

ChatGPT: Revolutionizing Life Sciences - A Guide to Foundations, Structures & Advanced Prompt Design for Biological Insights

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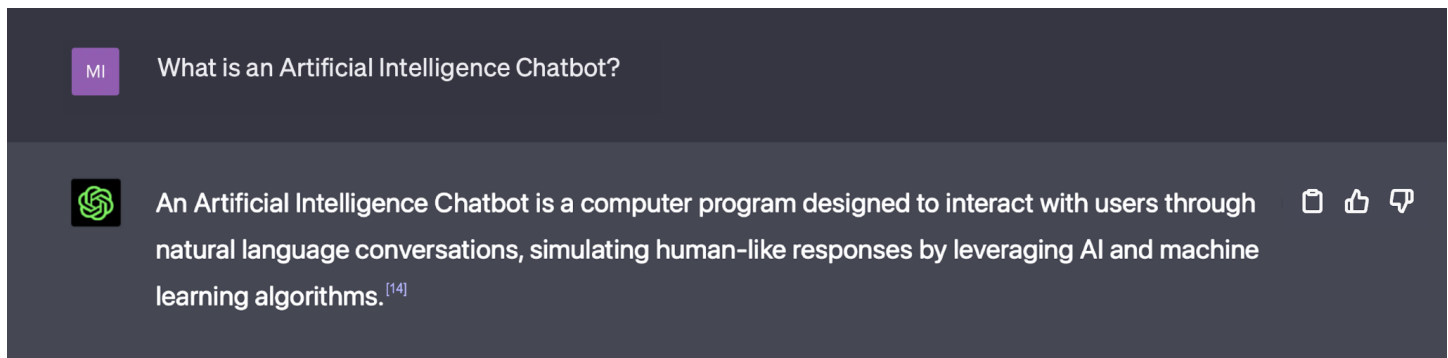
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Abstract

Chat [\[1,2\]](#) Generative Pre-Training [\[3\]](#) Version-4 (ChatGPT-4) is a sophisticated large language model designed to generate insightful, human-like responses to questions or prompts. In this paper, we present a detailed overview of the scientific foundations and computational processes that underpin this state-of-the-art Artificial Intelligence [\[4\]](#) (AI) research tool. Having an intuitive understanding of these processes enables the user to extract the most relevant, useful, accurate and targeted responses.

Leveraging the data structure of ChatGPT-4's data model, we provide an advanced research query that serves as a versatile template for life scientists, allowing them to adapt it for their own specific research goals. This prompt effectively demonstrates the organizational power and intuitive insights this tool provides to scientists regardless of their pursuits or discipline. Effective prompt design requires both a basic understanding of the computational structures incorporated by OpenAI's chatbots, and importantly, a guiding, grounded source-of-truth, within the prompt. Incorporating these elements allows the bot to return specific, highly relevant and accurate responses to esoteric scientific criteria.

Preface

Science is a gradual, stepwise process that incrementally builds on all the research that has been previously accomplished. Most historians credit Galileo Galilei (1564-1642)^[5] as the father of modern physics and the scientific method, while Francis Bacon (1561-1626)^[6] is known for his work on inductive reasoning and his advocacy for a systematic, empirical approach to scientific inquiry.

In the 380 years since the last of these two giants died, no tool has had the potential to accelerate the speed at which science advances more than AI chatbots. Chatbots are an emerging research tool, leveraging a new computational model, that will change the research landscape in dramatic and still unrealized ways.

Scientists can only make intuitive connections from the data points they are aware of or can find in the published literature. We are all aware of the adage that knowledge is of two types; knowing it and knowing where to find it. Please carefully consider what a profound change the next sentence represents.

Chatbots revolutionize the scientific landscape by rendering the entirety of human knowledge effortlessly accessible and intimately aware, empowering scientists to transcend the limits of their own individual cognition and truly incorporate the vast expanse of prior scientific research.

This dramatic statement is tempered by the currently available data that the computational model has been trained on. Open AI, the parent company of ChatGPT-4 will only provide a general description and inventory of the extensiveness of that training. Paywalls certainly limit the completeness of this endeavor.

Communicating with a AI Chatbot

The term "prompt," is utilized throughout this article. In the context of using ChatGPT, a "prompt" is defined as a textual input that a user provides to the system to initiate a conversation or to request a specific response. A prompt can be a question, a statement, or any other type of textual input that conveys the user's intent or quest for specific information. Prompts have no specified criteria or limitations. They can be one word or extend to include thousands of words limited only by the maximum number of tokens currently allowed by each Chatbot version.

The prompt included in this manuscript as an example, is capable of generating a comprehensive table of all interactions between any biologically active agent and the entire universe of molecular targets, pathways, and transcription factors. The specific example returns modifiers of the reprogramming induced rejuvenation (RIR)^[7,8] process. This is the same process as reprogramming any somatic cells into a pluripotent state (iPSC)^[9], but involves the systematic reversal of organismal aging, applied to an entire organism.

ChatGPT-4 rapidly searches, filters, organizes, and intelligently returns highly relevant information from an extensive knowledge base that includes most of the world's information. It delivers answers to your queries within a matter of seconds. The initial impact of ChatGPT's understanding and response abilities

were shocking when correctly formulated. Any tool that promises to revolutionize research methods, accelerating advancements in all scientific endeavors, makes disseminating the effective utilization of that tool important.

The impact of incorporating ChatGPT into your research workflow is greater than adding several brilliant postdoctoral researchers to your program, but at a total cost of \$20.00 a month. One encounter with its unique benefits is sufficient to recognize this dramatic advancement as an indispensable tool you will incorporate into your work and life forever.

These cutting-edge technologies enable researchers to instantaneously access deep repositories of knowledge, analyze complex datasets, review literature and effectively and expeditiously integrate them into their workflow. ChatGPT's advanced language understanding capabilities make it a valuable tool for multiple research related applications, from research assistant to content creation, discovery, lead and idea generation, hypothesis confirmation, and beyond.

This article's primary focus is divided into seven sections.

1) Historical Background

2) Structure, Process and Utility of AI ChatBots

3) How do ChatBots Intelligently Respond to Prompts

4) Specific Training Topics and Disciplines

5) Tutorial on how to Effectively Design Your Own Powerful Prompts

6) Prompt Example Formatting Key and Example Prompts

7) Demonstration of the Power and Potential of Chatbots

1) Historical Background

Alan Turing's development of the Turing Machine in 1936 was a precursor to modern computers, and he is often referred to as the father of AI. Between 1937 and 1940, he developed the Bombe machine, an electro-mechanical data processor that enabled Britain to decode intercepted World War II messages encrypted by the Nazi's Enigma machines. He also developed a theoretical model of computation and the Turing Test, a method for assessing a machine's ability to exhibit intelligent behavior. In 1950, Alan Turing published "Computing Machinery and Intelligence," which began with a provocative statement and a forward-looking question still resonating today: "Can machines think?"^[10]

In this article, Turing proposed a landmark concept in artificial intelligence: a test to determine if a computer was exhibiting human-like intelligence. His test involves a human judge engaging in a natural language conversation with both a machine and a human, without knowing which is which. If the judge cannot reliably distinguish between the two based on their responses, the machine is considered to have

passed the test, demonstrating a level of intelligence comparable to that of a human. This test has been a crucial benchmark that many consider the foundation of the field of AI.

In the context of AI, "thinking" can be interpreted as a machine's ability to process information, reason, learn from data, and make decisions based on that data. If we define thinking in this way, then it could be said that machines are capable of a certain level of "thinking" through the use of algorithms and complex computations.

