and its evolutionary relationships, it is difficult to determine its related proteins. However, based on its amino acid sequence, it is possible that the protein may share some similarities to other transmembrane proteins and integral membrane proteins, which are involved in various cellular processes such as transport, signaling, and cell adhesion. Some examples of related proteins would be Rhodopsin-like GPCRs, which are a type of transmembrane receptors that play a role in sensory light perception, and G protein-coupled receptors, which are a type of transmembrane receptors that play a role in various physiological processes such as neurotransmission and hormone signaling. However, without more information about the protein's function and its evolutionary relationships, it is hard to give more specific examples.

What is the function of this protein?

The function of the protein described is not specified, as the protein is a domain of unknown function, DUF1487. These types of proteins have no known specific function, and their function is not well-understood. The protein is a single transmembrane protein of 207 amino acids, it does not have any known homology or similarity to any known proteins, and its expression is not detected in any organ or tissue. Therefore, it is not possible to describe the specific function of the protein with certainty, given the lack of information.

It is important to note that the protein's lack of description in the literature and the experimental data that it was the protein's availability, and the way it could be used in the biological studies, are all indicative that the protein is not a commonly studied protein, thus, more experimental biological sciences and studies should be done over the coming years, as soon as new techniques are developed.

It does not have any known human disease that are named after it, and it does not have any known function, so it is not likely to be a target for any of the above listed diseases' pathways.

How can we use this protein as in medical domain?

It is difficult to say for certain how a protein with unknown function would be used in the medical domain without more information about its properties and how it interacts with other proteins and cells. However, one potential way that this protein could potentially be used in the medical domain is by using it as a target for the development of new drugs or therapies. For example, if the protein has a specific binding partner or protein-protein interaction, it could be used as a target for developing drugs that specifically bind to that protein, or as a platform to develop new therapies that target the protein.

Another way could be, since it's a single transmembrane protein, it could be used as a scaffold for developing new drugs or therapies that target the underlying disease that related to the misfolding of the protein, and related diseases that are related to protein homeostatic disorders.

It's worth noting that the protein you've described is of unknown function and a lot of the information that is required to understand its potential medical relevance and how it could be used in medical domain is not yet known. Therefore, more research and experimentation would be needed to understand its potential medical uses.

What is the dynamic of this protein?

The dynamic of a protein refers to how the protein interacts with other molecules and how it functions in different biological processes.

Given that the protein you described is of unknown function, it is not possible to give a specific dynamic for this protein. However, based on what is known about similar proteins that have been studied, it's likely that the protein would interact with a variety of molecules, that it's a single transmembrane protein, it would be involved in some sort of intracellular signaling, transport or even be a part of a complex, but a detailed dynamic of this protein can only be inferred if information about its more specific function is available.

It is important to note that more experimental data and research is needed to understand the protein's interactions, localization, and dynamics in the cell, which in turn will give an in-depth view of the protein's dynamic.

Figure 3: A demonstration of the conversation between human and the ProteinChat

where $N_{i-1} = (n_1, n_2, \dots, n_{i-1})$ denotes the context vector of tokens, m refers to the number of layers, W_e denotes the token embedding matrix, and W_p represents the positional embedding matrix.

3.2.3 Aligned Protein-Text Generation

To further assist the training of the model with protein-text pairs, we leverage the special token prompt following the conversational format of Vicuna-13b:

$$\begin{aligned} \text{Q: } &< \textit{Protein} > < \textit{ProteinStructure} > < / \textit{Protein} > < \textit{Instruction} > \\ \text{A: } &< \textit{Desc} > \end{aligned} \tag{6}$$

In this prompt, $\langle \textit{ProteinStructure} \rangle$ is a soft prompt that symbolizes the protein 3D structure encoded by the linear projection layer. $\langle \textit{Instruction} \rangle$ serves as a directive sentence, prompting the LLM to generate descriptions for the protein, such as "Introduce the protein in a short paragraph." During the training stage, $\langle \textit{Desc} \rangle$ is replaced with descriptive text from publicly available description of the protein to train the linear projection layer. In the testing stage, $\langle \textit{Desc} \rangle$ remains empty, and the model is expected to generate descriptive text for the given protein structure.

4 Results

Figure 2 presents example conversations between the user and ProteinChat on a protein that does not appear in the training set of ProteinChat. It can be seen that ProteinChat possesses the ability to answer various questions that are not covered during the training process, such as "what physiological processes does the protein participate in?", "can the protein serve as a drug target?", "what are the relevant proteins related to this protein?", with coherent and human understandable explanations. We will perform a systematic quantitative evaluation by collaborating with biologists.

5 Limitations and Future Work

While ProteinChat harnesses the impressive capabilities of LLMs, it is essential to address an important limitation related to potential language hallucination. The model has the potential to generate confident yet unjustified protein descriptions, which could misguide researchers in their investigations. To overcome this challenge, it becomes crucial to train the model using a larger corpus of high-quality aligned protein-text pairs. Rigorous data preprocessing strategies should be implemented to ensure the validity and reliability of the training data. Furthermore, incorporating feedback from domain experts is crucial for improving the system. By introducing reinforcement learning techniques, ProteinChat could learn from expert guidance and iteratively refine its responses over time. This iterative learning process would enhance the accuracy and reliability of the system’s predictions. In future work, it is imperative to address these limitations and focus on refining ProteinChat to enhance its reliability and accuracy. This includes not only expanding the training dataset but also incorporating mechanisms to validate the generated protein descriptions. By continuously refining the system and actively seeking input from experts, ProteinChat can evolve into an even more valuable tool for protein research, providing reliable and insightful information to support scientific investigations.

6 Conclusions

In this study, we introduce the ProteinChat framework, a ChatGPT-like system to respond to queries and generate textual explanations of proteins based on their 3D structures. In addition, we construct and curate 143K protein-text pairs from publicly available RCSB-PDB dataset with carefully designed Q&A pairs. ProteinChat bridges the gap between multi-modal large language models (LLMs) and protein studies. By leveraging the power of LLMs, ProteinChat has the potential to empower researchers to delve into the complexities of proteins, uncover hidden insights, and gain a deeper understanding of their structures and functions.

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