

# A Survey of Large Language Models in Medicine: Principles, Applications, and Challenges

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## Abstract

Large language models (LLMs), such as ChatGPT, have received substantial attention due to their impressive human language understanding and generation capabilities. Therefore, the application of LLMs in medicine to assist physicians and patient care emerges as a promising research direction in both artificial intelligence and clinical medicine. To reflect this trend, this survey provides a comprehensive overview of the principles, applications, and challenges faced by LLMs in medicine. Specifically, we aim to address the following questions: 1) How can medical LLMs be built? 2) What are the downstream performances of medical LLMs? 3) How can medical LLMs be utilized in real-world clinical practice? 4) What challenges arise from the use of medical LLMs? and 5) How can we better construct and utilize medical LLMs? As a result, this survey aims to provide insights into the opportunities and challenges of LLMs in medicine and serve as a valuable resource for constructing practical and effective medical LLMs. A regularly updated list of practical guides on medical LLMs can be found at <https://github.com/AI-in-Health/MedLLMsPracticalGuide>.

## Contents

<b>1</b>	<b>Introduction</b>	<b>4</b>
<b>2</b>	<b>The Principles of Medical Large Language Models</b>	<b>6</b>
2.1	Pre-training . . . . .	6
2.2	Fine-tuning . . . . .	8
2.3	Prompting . . . . .	9
<b>3</b>	<b>Biomedical NLP Tasks</b>	<b>10</b>

3.1	Discriminative Tasks . . . . .	10
3.2	Generative Tasks . . . . .	10
3.3	Performance Comparisons . . . . .	12
<b>4</b>	<b>Clinical Applications</b>	<b>12</b>
4.1	Medical Diagnosis . . . . .	13
4.2	Formatting and ICD-Coding . . . . .	13
4.3	Clinical Report Generation . . . . .	14
4.4	Medical Education . . . . .	14
4.5	Medical Robotics . . . . .	15
4.6	Medical Language Translation . . . . .	15
4.7	Mental Health Support . . . . .	16
<b>5</b>	<b>Challenges</b>	<b>16</b>
5.1	Hallucination . . . . .	16
5.2	Lack of Evaluation Benchmarks and Metrics . . . . .	17
5.3	Domain Data Limitations . . . . .	17
5.4	New Knowledge Adaptation . . . . .	17
5.5	Behavior Alignment . . . . .	18
5.6	Ethical, Legal and Safety Concerns . . . . .	18
<b>6</b>	<b>Future Directions</b>	<b>18</b>
6.1	Introduction of New Benchmarks . . . . .	18
6.2	Interdisciplinary Collaborations . . . . .	19
6.3	Multimodal LLM Integrated with Time-Series, Visual, and Audio Data . . . . .	19
6.4	Medical Agents . . . . .	19
<b>7</b>	<b>Conclusion</b>	<b>20</b>
<b>A</b>	<b>Appendix: Background</b>	<b>42</b>
A.1	Formulation of Large Language Model (LLM) . . . . .	42
A.1.1	Language Model - Transformer . . . . .	42
A.1.2	Large-scale Pre-training . . . . .	42
A.1.3	Scaling Laws . . . . .	42
A.2	General Large Language Models . . . . .	43
A.2.1	Encoder-only LLM . . . . .	43
A.2.2	Decoder-only LLM . . . . .	44
A.2.3	Encoder-decoder LLM . . . . .	44
<b>B</b>	<b>Appendix: Discriminative Tasks</b>	<b>44</b>
B.1	Question Answering . . . . .	44
B.2	Entity Extraction . . . . .	45

B.3	Relation Extraction . . . . .	46
B.4	Text Classification . . . . .	47
B.5	Natural Language Inference . . . . .	48
B.6	Semantic Textual Similarity . . . . .	49
B.7	Information Retrieval . . . . .	49
<b>C</b>	<b>Appendix: Generative Tasks</b>	<b>51</b>
C.1	Text Summarization . . . . .	51
C.2	Text Simplification . . . . .	52
C.3	Text Generation . . . . .	52

# 1 Introduction

Over the past few years, a wide range of general large language models (LLMs) [1, 2], such as PaLM [3], LLaMA [4, 5], GPT-series [6, 7, 8], and ChatGLM [9, 10] have emerged and advanced the state-of-the-art in various natural language processing (NLP) tasks, including text generation, text summarization, and question answering. Inspired by the great success of general LLMs, the development and application of medical LLMs have gained growing research interests as they aim to assist medical professionals and improve patient care [11, 12, 13]. To this end, several endeavors have been made to adapt general LLMs to the medicine domain, leading to the emergence of medical LLMs [14, 15, 16, 17, 18, 19, 20, 21]. For example, based on PaLM [3], MedPaLM [14] and MedPaLM-2 [15] have achieved a competitive score of 86.5 compared to human experts (87.0 [22]) in the United States Medical Licensing Examination (USMLE) [23]; based on publicly available LLMs, e.g., LLaMA [4, 5], several medical LLMs, including ChatDoctor [19], MedAlpaca [16], PMC-LLaMA [22], BenTsao [17], and Clinical Camel [18], have been introduced.

Although existing medical LLMs have achieved promising results, there are some key issues in their development and application that need to be addressed. First, many of these models primarily focus on biomedical Natural Language Processing (NLP) tasks, such as dialogue and question answering, often overlooking their practical utility in clinical practice [12]. Recent research has begun to explore the potential of medical LLMs in various clinical scenarios, including Electronic Health Records (EHRs) [24, 25], discharge summary generation [13], health education [26], and care planning [27]. However, they mainly perform case studies and invite clinicians to perform the human evaluation on a small number of samples, and thus lack a standard evaluation dataset for evaluation. Second, most existing medical LLMs evaluate their performances mainly on medical question answering, neglecting other biomedical tasks, such as text summarization, relation extraction, information retrieval, and text generation. These gaps in the current research and application of LLMs in medicine motivate this survey to offer a comprehensive review of LLM development and applications in medicine. This survey aims to cover various topics, including existing medical LLMs, various biomedical tasks, clinical applications, and the associated challenges.