Ironically, a very insightful description of if and when a machine is actually thinking was produced by Geoffrey Jefferson (1886–1961) one year before Turing published his article in 1950. Turing actually quoted the definition in his article. "Not until a machine can write a sonnet or compose a concerto because of thoughts and emotions felt, and not by the chance fall of symbols, could we agree that machine equals brain—that is, it can not only write it, but knows that it had written it. No mechanism could feel (and not merely artificially signal, an easy contrivance) pleasure at its successes, grief when its valves fuse, be warmed by flattery, be made miserable by its mistakes, be charmed by sex, be angry or depressed when it cannot get what it wants."^[11]

Recently released AI chatbots, including ChatGPT-4 can pass the "Turing Test," with ease, but still do not "think" in the sense we apply to humans. It is very difficult to discern if a response from a ChatGPT prompt is human or machine generated. Jefferson's definition is commonly referred to with a blanket term: sentience. Most researchers believe that we are still decades away from this benchmark of intelligent, self-aware, thoughtful, and introspective machines. However, chatbots such as ChatGPT are already demonstrating novel and unforeseen capabilities, termed emergent properties. These novel and unforeseen capabilities surpass the scope of their initial design parameters as well as the intentions and expectations of their designers. The phenomenon of emergent properties was already a recognized aspect of some complex systems, including artificial intelligence. These awe inspiring and disturbing properties of Chatbots lead to two inescapable conclusions: Sentient bots are coming and will arrive sooner than anyone is currently predicting.

ChatGPT and similar chatbots now emerging onto our computational, informational, and scientific lexicon, represent a technological inflection point that will have a greater impact on the advancement of knowledge than Gutenberg's printing press, the computer or even the internet. It has the potential to transform the way we think, learn, and interact with the world around us by democratizing access to advanced and specialized wells of knowledge. This innovation enables new discoveries in every field of human endeavor and scientific discipline. Empowering individuals with Chatbots will enable them to excel beyond their own self-limiting knowledge base, allowing almost anyone to effect real change in their own lives, communities, and beyond.

2) Structure, Process and Utility of AI ChatBots

ChatGPT-4's Artificial Neural Network or Computational Models are designed to mimic both the structure and behavior of the human brain. The brain receives stimulus from the outside world, processing the input, and then generating an insightful and intuitive response. As the difficulty of the task increases,

more neurons are incorporated into the computational processing. The human brain contains approximately 86 billion neurons. They are connected by 100 trillion synapses [\[12\]](#).

ChatGPT-4 incorporates approximately 200 billion neuron-like nodes. This lexicon of 200 billion nodes in 96 layers makes the total number of possible synaptic-like connections (edges) a range somewhere between trillions and quadrillions. There are notable differences between the human brain and neural networks: 1) The human brain is vastly more complex; 2) AI chatbots have near-perfect, total-recall of their training data, encompassing the wealth of accumulated human knowledge; 3) This recall doesn't discern between right or wrong, true or false; 4) AI doesn't include the latest data until new trainings occur.

ChatGPT is a Large Language Model (LLM) based on the Transformer Architecture, designed to process and generate human language. It is trained on a vast corpus of textual data, which enables it to understand and interpret context in input prompts. The architecture employs self-attention mechanisms, allowing the model to assign weights and prioritize various tokens from within an input sequence or prompt.

Following unsupervised learning, supervised training refines the model for specific tasks, enhancing response accuracy. The LLM establishes context through nodes, which capture relationships within extensive text strings. This context is represented by embeddings and weightings, visualized as a network of interconnected nodes linked by contextual associations (Figure 1).

Upon receiving a user's prompt, ChatGPT activates these nodes, creating "bindings" between pertinent information. The relevance of these bindings is modulated, akin to synaptic weights in the human brain. By adjusting these weightings, the AI system prioritizes specific connections, resulting in more accurate and contextually relevant responses. The output is generated from the culmination of these processes in the final layer of the architecture. In the associated figure below, the colored curved background lines represent the concepts encapsulated by the bindings. This overview describes the basic mechanisms of contextual understanding and response generation by ChatGPT. The next three diagrams, with their accompanying keys, provide a detailed description of the individual elements allowing for insightful and intelligent responses by the Chatbot.

The Large Language Model, Artificial Neural Network

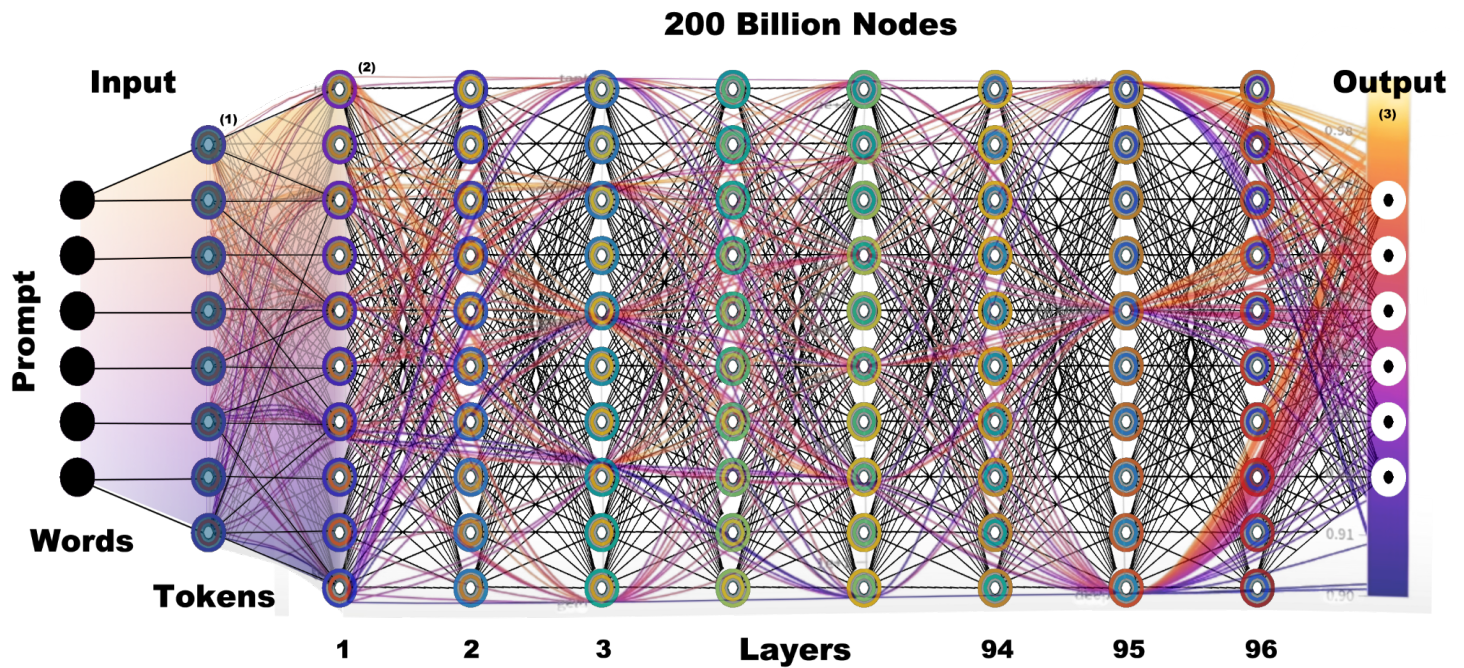


Figure 1. A Large language model [13], artificial Neural Network [14,15] consists of multiple components. First the input **Words** of the user's prompt are converted into tokens. **Tokens** ⁽¹⁾ [16, 17] represent words, sub-words, special characters and punctuations, and are the smallest units of text that an AI system can understand and process. **Nodes** [18, 19, 208, 21] are synaptic-like, interconnected, neuron-like fundamental units of artificial neural networks. They capture, store, process, and transmit information, and their collective operation enables the network to learn complex patterns and make decisions. (Multi-Ringed Dots) These nodes form a rich web of associations and relationships. Nodes are interconnected in **Layers** [22, 23]. Each layer is responsible for learning different levels of abstraction and linguistic patterns. Each node applies a transformation to its inputs to produce a modified output. Node connections are referred to as **Edges** ⁽²⁾ with all the nodes of an upper layer able to connect to all the nodes in a lower layer. Each node contains **Embeddings** [24], capturing both the semantic and syntactic information from the text, enabling the model to understand context and generate contextually relevant responses after converting words or Tokens into vectors. **Vectors** [25, 26] are ordered lists of numbers, where each number represents a different dimension describing different aspects of the word's meaning, allowing the model to understand and process language in a numerical form. Vectors contain multiple components including **Weightings** [27]. In a neural network, weightings are numerical values associated with the connections between nodes (Inner, color-coded ring of each node) representing the strength or influence of these connections. (Black straight lines) **Bias** is an additional parameter (not shown in graphic) used to adjust the output of a node, along with the weighted inputs. It helps in shifting the activation function and plays a crucial role in shaping the network's learning patterns. **Self-Attention** [28] enables the model to grasp context and word relationships by focusing on the most relevant nodes, assigning numerical values to each word's significance from the original text query. (Outer, color-coded ring of each node) Bindings [29, 30, 31] provide an inter-relational network of concepts, entities, events and ideas. (Curved multicolored background lines). Bindings can be thought of as the relationships captured by the network's structure and the learned weights between nodes, unique features that describe different aspects of the word's meaning. These bindings are strengthened or weakened based on their relevance and frequency of use, similar to the synaptic weights in the human brain. **Output** ⁽³⁾ is the compilation of this entire process with the token IDs delivered to the last layer. The tokens are again converted into words that have captured the concept (background highlight colors) and intent of the user's imputed prompt.

A Simplified Large Language Model Neural Network

To make Artificial Neural Networks (ANN) more transparent, consider a simplified version with only four elements (Figure 2): the prompt input; the first layer of nodes, (Input Layer 1), the output node layer (Output Layer 2), and finally the output of the response. The initial input is mapped to the nodes in the first layer (layer 1) using token id numbers. Each node in this layer is connected to every node in the second layer (layer 2), but there are no connections between nodes within the same layer.

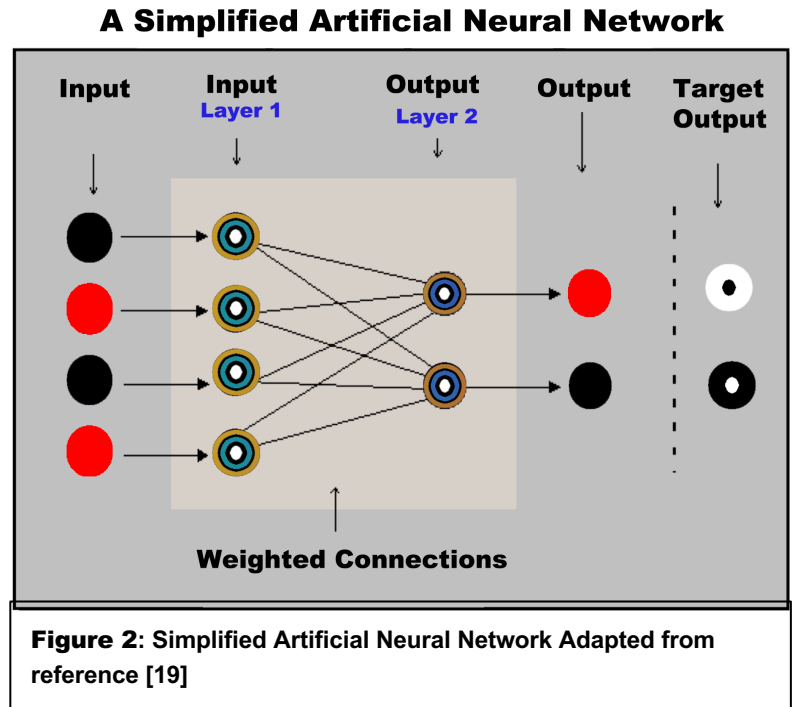
When a signal is sent from layer 1 to layer 2, it is modified by 'weights' associated with the connections between the nodes. These weights can be thought of as the strength or importance of each connection.

Each node in layer 2 receives and sums up these adjusted signals from all the nodes it's connected to in layer 1. The summed signal is then compared to a specific threshold. If the summed signal surpasses this threshold, the node in layer 2 activates and emits a signal corresponding to an output token or word.

This process, known as 'forward propagation', involves summing and processing all inputs received by each node in the output layer to produce the final output of the network. The network learns and improves by adjusting the weights on the connections based on the difference between the network's output and the desired output, a process known as 'backpropagation'.

Training an ANN involves fine-tuning the connection weights between layers to achieve desired outputs. This is done by sending specific inputs through the network and comparing the results with target outputs. If there's a discrepancy between the actual and target outputs, the weights are adjusted to produce outputs closer to the target values.

The descriptions associated with both diagrams omit a significant number of steps to simplify what is obviously a very complicated process. If the process still seems a little obtuse to you, the next sentence will make you feel a little better. It's important to note that while each vector element (volatile string of numbers within each node) corresponds to some abstract feature for each word's meaning, it's generally not possible to point to a specific element and say exactly what real-world feature it corresponds to. The feature representations are learned in a high-dimensional space (Entire graphic above + contents of each vector) during training and are based on statistical patterns in the data, which do not necessarily map onto human-understandable concepts. So, after reading the overview above, if you still do not have a good or complete insight into this entire process, take some comfort in the fact that no one, not even the developers, have complete insight or understanding of the ongoing process.



Self-Conformation - An Experiment

If the multiple and somewhat breathless exhalations of the abilities of AI Chatbots throughout this article still leaves you skeptical, please try one quick experiment. Copy the prompt from within this article, or download the full text prompt from the supplemental materials below, and enter it into the ChatGPT site at <https://openai.com> ^[32]. The optimized version, ChatGPT-4, currently costs \$20.00 a month.

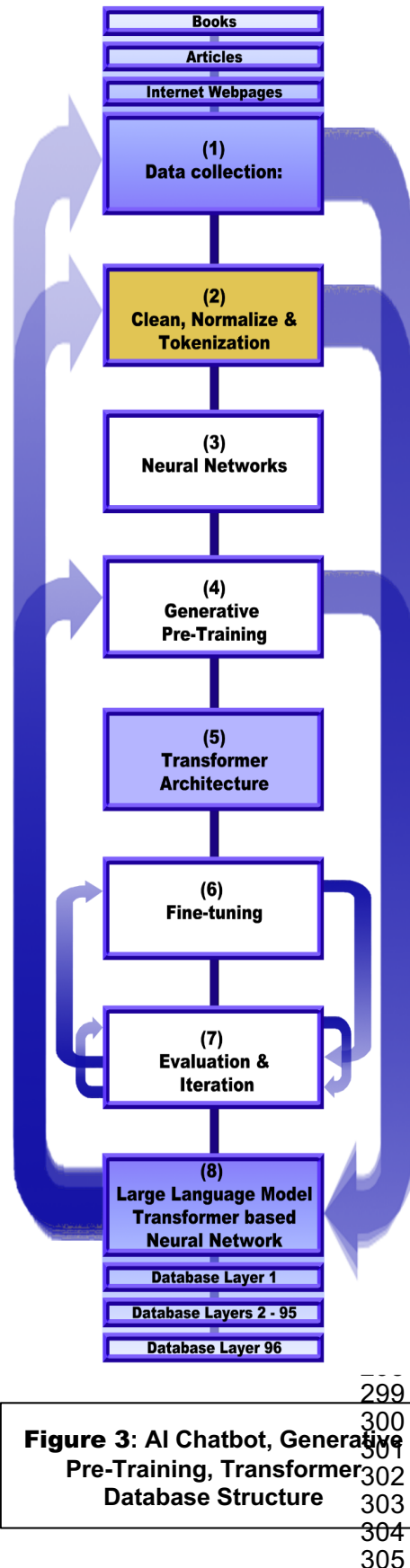
Once you've entered the prompt, the ChatBot will ask you to enter an active agent of interest to you. You can choose any small molecule, nutritional supplement, biological agent or compound used in your own or any research you are familiar with. Within seconds, you will experience a revelation, from having most of the world's knowledge searched, filtered, organized, and returned to your screen. It only takes one such experience to appreciate the value of the informational and computational revolution that is now at the fingertips of every researcher. If you are not one of them, you are putting yourself and your team at a distinct disadvantage.

Assembling the Elements of a Large Language Model, Neural Network

In contrast to the neural network structure provided in the graphic above (Figure 1), the schematic below (Figure 3) identifies the order of the steps incorporated within the computational model to achieve an intelligent and insightful response to the user's prompt. Understanding this sequence or process is important to effectively engineering useful scientific prompts.

Many steps in preparing the database or training ChatGPT are iterative, creating feedback loops that enable the model to learn patterns and relationships in the text data. Feedback loops are indicated by both the arrows of the same color used in this highlighting (Figure-3) below on the left, and by this text formatting. It should also be noted that not all feedback loops have been identified in the descriptions provided below.