With this objective, as shown in Figure 1, this survey seeks to answer the following questions:

1. What are LLMs? How can medical LLMs be effectively built? (**Section 2**)
2. How are the current medical LLMs evaluated? What capabilities do medical LLMs offer beyond traditional models? (**Section 3**)
3. How can medical LLMs be applied in clinical settings? (**Section 4**)
4. What challenges should be addressed when implementing medical LLMs in clinical practice? (**Section 5**)
5. How can we optimize the construction of medical LLMs to enhance their applicability in clinical settings, ultimately contributing to medicine and creating a positive societal impact? (**Section 6**)

For the first question, we summarize the principles of existing medical LLMs, detailing their basic structures, the number of parameters, and the datasets used for model development. Additionally, we provide insights into the construction process of these models. This information is valuable for researchers and medical practitioners looking to build their own medical LLMs tailored to specific needs, such as computational limits, private data, and local knowledge bases. For the second question, we conducted an extensive survey on the performances of existing medical LLMs across ten biomedical NLP (discriminative and generative) tasks. This analysis will allow us to understand how medical LLMs outperform traditional medical AI models in different aspects. By showcasing their abilities, we aim to clarify the strengths that medical LLMs bring to the table when deployed in clinical settings. The third question focuses on the practical application of medical LLMs in clinical settings. We provide guidelines and insights into seven clinical application scenarios, offering specific implementations of medical LLMs and highlighting which abilities are used for each scenario. The fourth question emphasizes the challenges that must be overcome when deploying medical LLMs in clinical practice. These challenges include issues such as hallucination (*i.e.* generation of coherent and contextually relevant but factually incorrect outputs) [53, 63, 64], explainability [65], ethical, legal, and safety concerns [66]. We also advocate a broader evaluation of medical LLMs, including such aspects as trustworthiness [67], to ensure their responsible and effective use in clinical settings.

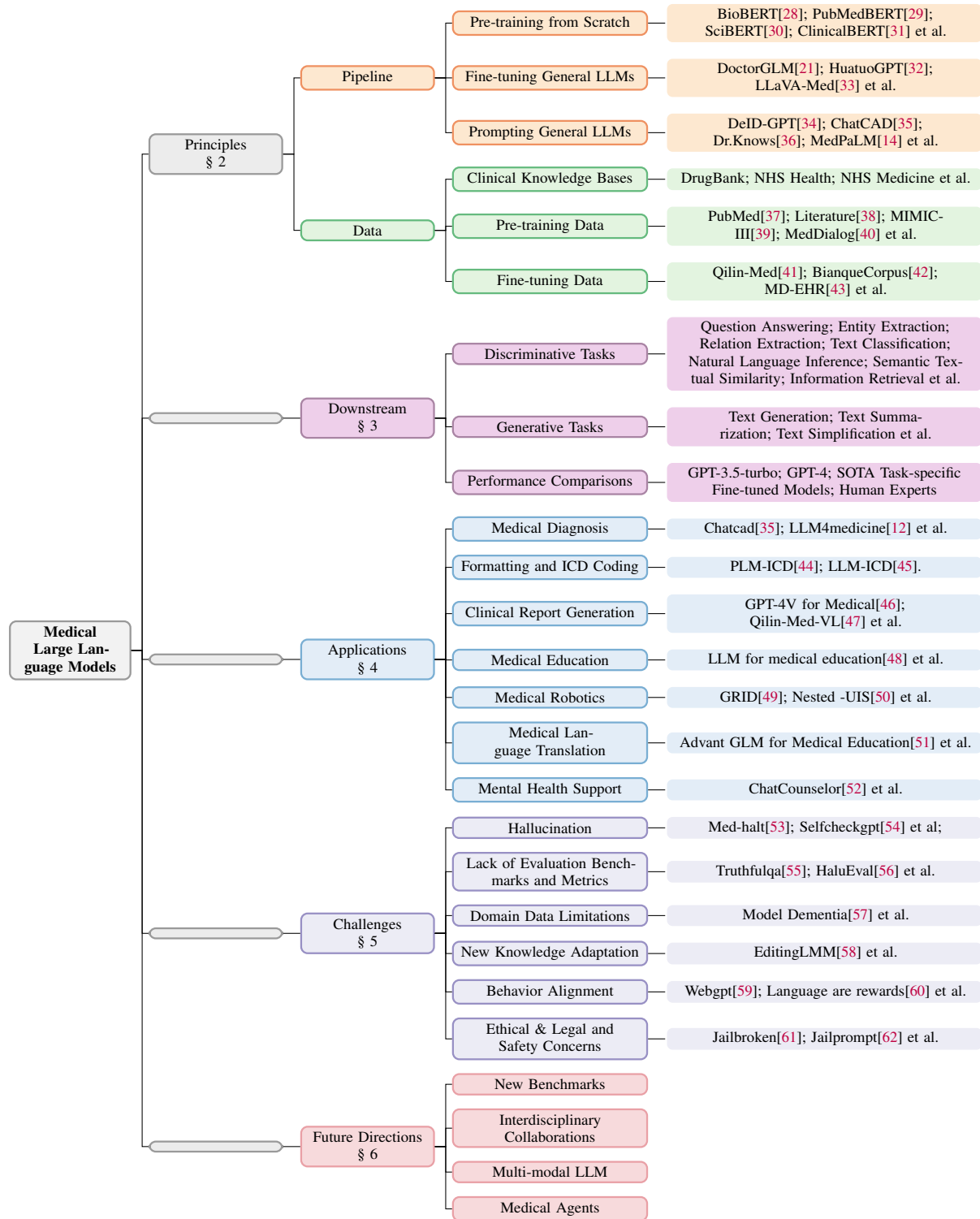


Figure 1: An overview of the practical guides for medical large language models.