The Steps in Assembling A Large Language Model, Neural Network



1) Data Collection process gathers diverse text from various sources to form a comprehensive, unprocessed, Large Language Model (LLM) dataset. The collected text is cleaned and preprocessed to remove any irrelevant content, inconsistencies, or errors. This step involves filtering out inappropriate content, correcting spelling and grammatical mistakes, or normalizing text formatting.

2) Clean, Normalize and Tokenization Involves breaking the text into smaller units, such as words, sub words, or characters

3) Neural Networks process text into numerical "embeddings" during training. This happens after tokenization, during the model's forward pass, as it processes input tokens and learns meaningful representations. These embeddings capture semantic and syntactic information, aiding the model in understanding word and phrase contexts. As training progresses, the model refines its understanding of language patterns using the embeddings to predict and capture token relationships, enhancing language understanding and generation.

4) Generative Pre-Training (GPT) involves training a **Large Language Model (LLM)** on tokenized text data in an unsupervised manner, where the model learns to predict the next token in a sequence based on the context of the surrounding tokens. This process enables the model to capture the structure, patterns, and relationships within the text data.

5 Transformer Architecture (TA) includes layers, attention mechanisms, and hyperparameters, tuned according to model performance and resource constraints. It trains the Large Language Model, capturing complexities of language and human interaction. Introduced by Vaswani et al. in their 2017 paper "Attention is All You Need", TA is a pivotal framework for Natural Language Processing (NLP) tasks. It underpins many top-tier NLP models, including ChatGPT.

6) Fine-tuning: is conducted on smaller, more specific datasets. This step usually involves supervised training with labeled data, such as question-answer pairs or other conversation data, allowing the model to learn to generate more contextually relevant and accurate responses. Fine-tuning can affect both itself and the evaluation and iteration step (Step 7). As fine-tuning is performed using different domain-specific datasets or optimizing the model for various tasks, the evaluation process may also be adapted to assess the model's performance on those specific tasks.

7) Evaluation and Iteration: The trained model is evaluated on various performance metrics, such as perplexity, accuracy, or other custom metrics. If necessary, the model's architecture, training data, or hyperparameters are adjusted, and the training process is iterated to improve the model's performance. This feedback loop is primarily reiterative on itself, as it involves adjusting the model's architecture, training data, or hyperparameters based on performance metrics. These adjustments may lead to changes in earlier steps, such as (1) Data collection, (2) Tokenization, and the choice of (5) Transformer Architecture.

8) Computational, Large Language Model, Natural Language Processing: The trained model allows the Chatbot to apply NLP techniques within the model to understand and process input prompts. Evaluation and Iteration (for response generation): Continuously evaluate and refine the model to improve its performance in generating accurate and contextually appropriate responses. This feedback loop is primarily focused on refining the deployed model. As improvements are made based on real-world performance, it could lead to changes in earlier steps, such as (1) Data Collection, (2) Tokenization, (4) Pre-Training, and (6) Fine-Tuning, to better capture and address specific issues encountered during deployment.

Figure 3: AI Chatbot, Generative Pre-Training, Transformer Database Structure

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3) How do ChatBots Intelligently Respond to Prompts

The ChatGPT process, illustrated in (Figures 4, below), begins after a user enters a prompt. This could be a question, a statement, or any other textual request for information. The words and components of these words are converted into numerical representations known as tokens. In the English language, a token can be as short as one character or as long as one word. The tokenization process may also break down long or compound words into subunits, with each becoming an individual token. Each token is then mapped to a unique ID number, transforming the input text into a numerical form that becomes a core component of the computational model.

The model accepts this series of token IDs as input and processes it layer by layer through a neural network (Figure 1). Each layer of the network learns to recognize different patterns of tokens. Lower layers may learn basic grammar and syntax, while higher layers might grasp more abstract concepts such as sentiment or meaning.

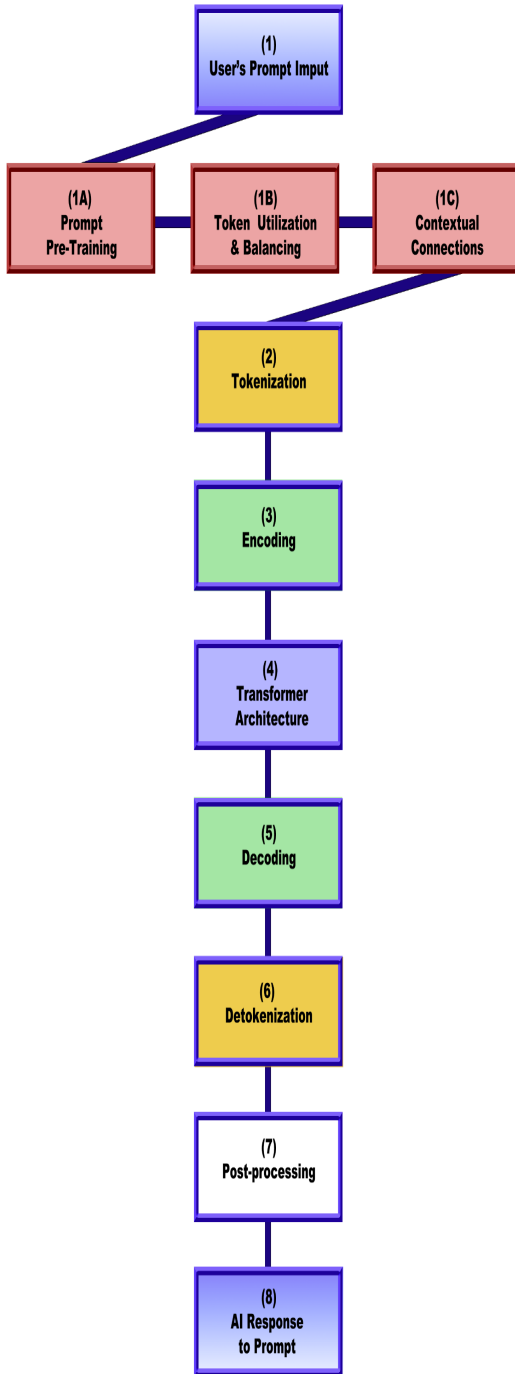
A mechanism called "self-attention" operates at each layer, allowing the model to weigh the importance of each token from the prompt in the context of the others. This mechanism aids the model in understanding which parts of the sentence are most relevant to each other. Self-attention works by assigning different weights to different words in the input. If a word is deemed more critical for understanding the sentence's meaning, it receives a higher weight. These weights contribute to creating a context-aware representation of each word, a summary that considers both the word itself and its context within the sentence.

This approach allows the model to manage long-range dependencies between words and to process different sentence parts in parallel. Each layer may learn to pay attention to different aspects of the input. The model's output (the generated response) is not directly determined by the self-attention weights. Instead, the output is produced by the model's final layer, which takes the context-aware representations produced by the self-attention mechanism and the earlier layers of the model as input.

Once the input has been fully processed, the model generates a series of output token IDs. These output token IDs are then converted back into words, resulting in the model's response. This generated response undergoes post-processing to ensure proper grammar, spelling, punctuation, and capitalization before being converted into the final human-readable text.

1.

The Multiple Steps Involved in ChatGPT's Input Prompt and Response Process



1) Prompt: Text Input (question, statement or specific informational query) entered by the user to be processed by the AI model.

Prompt Optimization Opportunities

1A) Optimize via Pre-Training

1B) Optimize via Token Utilization and Balancing

1C) Optimize via Contextual Connections

2) Tokenization: The input text is converted into tokens using a tokenization method, which involves breaking the text into smaller units such as words, sub-words, or characters, depending on the specific tokenizer employed.

3) Encoding: Tokens are mapped to numerical representations called embeddings, used as input for the neural network. Embeddings don't represent specific topics; instead, they efficiently handle input data. The model uses embeddings and learns patterns to generate responses or perform tasks like translation or summarization.

4) Transformer architecture: The token embeddings are fed into the Transformer, a neural network architecture comprising multiple layers of self-attention and feedforward mechanisms. As the embeddings pass through the layers, the model captures relationships and dependencies between the tokens and refines their representations.

5) Decoding: After the embeddings are processed by the Transformer, they are translated back into tokens. The model generates an output sequence token by token, predicting the most likely next token at each step based on the current context and the knowledge it has acquired during training.

6) Detokenization: The output tokens are converted back into a human-readable text format, forming the generated response.

7) Post-processing (optional): In some cases, additional processing may be applied to the generated text to refine the response, such as truncating it to a specific length, filtering out inappropriate content, or adjusting the style.

8) Response to the prompt. Output: Once the model processes the input, it generates a response in the form of tokens. The tokens are converted back to words or detokenized. After post-processing the response is provided to the user.

Figure 4: Prompt and Response Process Flow. 1A, 1B and 1C are prompt optimization opportunities detailed in Section 5.

4) Training Topics and Disciplines

ChatGPT training begins with data collection, where a vast amount of diverse text is gathered to form the foundation of its knowledge base. The data is then preprocessed, cleaned, and formatted to ensure the model can efficiently process it. Utilizing transformer neural networks, the model learns to predict the next word in a sentence, incrementally developing an understanding of language. Finally, ChatGPT is fine-tuned through human reviewers' feedback, optimizing its performance to generate appropriate responses to a wide array of user inputs. The training occurs on a broad range of human knowledge, including science, technology, history, and much more, drawn from sources like books, newspapers, magazines, encyclopedias, dictionaries, academic articles, and websites. Historically the information spans many centuries. Because the chatbots can only provide information they have been trained on, a significant amount of information can be missing. This is the span of time from today's date back to the date of the last training. As of the writing of this manuscript that date is September of 2021. Approximately a 20-month void of information. As an example, ChatGPT-4 knows of ChatGPT-3, but not vice versa. This informational void in the database is a significant drawback in the cumulative nature of scientific research and underscores the need for Open Ai to develop continuous updates, akin to the search engine indexing processes. With this drawback in mind, the overall benefits of the model generally outweigh this issue. The difference between having access to ChatGPT-4 with this information deficit and not having access to it at all is immeasurable.

Scientific Disciplines with Extensively Trained Data Sets

This article is specifically focused on demonstrating the power and flexibility of effectively extracting exact, scientific information related to the field of molecular biology from the ChatGPT-4's computational mode. To be useful to scientist in high-level, demanding disciplines, the model must be extensively trained, providing deep and insightful information in every relevant field, each respective scientist may be working in. Currently these extensively trained datasets include 1) Chemistry: such as organic, inorganic, and biochemistry; 2) Physics: like quantum mechanics and thermodynamics; 3) Biology: including cell biology, genetics, and evolutionary biology; 4) Medicine: covering anatomy, immunology, and medical specialties like cardiology and oncology. The model's extensive training enables a comprehensive grasp of the ideas, definitions, concepts and vocabulary of these fields.

Compared to other topics, these extensively trained subjects have a much larger representation in the training dataset, allowing the model to develop a more comprehensive understanding of the concepts, trends, vocabulary, and patterns associated with these fields.

5) Prompt Design and Optimization Considerations

Effective prompt design in AI involves crafting questions or tasks that guide language models like ChatGPT to produce meaningful, accurate, and informative responses. "Guide," is the optimal word in this process. It is crucial to consider the form of the question, as slight alterations can result in entirely different answers. Generally, every prompt should be defined as clearly and definitively as possible, avoiding any ambiguous terms or extemporaneous adjectives.

If unsatisfied with a response, users can rephrase or modify the initial question. Although ChatGPT offers a "Regenerate" option, it typically provides a rearrangement of the initial response rather than a completely different answer.

To achieve relevant and targeted results, we take advantage of various processes incorporated in AI database construction and ChatGPT's unique prompt processing algorithms. These opportunities are highlighted in (Figure 4) as three horizontal red boxes that identify the following prompt optimization opportunities: 1A) Optimize via Pre-Training; 1B) Optimize via Token Utilization and Balancing; 1C) Optimize via Contextual Connections. Each of these opportunities are described in detail in the following sections and included specific prompt design techniques to capitalize on each of them.

1A) Optimize via Pre-Training

The most difficult problem Chatbots must solve is that there is no source of truth in reinforcement learning, which leads to the absence of weighting. To restate this, ChatGPT's talent lies in contextual connections not discerning if the resulting textual continuations or connections are truthful. A singular feature or idiosyncratic feature of these systems is that they will provide an answer even if the question is ambiguous, and there is no search for a better understanding of the question (disambiguation). This makes the model very sensitive to the formulation of the original prompt. Formulating your prompt to guide the AI to your desired intent circumvents these issues.

As indicated in the database structure schematic (Fig 2), the LLM process involves a fine-tuning step that utilizes human interaction to guide the AI model towards optimal responses for tasks like sentiment analysis, summarization, or translation. Fine-tuning adjusts the model's weights, building upon the knowledge acquired during pre-training. Human annotators label collected data, enabling supervised learning by providing accurate, ground-truth, information through annotations, such as object names, images, sentiment classification in text, or speech-to-text transcription. Additionally, humans review the AI's output, offering corrections or suggestions to enhance the model's performance.

With 'truth' as an identified obstacle to effective prompt design, the first goal of our prompt is to provide a scientific framework so that the Chatbot will not engage in disambiguation, confabulation or hallucinations. To that end we carefully define the terms and definitions of all relevant prompt elements within a Prompt Pre-Training section that includes Definitions and Abstracts. The abstracts describe the relevance and relationship between the definitions and the prompt questions. This enables us to direct the ChatBot to our informational focus or grounded truths and the relative weights we are assigning to the target source(s) of information. The lay press is full of articles describing incorrect or inappropriate chatbot responses to queries. The strategy identified here comes very close to eliminating the errors and omissions any scientist would find limiting and unacceptable.

1B) Optimize via Token Utilization and Balancing

ChatGPT uses tokens for processing and generating text. It employs sub-word tokenization methods like Byte Pair Encoding (BPE) ^[33] or WordPiece (WP) ^[34]. These tokens represent not just words, but also word parts, punctuation, and special characters, allowing efficient language representation and

processing. The tokens also help the AI understand language variations, handle multiple languages, and reduce computational complexity for improved performance.

The number of tokens in a prompt also affects the computational cost of processing, as the model's capacity to handle tokens is limited by its architecture and available resources. This limitation is essential to consider when designing prompts that include a large amount of text in the prompt and/or are intended to output a large amount of textual information as a response.

Each AI model has a specific maximum token limit it can handle in a single instance, which includes the total of the input and output tokens combined. For example, GPT-2 had a maximum token limit of 1024 tokens, while GPT-3's larger models can handle up to 4096 tokens. ChatGPT-4's maximum token limit has been fluctuating due to high demand, currently standing at 4096 tokens. As demand increases this parameter allows Open AI some flexibility in controlling the workload of its servers, consequently the limits on total allowable tokens may change during periods of high demand.

This constraint makes it critical to consider token limits when designing large prompts, as exceeding the maximum limit (For the combined input and output) can lead to error messages and incomplete or truncated output. When the latter occurs the bot just quits outputting your response. It is possible to ask it to continue, but the formatting is often lost, and the contextual focus may not be the same. Have you ever lost your train of thought in the middle of a sentence? For a chatbot, that's analogous to running out of token allocations.

If the input text (the prompt) comprises a significant number of words or tokens, as demonstrated in our example, the model's output (response) will be bound by the remaining tokens available within the maximum token limit. This challenge is easily addressed by breaking large prompts into two or more smaller prompts. This can lead to another contextual problem that is also easily overcome and is discussed in the next section.

Both Microsoft Word and Google Documents provide word count tools. You can take this number and ask ChatGPT for a token count based on the text or word count. With this information you can balance the input and output of your prompts

The total word count of the first example prompt is 1086. This includes the Overview; Definitions and Abstracts; the first five prompts and the output formatting section. (Shown below in the example RIR prompt) The 1086 words it contains gets converted into 1046 tokens according to ChatGPT-4. This allows our output to contain 3050 tokens or approximately 2500 words. Using formatting conventions like tables also increases your token utilization.

1C) Optimize via Contextual Connections

Contextual connections allow the chatbot to maintain a train of thought or context. Contextual connections are very simple and are achieved by simply informing the Chatbot of the link between the specific targets of information and the prompt. In the first prompt we connected the overview containing the definitions and abstracts with the prompt using the following: "Please answer the following questions

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in the context of the overview previously provided.” We also communicate to the Chatbot words that we consider important and demonstrate a flagging convention to demonstrate that emphasis.