For the final question, we offer insights into future directions for developing medical LLMs. This section serves as a guide for researchers and practitioners looking to advance this field and maximize the potential of medical LLMs in medicine.

In summary, this survey makes several contributions:

1. We provide a comprehensive survey of large language models in medicine and summarize their evaluations in ten biomedical downstream tasks.
2. We highlight the clinical applications of medical LLMs and offer practical guidelines for their deployment in various clinical settings.
3. We identify and discuss the challenges of applying medical LLMs in clinical practice, aiming to inspire further research and development in this area.

By addressing these questions and providing a holistic perspective on medical LLMs, we hope to foster deeper understanding, broader collaboration, and faster advancement in the field of medicine AI. The overall structure of the survey is as follows: Section 2 reviews existing research on LLMs and medical LLMs, emphasizing how to efficiently construct medical LLMs; Section 3 summarizes the performance of existing medical LLMs on ten representative biomedical AI tasks; Section 4 details how medical LLMs are applied in medicine; Section 5 delves into the challenge of existing medical LLMs; Section 6 introduces several potential opportunities to improve medical LLMs in terms of development and deployment. The conclusion of the paper is given in Section 7. Finally, we provide a more detailed background, including technical details and model development, of the general large language model in Appendix A for reference. Appendix B and C illustrate the detailed performances of LLMs on the downstream tasks.

## 2 The Principles of Medical Large Language Models

The adoption of LLMs in medicine is receiving increasing research interest. In this section, for clarity, we focus on summarizing the principles of medical large language models, putting the detailed introduction to the background of general LLMs in Appendix A. Existing medical LLMs are mainly pre-trained from scratch, fine-tuned from existing general LLMs, or directly obtained through prompting to align the general LLMs to the medical domain. Therefore, we introduce the principles of medical LLMs in terms of these three methods including: pre-training, fine-tuning, and prompting. Table 1 summarizes the details of the medical LLMs that are currently available.

### 2.1 Pre-training

Pre-training typically involves training an LLM on a large corpus of medical texts, including both structured and unstructured text, to learn rich medical knowledge. This corpus may include electronic health records (EHRs) [78], clinical notes [24], DNA sequence [98], and medical literature [31]. In particular, PubMed [37], MIMIC-III clinical notes [39], and PMC literature [99], are three widely used medical corpora for medical LLM pre-training. For example, PubMedBERT [29] is pre-trained on PubMed; ClinicalBERT is pre-trained on MIMIC-III; while BlueBERT [69] combines both corpora for pre-training; BioBERT [28] is pre-trained on PubMed and PMC. The internal UF Health clinical corpus (EHRs) is further introduced in pre-training GatorTron [24] and GatorTronGPT [78]. MEDITRON [79] is further pre-trained on Clinical Practice Guidelines (CPGs), which are used to guide healthcare practitioners and patients in making evidence-based decisions about diagnosis, treatment, and management.

Pre-training objectives for medical LLMs typically involve the commonly used masked language modeling, next sentence prediction, and next token prediction<sup>1</sup> but are refined to fit the needs of the medical domain. After pre-training, these medical LLMs are typically fine-tuned and evaluated on various downstream tasks to assess their understanding and generation capabilities. Currently, the widely-used downstream tasks for evaluating the medical LLMs [24, 78] are the question answering (QA)[23] and named entity extraction (NER), where the former task requires the model to generate responses/answers to questions using the medical knowledge it has learned, which is crucial for applications such as diagnostic support and medical research, and the latter task involves identifying

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<sup>1</sup>Please refer to Section A.1.2 for the introduction of these three pre-training objectives.

Table 1: Summary of existing medical-domain LLMs, in terms of their model development, the number of parameters, the pre-training/fine-tuning datasets, and the data source.

Domains	Model Development	Models	# Params	Data Scale	Data Source
Medical-domain LLMs (Sec. 2)	Pre-training (Sec. 2.1)	BioBERT [28, 68]	110M	18B tokens	PubMed [37]
		PubMedBERT [29]	110M/340M	3.2B tokens	PubMed [37]
		SciBERT [30]	110M	3.17B tokens	Literature [38]
		ClinicalBERT [31]	110M	112k clinical notes	MIMIC-III [39]
		BlueBERT [69, 70, 71]	110M/340M	>4.5B tokens	PubMed [37] MIMIC-III [39]
		BioCPT [72]	330M	255M articles	PubMed [37]
		BioGPT [73]	1.5B	15M articles	PubMed [37]
		BioMedLM [74]	2.7B	110GB	PubMed [75]
		OphGLM[76]	6.2B	20k dialogues	MedDialog [40]
		GatorTron [77, 24]	8.9B	>82B tokens 6B tokens 2.5B tokens+0.5B tokens	EHRs [24] PubMed [37] Wiki+MIMIC-III [39]
		GatorTronGPT[78]	5B/20B	277B tokens	EHRs [78]
		MEDITRON [79]	70B	48.1B tokens	PubMed [37] Clinical Guidelines [79]
	Fine-tuning (Sec. 2.2)	DoctorGLM [21]	6.2B	323MB dialogues	CMD. [80]
		BianQue[42]	6.2B	2.4M dialogues	BianQueCorpus [42]
		ClinicalGPT [43]	7B	96k EHRs 192 medical Q&A 100k dialogues	MD-EHR [43] VariousMedQA [81, 23] MedDialog [40]
		Qilin-Med [41]	7B	3GB	ChiMed [41]
		ChatDoctor[19]	7B	110k dialogues	HealthCareMagic [82] iCliniq [83]
		BenTsao [17]	7B	8k instructions	CMeKG-8K [84]
		HuatuoGPT [32]	7B	226k instructions&dialogues	Hybrid SFT[32]
		Baize-healthcare [85]	7B	101K dialogues	Quora+MedQuAD[86]
		MedAlpaca [16]	7B/13B	160k medical Q&A	Medical Meadow [16]
		AlpaCare [87]	7B/13B	52k instructions	MedInstruct-52k [87]
		Zhongjing [88]	13B	70k dialogues	CMtMedQA [88]
		PMC-LLaMA [22]	13B	79.2B tokens	Books+Literature[89] MedC-I [22]
		CPLLM [90]	13B	109k EHRs	eICU-CRD [91] MIMIC-IV [92]
		Clinical Camel [18]	13B/70B	70k dialogues 100k articles 4k medical Q&A	ShareGPT [93] PubMed [37] MedQA [23]
		MedPaLM 2 [15]	340B	193k medical Q&A	MultiMedQA [15]
	Prompting (Sec. 2.3)	DeID-GPT [34]	ChatGPT/GPT-4	Chain-of-Thought [94]	-
		ChatCAD [35]	ChatGPT	Zero-shot Prompting	-
		Dr. Knows [36]	ChatGPT	Zero-shot Prompting	UMLS [95, 96]
		MedPaLM [14]	PaLM (540B)	40 instructions	MultiMedQA [15]
		MedPrompt [97]	GPT-4	Few-shot Prompting Chain-of-Thought [94]	-