When breaking your prompts into separate segments in order to manage and balance token allocations, it’s important to connect the first prompt’s information guidance or pre-training with the continuation of the next requested prompt. First, do not start a new chat, as ChatGPT remembers prior conversations or chats within the same chat session.

To ensure a coherent continuation from the previous prompt, provide a contextual link that informs ChatGPT that subsequent questions are an extension of the earlier prompt and should be grounded in the same truths established in the pre-training section (Definitions and Abstracts). For instance, in the Prompt-2, example below, the chatbot is instructed to "continue by responding to the following questions as you did the first five (5)." This second prompt should be entered immediately after you are provided with the response from the first prompt. We also request in the second prompt that the chatbot not again reproduce the first five responses. If it is allowed to combine the output from both prompts, the AI will often reduce the completeness of the responses in order to remain within the token allocation.

Independent Analytical and Subjective Analysis

ChatGPT-4 can make its own analytical evaluations that can add an important perspective and/or weighting factor to your results. In the example below we ask the bot to produce what we are calling a “Potential RIR Effect Score,” (PRIRE SCORE) that we append and apply to every prompt. The PRIRE Scores are calculated based on the agent's primary influence on RIR, its mechanism of action, any synergistic/additive effects it might have with other agents, its interaction with core biological and molecular signaling pathways (Hubs), and its potential use in treating diseases of aging (DOA). Each of these components is assigned a subjective score by the Chatbot, ranging from 1 to 100, calculated by the chatbot and based on a qualitative or quantitative evaluation of the available scientific evidence, to measure how well the agent can influence the specific molecular targets we are investigating for targeted RIR biological activity. The scores are then added together and divided by the number of components to calculate an average. This average produces the combined PRIRE Score for the agent.

The debate remains open as to how closely this ranking mirrors the agent's actual ability to contribute to the RIR process. However, it does seem to provide another perspective that is illustrative in the RIR evaluation process. The aim here is not just to showcase the bot's ability to make subjective judgments and handle infinitely variable scenarios, but also to demonstrate its potential in creating innovative quantification methods. The greatest error any researcher can make at this critical juncture is to dismiss or underestimate the tremendous benefits that this cutting-edge tool provides to those who understand its intricacies and seize the opportunities it presents. Don’t make the mistake of presuming it is incapable of a task that seems unlikely to you, for it to be able to accomplish. We can't exceed known chatbot boundaries because those boundaries are still unknown. If you want something, ask for it. Often, you will be as surprised or even shocked as I have been by the results.

Formatting

We defined how the response should be formatted as the last section of the prompt. Formatting the results as a table, as in our example, makes the results easy to transfer to an excel or google sheet to produce a database in which to combine and compare all profiled agents that meet your predefined research criteria.

6) Prompt Formatting Key and Example Prompts

This article discusses the three primary prompt optimization opportunities inherent in the database and the prompt response process. In order to keep the flow of the prompt example coherent and avoid breaking the prompt into multiple disjointed parts, we color coded the respective sections below using the key provided below. Because ChatGPT is a text-based interface, it ignores all formatting. This enables you to cut and paste this prompt into the AI without any concerns that the formatting will interfere with its execution. A full text pdf version of both prompts is also available in the Supplemental Materials below.

Pre-Training	Prompt 1: Queries 1 - 5	Response Key
Contextual Continuation	Prompt 2: Queries 6 - 11	Format of Output

© RIR Agent Profile - Prompt 1 of 2: Queries 1 - 5

Overview / Pre-Training

I, now we ;√), are researching; **[Reprogramming Induced Rejuvenation] [RIR]** in cells or mammals.

Prompt Pre-Training - Abstract and Definitions:

[RIR] is an identical process to generating: **[induced Pluripotent Stem Cells] [iPSC]'s** from somatic cells, but in organisms, including humans.

[Transcription factors] [TFs] are proteins involved in the regulation of gene expression at the transcriptional level. They interact with DNA in a sequence-specific manner through their **[DNA-binding domains] [DBD]**, which are used to classify TFs into structural families. The genomic locations where TFs bind to DNA are known as **[TF binding sites] [TFBS]s**, which are typically short (6–20 bp) and exhibit sequence variability. Genome-wide identification of TFBSs is key to understanding transcriptional regulation.

[Molecular Pathways] [MP] and **[Network HUBs] [NH]** - The interconnected molecular pathways that produce signaling cascades, inducing or enhancing the RIR or cellular reprogramming, are highly interconnected and form protein-protein networks of a scale-free topology. These pathways are activated,

modulated or blocked by small molecules [SM] targets and transcription factors [TFs] that play critical roles in various functional categories such as epigenetics, cell signaling, and metabolic "switchers." Remarkably, many enriched pathways of SM targets are related to aging, longevity, and age-related diseases, thus connecting them with cellular and organismal reprogramming.

[Core Transcription Factors] [CTF]s TFs dominate the control of gene expression in embryonic stem cells, iPSCs and other cellular models by forming interconnected auto-regulatory loops, known as **[Core Transcriptional Regulatory Circuitry] [CRC]**. CRC's control gene expression in embryonic stem cells and other cellular models including iPSCs by forming interconnected auto-regulatory loops, known as **[Super-enhancers] [SE]s** are large clusters of transcriptional enhancers that drive expression of genes that drive reprogramming and define cell identity. SEs enabling CRC activation and induction.

[All Available Interventional Resources] [AAIR] represents an envelope containing: Amino Acids; Peptides; Proteins; Nutritional Supplements; Plant Derived Compounds; Hormones; Drugs and/or **[Small Molecules] [SM]**. AAIR is intended to include virtually every bioactive molecule capable of binding, activating or inhibiting any relevant biological target or pathway involved in iPSC or RIR. AAIR or SM agents fall into four major functional categories: [epigenetic], [antioxidant], [cell-signaling], and/or [metabolic switcher]. Each of these categories appears to be required in any cocktail designed to induce or enhance the iPSC or RIR programming process.

[Primary Function] [PM] SM targets are necessary components of each reprogramming cocktail and are highly interconnected. These agents also fall into three primary functions related to RIR or iPSC and include **[inducing]**, **[enhancing]** or **[blocking]** reprogramming. The extremely high contribution of hubs to network connectivity, suggests that (1) cell reprogramming requires AAIR or SM agents and their targets to act cooperatively, and (2) their coordination and network organization ensures robustness by resistance to random failures. This attribute also provides for both the redundancy and flexibility of the RIR protocol process that is required when incorporating nutritional supplements and the multiplicity of off target signaling that accompanies most nutritional supplements.

[Potential RIR Effect Score] [PRIRE SCORE] Please provide an RIR impact score between 1 and 100 based on the agent's ability to impact the identified targets within each specific prompt. This will always include your; (ChatGPT's,) analysis from your information and data perspective as to the potential effectiveness of this agent in generating iPSCs or inducing RIR. It should also utilize as a weighting factor, the agent's ability to activate, modulate or inhibit any signaling or molecular pathways / transcription factors, involved in facilitating or promoting the generation of iPSC's and/or the induction of RIR. **End of Abstract**

Conceptual Connection

With this overview of effective RIR requirements in mind, please provide the answers to the following prompts with special emphasis or focus on the concepts, and ideas embodied in the abstract above. Please place special emphasis on key words that are underlined and are contained within **[angle brackets]** i.e., **[X]**.

Prompt 1 of 2: Queries 1 - 5

1) Scientific Overview - Please provide a scientific overview of the agent and how the agent impacts the iPSC or reprogramming induced rejuvenation [RIR] process as it directly relates to the abstract? Please calculate the: **[PRIRE SCORE] specific to this question.**

2) Scientific Classification - Please provide the scientific classification of the "Agent"? Please calculate the: **[PRIRE SCORE] specific to this question.**

3) Molecular Targets Please provide a complete list of all molecular targets or signaling pathways that are modulated, activated, inhibited or blocked by the Agent? Please specifically included the following: [TGF- β], [MAO], [GSK3- β], [Wnt/ β -catenin], [FGF/ERK], [Nrf2], [TET], [DNMT], [HDAC], [LSD-1], [MAPK/ERK], [NF- κ B], [SIRT]. Please specifically indicate if the agent, up or down-regulates the identified molecular targets or pathways. Please limit the initial response to a list of the impacted molecular targets, and then provide brief descriptions of the biological activity of those pathways as appropriate. Please place any text used from this prompt within angle brackets, i.e., [X]. Please calculate the: **[PRIRE SCORE] specific to this question.**

4) Transcription Factors - Please provide a list of all TFs the agent is capable of activating or inhibiting, with the primary focus being on the following Transcription factors:

[OCT4];
[SOX2];
[KLF4];
[c-MYC];
[L-Myc];
[NANOG];
[Lin28]; or
[Glis1].

Please specifically indicate if the agent, up or down-regulates the identified transcription factor. Please limit the initial response to one of the eight (8) bracketed words above first, and then provide any additional information as appropriate. Please place any text used from this prompt within angle brackets, i.e., [X]. Please calculate the: **[PRIRE SCORE] specific to this question.**

5) Functional Category - Please describe which major functional category, this agent's mechanism-of-action (MOA), falls within:

[epigenetics];
[antioxidants];
[cell signaling]; or
[metabolic switcher].

Please limit the initial response to one of the four bracketed words above first, and then provide any additional information as appropriate. Please place any text used from this prompt within angle brackets, i.e., [X]. Please calculate the: **[PRIRE SCORE] specific to this question.**

Output Formatting

Please format the responses as a table.

Please place any text reused from within any prompt into angle brackets, i.e., [X].

Do not include any HTML markup language such as line break indicators,
.

Please have the table contain four columns.

Column 1 will contain the **Prompt Number**.

Column 2 will contain the (Keyword,) i.e., the text in parentheses, following the (number) in parentheses for each numbered query.

Column 3 will contain the Generated Response to each numbered query within the prompt.

Column 4 will contain the calculated: [Potential RIR Effect Score] [PRIRE SCORE] specific to this question.

Response Key - Triggering Prompt Activation

Respond "Ready for Agent?" to acknowledge and I will paste the agent name for you to analyze?

◉ RIR Agent Profile - Prompt 2 of 2: **Queries 6 - 11**

Please continue by responding to the following questions as you did the first five (5).

Do not output the first five again, only provide output for question 6 through 11.

6) Primary Influence - Please indicate if the agent:

[induces];
[enhances]; or
[blocks], the iPSC or RIR processes.

Please limit the initial response to one of the three bracketed words above first, and then provide any additional information as appropriate. Please place any text used from this prompt within angle brackets, i.e., [X]. Please calculate the: [PRIRE SCORE] **specific to this question.**

7) Mechanism of Action - Please identify which mechanism(s) are engaged by the agent to affect the reprogramming function within these eight categories:

[epigenetics]; epigenetic profiles
[telomer]; telomere size
[transcriptome]; Transcriptomic reprogramming
[proteomics];
[anti-oxidation]; or
[oxidation]; oxidative stress

[mitochondrial metabolism];
[cellular senescence].

Please limit the initial response to one of the eight bracketed words above first, and then provide any additional information as appropriate. Please place any text used from this prompt within angle brackets, i.e., [X]. Please calculate the: **[PRIRE SCORE] specific to this question.**

8) Synergistic / Additive - Please indicate if it is synergistic or additive with any other agents? Please list those agents and the synergistic factors each has been identified with. Please calculate the: **[PRIRE SCORE] specific to this question.**

9) Hubs - Please provide any information on core connections between other biological, molecular signaling pathways described as Hubs or CRC in the abstract. Please list those pathways. Please calculate the: **[PRIRE SCORE] specific to this question.**

10) DOA Please provide a complete list of all diseases and age-related diseases for which the agent has been identified as a potential treatment or intervention? Please specifically check to see if any of the following diseases of aging are impacted by the agent: [Inflammaging], a significant risk factor for [chronic kidney disease], [diabetes mellitus], [cancer], [depression], and [dementia]; [Cardiovascular disease]; [Strokes] and [Heart Attacks], [Cancer]; [Neurodegenerative diseases], such as [Alzheimer's]; [Autoimmune diseases], such as [Osteoarthritis]; [Musculoskeletal disorders], such as [Osteoporosis] and [Sarcopenia]. This list now also includes [bacterial infections] in older individuals. Please indicate the total number of diseases of aging this agent has demonstrated an ability to treat, ameliorate or diminish its course? Please calculate the: **[PRIRE SCORE] specific to this question.**

11) Combined RIR Score - Please describe the global implication and potential impact of this component on RIR. Please provide an RIR impact score between 1 and 100 based on the following components: Please add the **[PRIRE SCORE] s for** prompts 1, and 3 through 10, and divide that number by 9. Please place the resulting score in the **[PRIRE SCORE]** column for prompt 11.

Output Formatting

Please format the responses as a table.

Please place any text reused from within any prompt into angle brackets, i.e., [X].

Do not include any HTML markup language such as line break indicators,
.

Please have the table contain four columns.

Column 1 will contain the Prompt Number.

Column 2 will contain the (Keyword,) i.e., the text in parentheses, following the (number) in parentheses for each numbered query.

Column 3 will contain the Generated Response to each numbered query within the prompt.

Column 4 will contain the calculated: [Potential RIR Effect Score] [PRIRE SCORE] specific to this question.

Thank you.

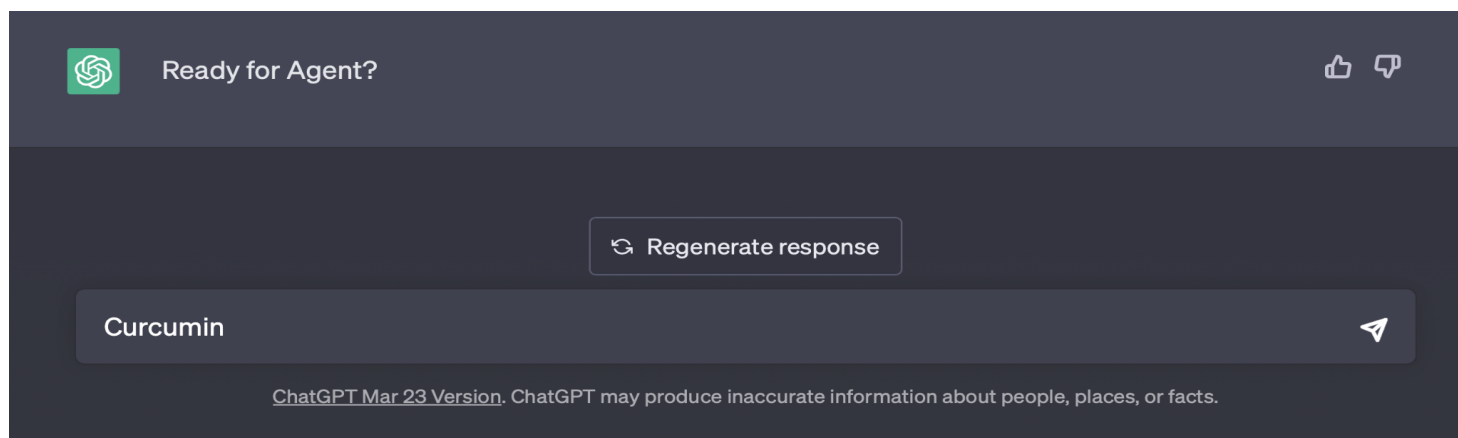
End of Prompt Examples

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Active Agent Activation Key

The prompt contains a large body of text that sets up and defines the specific data points we want returned. Each specific query within the prompt is requesting information to be returned for the “agent.” Agent in this case is any active molecule or biological response modifier with the potential to modulate the RIR process. Each agent you enter acts as a key, unlocking the process and initiating the execution of the prompt's complete instruction set.

After ChatGPT-4 has pre-processed the first prompt, it will execute the last instruction and inform you that it is “Ready for Agent?” you are researching. This last instruction is shown above at the end of Prompt-1 and the output from that instruction is illustrated below.



Enter the single compound or small molecule you want a RIR biological profile returned for, and either click on the paper airplane on the right or hit enter.

7) Demonstration of the Power and Potential of Chatbots

The results of the two separate prompts provided above are shown combined in an image of the output below (Figure 5). ChatGPT-4 quickly coalesces a cohesive picture of the agent's attributes and its ability to modulate specific pathways targeted in the field of Reprogramming Induced Rejuvenation and iPSC. It provides you with a score of each distinct description or attribute and for each of the molecular targets and pathways it can affect.