medical entities such as diseases, treatments, and medications from the text. Specifically, the two benchmarks BLUE [69] and BLURB [29] are widely used to provide a standard evaluation of models. BLUE (Biomedical Language Understanding Evaluation) benchmark [69] including ten public datasets, is used for evaluating the performance on NER, relation extraction, document classification, sentence similarity, and inference; BLURB (Biomedical Language Understanding & Reasoning Benchmark) [29] is a more comprehensive benchmark that includes thirteen datasets and further introduces the question-answering task.

## 2.2 Fine-tuning

Training LLMs from scratch typically requires much computational power, cost, and time. Therefore, lots of works [14, 15, 21, 19, 16, 41, 18] propose to fine-tune the general LLMs with medical data to learn domain-specific medical knowledge and obtain medical LLMs. Current popular fine-tuning methods include Supervised Fine-Tuning (SFT), Instruction Fine-Tuning (IFT), Low-Rank Adaptation (LoRA), and Prefix Tuning. The fine-tuned medical LLMs are summarized in Table 1.

**Supervised Fine-Tuning (SFT)** aims to leverage high-quality medical corpus, which can be physician-patient conversations [19], medical question-answering [16], and knowledge graphs [41, 17]. The constructed SFT data serves as continued pre-training data to further pre-train the general LLMs using the same training objectives, e.g., next token prediction. Therefore, SFT provides an additional pre-training phase to allow the general LLMs to learn rich medical knowledge and align with the medical domain, transforming them into specialized medical LLMs.

The versatility of SFT enables the development of diverse medical LLMs by training on different types of medical corpus. For example, DoctorGLM [21] and ChatDoctor [19] are obtained by supervised fine-tuning ChatGLM [9, 10] and LLaMA [4] on the physician-patient dialogue data, respectively. MedAlpaca [16] is fine-tuned using over 160,000 medical Q&A pairs sourced from diverse medical corpora. Clinicalcamel [18] has combined physician-patient conversations, clinical literature, and medical Q&A pairs to refine the LLaMA-2 model. In particular, Qilin-Med [41] and Zhongjing [88] are obtained by further incorporating the knowledge graph to perform supervised fine-tuning on the Baichuan [100] and LLaMA [4], respectively.

Overall, existing studies have demonstrated the efficacy of SFT in improving the performance of LLMs on medical tasks. It shows that SFT improves not only the model’s capability to understand and generate medical text but also its ability to provide more accurate clinical decision support [101].

**Instruction Fine-Tuning (IFT)** first constructs instruction-based training datasets [102, 101, 1], which are typically composed of instruction-input-output triples, e.g., instruction-question-answer. The primary goal of IFT is to further train LLMs to enhance their ability to follow various human/task instructions, align their outputs with the medical domain, and thereby produce a specialized medical LLM. Thus, the main difference between SFT and IFT is that the former focuses primarily on injecting medical knowledge into the LLM through continued pre-training, improving its ability to understand the medical text and accurately predict the next token, whereas IFT aims to improve the model’s *instruction following* ability and adjust its outputs to match that of the given instructions, rather than accurately predicting the next token [102]. As a result, in order to improve the performance of medical LLMs, SFT emphasizes more on the quantity of training data, while IFT emphasizes more on the quality and diversity of data rather than quantity. In other words, to enhance the performance of LLMs through IFT, it is important to ensure that the IFT data is of high quality and encompasses a wide range of medical instructions and medical scenarios. This diversity is essential for training medical LLMs to be able to accurately understand the various medical instructions.

For example, MedPaLM-2 [15] invited qualified medical professionals to develop the instruction data to fine-tune the PaLM. Meanwhile, BenTsao [17] and ChatGLM-Med [103] constructed the knowledge-based instruction data from the knowledge graph; Zhongjing [88] further incorporates the multi-turn dialogue as the instruction data to perform IFT. MedAlpaca [16] simultaneously incorporated the medical dialogues and medical Q&A pairs for instruction fine-tuning. Therefore, IFT has been proven to improve downstream performance. Since IFT and SFT can be used to improve performance in different aspects, there have been some recent works [88, 41, 87] that attempt to combine IFT and SFT to obtain more robust medical LLMs.