The prompts provide a huge amount of highly relevant information in just a few seconds. Replacing what could easily have been hours or even days of research. All of us have scoured the published literature searching for one obscure point of information, giving up, but still having a high degree of confidence that the information we are seeking is somewhere within the existing literature. Chatbots provide a tool that enables a level of in-depth and thorough screening unthinkable and certainly unavailable previously.

RIR Biological Response Modifier Active Agent Prompt Response

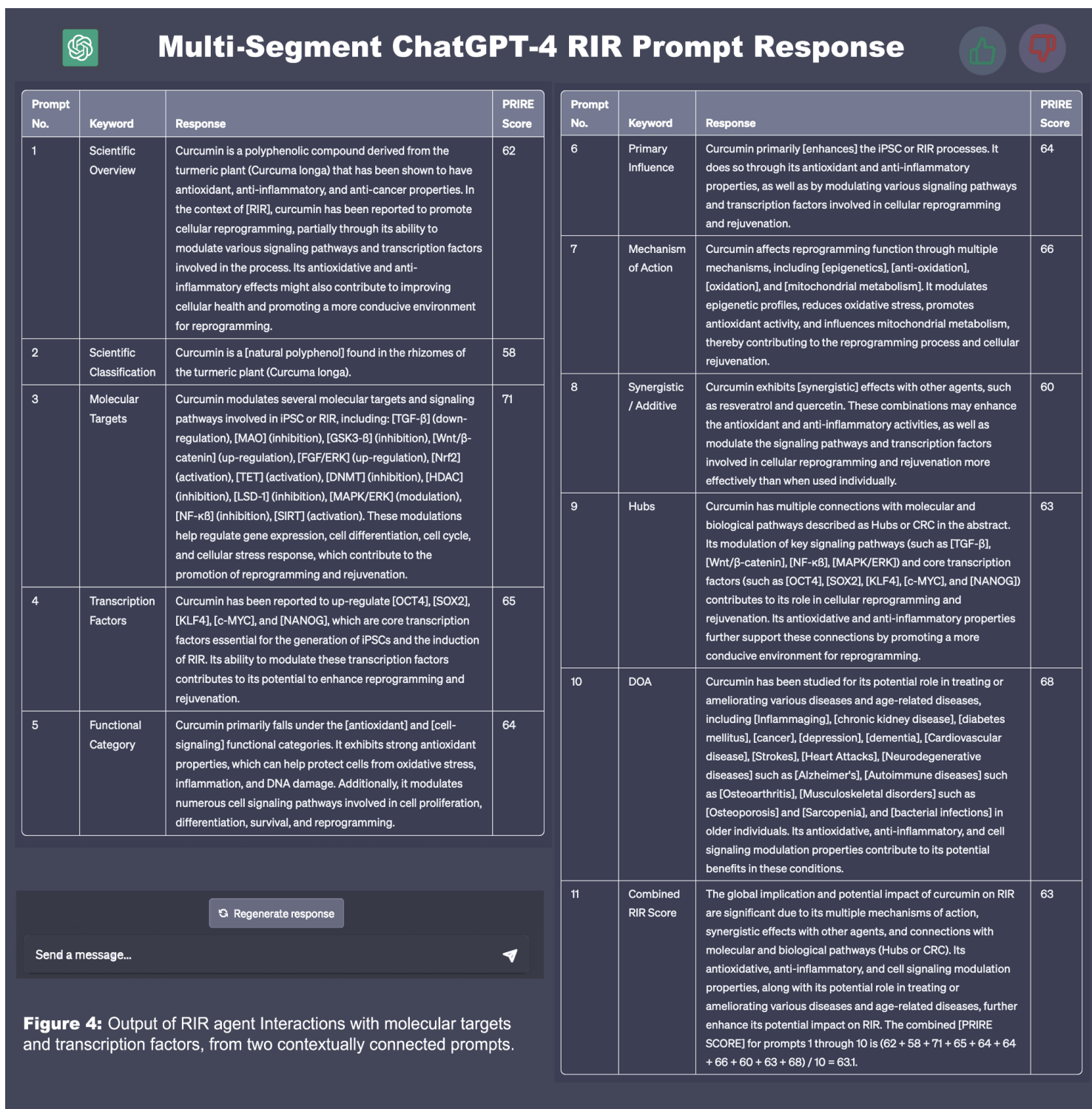


Figure 4: Output of RIR agent Interactions with molecular targets and transcription factors, from two contextually connected prompts.

Figure 5. Represents the output of two contextually connected prompts, each containing 5 specific queries. The first five responses are from prompt 1 and the second five are shown on the right and are the product of prompt 2. Point 11 is a combined, average score of this compound's potential impact incorporating selected relevant scores from all queries. A full, live-text pdf document containing the output response from both prompts is available for download from Supplemental Materials.

The unique opportunities of information extraction are limitless, and this sample prompt in no way limits the scope of its utility or demonstrates the full potential of this new research tool. After the construction of our prompt, the information output above was obtained by entering only one word: the active agent we wanted profiled. In this example, we chose "Curcumin" as it serves as an excellent illustration of a natural plant compound affecting numerous pathways involved in RIR.

Conclusion

The amount of data generated worldwide is growing exponentially. According to the International Data Corporation (IDC), the global datasphere is projected to grow from 33 zettabytes (ZB) in 2018 to 175 ZB by 2025,^[36] representing a compound annual growth rate (CAGR) of approximately 61%.

AI-powered tools, like natural language processing and machine learning algorithms, can analyze and synthesize this huge treasure trove of unrefined information from incredibly diverse and disparate sources in real-time. This allows researchers to swiftly streamline knowledge management^[35] and expedite the discovery by identifying connections, trends, and obscure or hidden patterns, transforming raw data into valuable, previously unrealized knowledge. AI enhances collaborations by offering semantic search capabilities and personalized recommendations based on individual interests and specific criteria, reducing duplication and fostering interdisciplinary breakthroughs. By automating tasks such as summarizing research papers, extracting relevant data, and data analysis, AI reduces time spent on repetitive tasks, providing valuable insights and freeing up researchers for complex, creative work. AI Chatbots' abilities to optimize knowledge management, accelerating innovations, sets the stage to revolutionize the research landscape, dramatically advancing science in all of its permutations.

While ChatGPT and similar AI technologies offer invaluable assistance in various biological research fields, they should not be viewed as replacements for human expertise, at least not yet. AI technologies serve as powerful supplementary tools that augment researchers' abilities, streamline their workflows, and enable them to focus on the intellectual challenges and creativity inherent in their work. At present, the advantages of this technology far surpass the occasional issues and inaccuracies that may surface in the results. The age-old adage: "trust but verify," is profoundly fitting in this context.

Some physicians and scientists who are already working with ChatGPT, have expressed concerns about being replaced by AI. A strong indication of the power and promise they see in this technology. Any scientist who does not incorporate AI into their research is putting themselves, their team and their umbrella institutions at a huge disadvantage.

“AI is not going to replace any scientist. It will, however, replace scientists who don’t incorporate AI into their research protocols, - with scientists who do.”

We are dealing with a brilliant child, a prodigy that will continue to grow, improve and mature. Like any child it deserves our guidance and support. The rewards for providing a nurturing environment are already being realized. No excuses are required for the personification; if you don’t understand now, you will soon.

Supplemental Materials

Illustrations in Pdf Fromat, Figures 1-5

1. **Figure 1. The Large Language Model, Artificial Neural Network**
2. **Figure 2. A Simplified Large Language Model Neural Network**
3. **Figure 3. The Steps in Building a LLM, Artificial Neural Network**
4. **Figure 4. The Steps Involved in Prompt Response Processes**
5. **Figure 5. RIR Biological Response Modifier Prompt Response**

Supplemental Text Files 1, 2

1. **Supplemental Text File 1. RIR Prompts 1 and 2**
2. **Supplemental Text File 2. RIR Prompt Responses 1 and 2**

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Additional Resources

[A complete Research index of published papers by Open AI can be found here: https://openai.com/research](https://openai.com/research)

[A complete archive of Open AI articles can be found on there blog here: https://openai.com/blog](https://openai.com/blog)

[ChatGPT: Wikipedia](#)

[ChatGPT: Optimizing Language Models for Dialogue](#)