After fine-tuning, most current medical LLMs (e.g., MedPaLM 2 [15] and Clinical Camel [18]) evaluated their performances on the multiple QA datasets (e.g., MedQA (USMLE) [23], MedMCQA [104], PubMedQA [105], and MMLU [106]).

**Parameter-Efficient Tuning** aims to significantly reduce computational and memory requirements for fine-tuning LLMs. The main idea is to keep most of the parameters in pre-trained LLMs unchanged by fine-tuning only the smallest subset of parameters (or additional parameters) in the LLMs. Commonly used parameter-efficient tuning techniques include low-rank adaptation (LoRA) [107], prefix tuning [108], and Adapter Tuning [109, 110]. In detail, 1) **LoRA**: In contrast to fine-



tuning full-rank weight matrices, LoRA preserves the parameters of the original LLMs and only adds trainable low-rank matrices into the self-attention module of each Transformer layer [107]. Therefore, it can significantly reduce the number of trainable parameters, thus improving the efficiency of fine-tuning while still enabling the fine-tuned LLM to effectively capture the characteristics of the downstream tasks. 2) **Prefix Tuning**: It takes a different approach by adding a small set of continuous task-specific vectors, i.e., "prefixes," to the input of each Transformer layer [1]. These prefixes serve as the additional context to guide the model's generation without changing the original pre-trained parameter weights. 3) **Adapter Tuning**: It involves introducing small neural network modules, known as adapters, into each Transformer layer of the pre-trained LLMs. These adapters are fine-tuned while keeping the original model parameters frozen [111]. Therefore, this approach allows for flexible and efficient fine-tuning, as the number of trainable parameters introduced by adapters is relatively small, yet they enable the LLMs to adapt to downstream tasks effectively. For example, for medical LLMs, DoctorGLM [21], MedAlpaca [16], Baize-Healthcare [85], Zhongjing [88], CPLLM [90], and Clinical Camel [18] adopted the LoRA [107, 112] to perform parameter-efficient fine-tuning to efficiently align the general LLMs to the medical domain.

In summary, parameter-efficient tuning is valuable for developing LLMs for specific domains or meeting unique needs. It decreases computational demands without harming performance.

## 2.3 Prompting

Although fine-tuning saves considerable computational resources and costs compared to pre-training, it still consumes computational resources as it still requires further training of the model parameters and the collection of high-quality fine-tuning datasets. Therefore, some works, e.g., MedPaLM [14], incorporates several "prompting" methods to efficiently align general LLMs, e.g., PaLM [3], to the medical domain without training any model parameters. Popular prompting methods include few-shot prompting, chain-of-thought prompting, self-consistency prompting, and prompt tuning.

**Zero/Few-shot Prompting** Zero-shot prompting aims to directly give an instruction to prompt the LLM to efficiently perform a task following the given instruction. Few-shot prompting presents the LLMs with a small number of examples or task demonstrations before requiring them to perform a task. This method allows the LLMs to learn from these examples or demonstrations to accurately perform the downstream task and follow the given examples to give corresponding answers [7]. Therefore, few-shot prompting allows LLMs to accurately understand and respond to medical queries. For example, in the medical domain, MedPaLM [14] significantly improves the downstream performance by providing the general LLM, PaLM [3], with a small number of downstream examples, e.g., medical Q&A pairs.

**Chain-of-Thought (CoT) Prompting** CoT prompting is a technique that can further significantly improve the accuracy and logic of model output. Specifically, through prompting words, the CoT prompting technique aims to prompt the model to generate intermediate steps or paths of reasoning when dealing with downstream (complex) problems [94]. Moreover, CoT can be combined with few-shot prompting by giving reasoning examples. Thus, medical LLMs can give reasoning processes when generating responses. In tasks involving complex reasoning, such as medical Q&A, CoT can effectively improve performance [14, 15]. In medical LLMs, DeID-GPT [34], MedPaLM [14], and MedPrompt [97] adopt the chain-of-thought prompting to assist LLMs in simulating a diagnostic thought process, thus providing more transparent and interpretable predictions or diagnoses. In particular, MedPrompt [97] directly prompts the general LLM, GPT-4 [8], to outperform the domain-specific medical LLMs.

**Self-consistency Prompting** Self-consistency prompting is built on CoT to further enhance the robustness of the response [113]. It encourages the model to perform multiple attempts to generate multiple answers to the same question and then select the most consistent answer across different attempts. Therefore, self-consistency prompting can improve results even when CoT is ineffective. This approach could be particularly useful in the medical domain [97], where consistency in diagnosis or treatment recommendation is crucial.

**Prompt Tuning and Instruction Prompt Tuning** Inspired by the great success of prompting and fine-tuning, prompt tuning [114, 110] is proposed to achieve improved downstream performances.

In detail, compared to the prompting methods mentioned above, which introduce discrete and fixed prompts, the prompt tuning method introduces learnable prompts, i.e., trainable continuous vectors, which can be optimized/adjusted during the fine-tuning process to better adapt to different downstream tasks, thus providing a more flexible way of prompting LLMs.

In contrast to traditional fine-tuning methods, which train all the model parameters, prompt tuning only requires tuning a very small set of parameters associated with the prompts themselves without extensively training the model’s parameters. Thus, it effectively aligns LLMs to the medical domain with minimal computational cost, accurately responding to medical problems [110, 109, 97].

Recently, MedPaLM [14] and MedPaLM-2 [15] propose to combine all the above prompting methods to achieve strong performances on various medical question-answering datasets. In particular, in the MedQA (US Medical Licensing Examination (USMLE)) dataset, MedPaLM-2 [15] achieves a competitive accuracy of 86.5 compared to human experts, surpassing existing state-of-the-art by a large margin (19%). Other medical LLMs that employ prompting techniques are listed in Table 1.

### 3 Biomedical NLP Tasks

In this section, we will introduce two popular types of downstream tasks: generative and discriminative tasks, which include ten representative downstream tasks that further build up clinical applications. We will first briefly describe the downstream tasks and their widely-used evaluation datasets, and then we will discuss LLMs that are suitable for the task and compare their performance in detail. Table 2 summarizes the details of widely used evaluation datasets for each downstream task. Figure 2 illustrates the performance comparisons between different LLMs. For clarity, We will only cover a general discussion of those downstream tasks and leave a more detailed definition of the downstream task and the performance comparisons in Appendix B and Appendix C. The performance comparison of discriminative tasks is shown in Fig. 2.

#### 3.1 Discriminative Tasks

Discriminative tasks aim to categorize or differentiate data into specific classes or categories based on given input data. These tasks involve making distinctions between different types of data, often to categorize, classify, or extract relevant information from structured text or unstructured text. As shown in Table 2, the representative discriminative tasks include Question Answering, Entity Extraction, Relation Extraction, Text Classification, Natural Language Inference, Semantic Textual Similarity, and Information Retrieval. Therefore, the typical input for discriminative tasks can be medical questions, clinical notes, medical documents, research papers, and patient EHRs. The output, which is often structured and categorized information derived from the input text, can be labels, categories, extracted entities, relationships, or answers to specific questions. As a result, in existing LLMs, the discriminative tasks are widely studied and used to make predictions and extract information from input text.

For example, based on medical knowledge, medical literature, or patient EHRs, the medical question answering (QA) task can provide precise answers to clinical questions, e.g., symptoms, treatment options, or drug interactions. Therefore, medical QA could be helpful in aiding clinicians in making efficient and more accurate diagnoses [14, 15, 12]. Entity extraction can automatically identify and categorize critical information (i.e., entities) such as symptoms, medications, diseases, diagnoses, and lab results from patient EHRs, thus helping in organizing and improving the management of patient data [160]. The following entity linking aims to link the identified entities in a structured knowledge base or a standardized terminology system, e.g., SNOMED CT [161, 162], UMLS [95], or ICD codes [163], which is critical in clinical decision support or management systems. Thus, this task allows for better diagnosis, treatment planning, and patient care.

#### 3.2 Generative Tasks

Different from discriminative tasks, which focus on understanding and categorizing the input text, generative tasks require the models to accurately generate a fluent and appropriate (new) text based on given inputs. The representative generative tasks include medical text summarization [164, 165], medical text generation [73], and text simplification [166]. In medical text summarization, the input and output are typically a long and detailed medical text, e.g., the “Findings” in radiology reports, and

Table 2: Summary of existing widely-used biomedical NLP datasets for evaluation.

Types	Tasks	Datasets	Data Scale	Data ScaleData Source
Discriminative Tasks (Sec. 3.1)	Question Answering (Sec. B.1)	MedQA (USMLE) [23]	61,097 multiple-choice QA pairs	51 medical textbooks
		MedMCQA [104]	194k multiple-choice QA pairs	AIIMS and NEET PG entrance exam
		MMLU [106]	300 multiple-choice QA pairs	Clinical Knowledge
		PubMedQA [105]	273,500 question-context-answer triples	PubMed [37, 115]
		BioASQ-QA [116]	4,721 QA pairs	BioASQ [117]
		EMRQA [118]	400k+ QA pairs	i2b2
		ChiCR [119]	105k QA pairs	12k clinical case reports
		COVID-QA [120]	2,019 QA pairs	147 articles (CORD-19 [121])
	Entity Extraction (Sec. B.2)	MASH-QA [122]	34,808 QA pairs	WebMD website
		Health-QA [123]	7,517 questions and 7,355 articles	1,235 website Patient’s articles
		NCBI Disease [124]	6,892 entity mentions	793 PubMed abstracts
		JNLPBA [125]	59,963 entity mentions	2,404 abstracts (GENIA [126])
		GENIA [126]	96,582 entity mentions	2,000 MEDLINE abstracts
		BCSCDR [127]	28,785 entity mentions	1,500 PubMed articles
		BC4CHEMD [128]	84,355 entity mentions	10,000 PubMed abstracts
		BioRED [129]	20,419 entity mentions	600 PubMed abstracts
Discriminative Tasks (Sec. 3.1)	Relation Extraction (Sec. B.3)	CMeEE [130]	24,850 entity mentions	938 files
		ADE [131]	21,160 entity mentions	2,972 documents
		2012 i2b2 [132]	30,690 entity mentions	310 discharge summaries
		2014 i2b2/UTHealth [133]	57,744 entity mentions	1,304 longitudinal medical records
		2018 n2c2 [134]	83,869 entity mentions	505 discharge summaries[39]
		Cadec [135]	9,111 entity mentions	1,253 posts
		DDI [136]	18,491 entity mentions	1,017 texts
		EU-ADR [137]	7,011 entity mentions	100 MEDLINE abstracts
	Text Classification (Sec. B.4)	BCSCDR [127]	3,116 relations	1,500 PubMed articles
		BioRED [129]	6,503 relations	600 PubMed abstracts
		ADE [131]	13,806 relations	2,972 documents
		2018 n2c2 [134]	59,810 relations	505 discharge summaries
		2010 i2b2/VA [138]	1,748 reports	clinical reports
		GDA [139]	869,152 relations	30,192 PubMed titles and abstracts
		DDI [136]	5,021 relations	1,017 biomedical texts
		GAD [140]	5,937 records	genetic records
Generative Tasks (Sec. 3.2)	Information Retrieval (Sec. B.7)	2012 i2b2 [132]	54,560 relations	310 discharge summaries
		PGR [141]	4,283 relations	1,712 abstracts
		EU-ADR [137]	2,436 relations	100 abstracts
		ADE [131]	20,967 sentences	2,972 documents
		2014 i2b2/UTHealth[133]	1,304 records	longitudinal medical records
		HoC [142]	5,310 sentences	1,499 PubMed abstracts
		OHSUMED [143]	50,216 abstracts	50,216 medical abstracts
		WNUT-2020 Task 2 [144]	10,000 tweets	10,000 tweets
	Semantic Textual Similarity (Sec. B.6)	Medical Abstracts [145]	14,438 abstracts	28,880 medical abstracts
		MIMIC-III [39]	52,724 discharge summaries	53,423 hospital admissions
		MedNLI [146]	14,049 sentence pairs	MIMIC-III [39]
		BioNLI [147]	40,459 sentence pairs	PubMed abstracts
		MedSTS [148]	174,629 sentence pairs	3M clinical notes
		2019 n2c2/OHNLNLP [149]	2,054 sentence pairs	113k clinical notes and MedSTS [148]
Generative Tasks (Sec. 3.2)	Text Summarization /Generation (Sec. C.1/Sec. C.3)	BIOSES [150]	100 sentence pairs	Text Analysis Conference (TAC)
		TREC-COVID [151]	8,691 3-level query-document relations	CORD-19 [121]
		NFCorpus [152]	712k 3-level query-document relations	NutritionFacts.org (NF) website
		BioASQ (BEIR) [153]	32,916 binary query-document relations	BioASQ [117]
		MIMIC-CXR [154]	128k Findings-Impression pairs	radiology reports
		MIMIC-III [39]	73k Findings-Impression pairs	radiology reports
	Text Simplification (Sec. C.2)	PubMed [37, 115]	36M+ citations and abstracts	biomedical literature
		PMC [99]	9,407,149 papers	biomedical and life sciences literature
		CORD-19 [121]	140k+ papers	COVID-19 literature
		MentSum [155]	24,119 post-TLDR summary pairs	24,119 Reddit posts
		MeQSum [156]	1,000 question-summary pairs	U.S. National Library of Medicine
		MultiCochrane [157]	7,755 abstract-summary pairs	Cochrane Library systematic reviews
		AutoMeTS [158]	3,300 sentence pairs	English Wikipedia [159]

a concise summarized text, e.g., the “Impression” in radiology reports, containing the most important medical information, enabling the medical professionals or patients to efficiently capture the key points without going through the entire text. For example, text summarization can help healthcare professionals in drafting clinical notes by summarizing patient information or medical histories. In medical text generation, e.g., discharge summary generation [167], the input can be medical conditions, symptoms, patient demographics, or even a set of medical notes or test results. The output can be a diagnosis recommendation of a medical condition or personalized instructional information

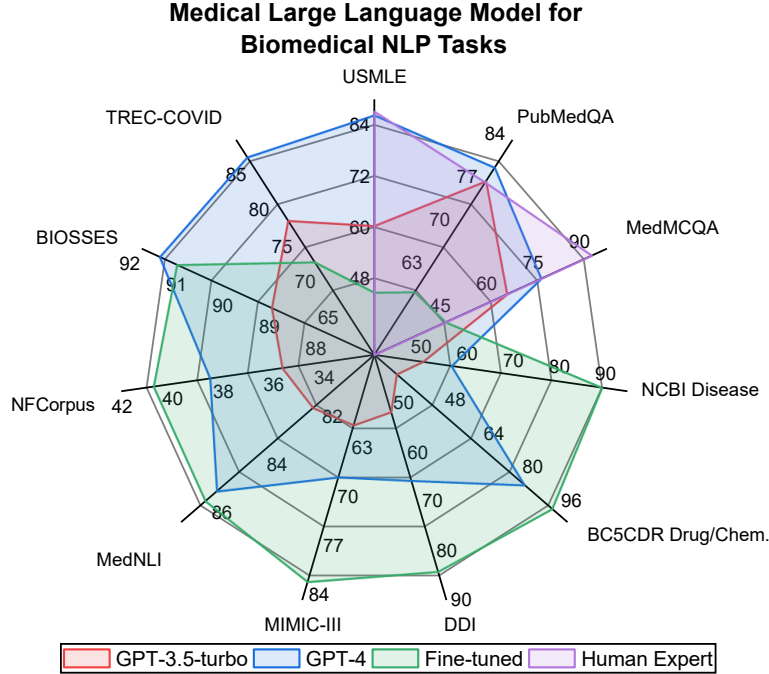


Figure 2: Performance comparison between the GPT-3.5 turbo, GPT-4, state-of-the-art task-specific fine-tuned models, and human experts, on seven downstream biomedical NLP tasks across eleven datasets. Please refer to Appendix B for details.

or health advice for the patient to manage their condition outside the hospital. In medical text simplification [166], the task aims to generate a simplified version of the input complex medical text by, for example, clarifying and explaining medical terms. For example, medical text simplification can help generate easy-to-understand patient education materials from complex medical texts. Therefore, it would be helpful in making medical information more accessible and understandable to a general audience, including patients, without altering the essential meaning of the text.

### 3.3 Performance Comparisons

As shown in Figure 2, existing strong general LLMs, i.e., GPT-3.5-turbo and GPT-4 [8], have achieved strong performance on existing downstream tasks. In particular, on the question answering datasets, i.e., MedQA (USMLE) [23], PubMedQA [105], MedMCQA [104], the GPT-4 (blue line) consistently achieves the state-of-the-art results, outperforms existing task-specific fine-tuned models, and is even comparable to human experts (purple line). However, on other tasks, the existing LLMs perform worse than the task-specific fine-tuned models. For example, on the entity extraction task (i.e., the NCBI disease dataset [124]), the state-of-the-art task-specific fine-tuned model BioBERT [28, 68] achieves an F1 score of 89.36, which significantly exceeds the GPT-4’s 56.73 F1 score. We hypothesize that the reason why LLMs can achieve excellent question answering performance is that the task is close-ended (i.e., the correct answer is already provided in multiple candidates), whereas most other tasks are open-ended (i.e., the model has to predict the correct answer from a large pool of possible candidates, or even without any candidates provided). This demonstrates that the current evaluation of LLMs should not be limited to medical question answering tasks, but should be evaluated more broadly. Overall, the comparison proves that the current general LLMs have a strong question answering capability, however, the capability on other tasks still needs to be improved.

## 4 Clinical Applications

This section discusses the clinical applications of LLMs. In each subsection, we introduce the application and discuss how LLMs perform this task, followed by challenges and future directions of LLMs in this specific use case.

## 4.1 Medical Diagnosis

Medical diagnosis involves the medical practitioner using objective medical data from tests and self-described subjective symptoms to conclude the most likely health problem occurring in the patient [168]. It is always important to diagnose a patient in an accurate and timely manner because the effectiveness of treatment for most diseases is extremely time-sensitive. For any illness, a missed or wrong diagnosis will often have negative consequences, ranging in severity from a minor inconvenience to death. For example, breast cancer has the highest mortality rate in the world because many communities lack trained personnel to perform proper checks [169]. Thus, incorporating LLMs into the medical diagnosis pipeline will increase the accessibility of professional healthcare [170, 12].

For example, a recently proposed method of using LLMs for medical diagnosis is through a graph model that returns the top paths regarding the pathology of diseases. Dr. Knows [36], a graph-based model that selects the top diagnosis cases with explainable paths trained on a real-world hospital dataset. The explainable paths come from the unified medical language system (UMLS) knowledge graph [95, 96]. The path encoder then generates a path representation, and the path ranker assesses the paths created for logical association with the input, generating a ranked list of probable disease diagnostics. Assessing the CUI-F score, a clinical metric that is a combination of CUI (concept identifier) recall and CUI precision, it is proven that when used on top of existing models, this method improves the aforementioned score by 8 percent to 18 percent depending on the base model chosen [36].

**Discussion** One distinct limitation of using LLMs as the sole tool for medical diagnosis is that it is completely reliant on the subjective inputs from the patient. Since LLMs are primarily text-based, they lack the inherent capability to analyze medical diagnostic imagery. Given that objective medical diagnoses frequently depend on visual images, LLMs are often unable to directly conduct diagnostic assessments as they lack concrete, visual evidence to support disease diagnosis [171, 172]. However, they can help with diagnosis as a logical reasoning tool to help improve accuracy in other vision-based models. For example, ChatCAD [35] utilizes the above logic in producing a diagnosis. Images are first fed into an existing computer-aided diagnosis (CAD) model to obtain tensor outputs. These outputs are translated into natural language, which is then fed into ChatCAD to summarize results and formulate diagnoses. ChatCAD achieves a recall score of 0.781, which is higher than the state-of-the-art model R2GenCMN’s 0.382. ChatCAD’s F1 score is also significantly higher than domain-specific model R2GenCMN [35]. We notice that although the more recent GPT-4V(vision) is capable of interpreting images in the general domain, an extension to the medical image domain is yet to materialize. Nevertheless, all aforementioned methods of implementing LLMs rely on image transformation into text beforehand. Other concerns include patient privacy, algorithm accountability, and the potential for bias [36].

## 4.2 Formatting and ICD-Coding

International classification of diseases (ICD) [173, 174] is a method of standardizing diagnostic and procedural information of a clinical session. Operations are recorded in the ICD code every time a patient visits a doctor in the individual’s electronic health records (EHR) to be referenced in the future. These codes are also for tracking health metrics, outcomes of treatments, as well as billing. There is a strong need to automate the ICD labeling process because it is time-intensive and often done by doctors themselves.

LLMs can help automate ICD coding by isolating medical terms from clinical notes and assigning corresponding ICD codes [45]. PLM-ICD [44] is an LLM fine-tuned for automatic ICD coding. It is fine-tuned as a multi-class classification model. In detail, the base model used in PLM-ICD is domain-specific with medicine-specific knowledge to enhance the ability to understand medical terms. In PLM-ICD, segment pooling, the algorithm that divides long input texts into shorter representations using LLMs, is used in cases where the input surpasses the maximum allowable length. To solve the issue of a large label set, the pre-trained language model is augmented with a label-aware attention mechanism to learn textual representations important to each label. Lastly, it relates the encoding to the augmented labels to output ICD codes for each clinical input. As a result of this, PLM-ICD produced a 92.6 macro AUC score and a 98.9 micro AUC score when implemented on the MIMIC-III full dataset [39], higher than scores of existing state-of-the-art models [44].



**Discussion** Addressing the potential biases and hallucinations in any LLM is paramount. Moreover, given that their algorithms have room for improvement, as evident from their AUC scores, it becomes crucial to establish a mechanism to detect and rectify these errors before they find their way into a patient’s Electronic Health Records (EHRs). Such a proactive approach is essential to prevent future confusion among healthcare professionals when interpreting medical records for diagnoses and medical procedures [175].

### 4.3 Clinical Report Generation

Clinical reports, e.g., radiology reports [176], discharge summaries [13], and patient clinic letters [177], refer to standardized documentation that healthcare workers must complete after each patient visit [178, 179]. It is closely linked to medical diagnosis as a large portion of the report is often diagnosis results. It is often tedious and time-consuming for clinicians and thus is often incomplete or error-prone for potentially overworked clinicians. Therefore, adopting LLMs for clinical report generation can provide an objective means of avoiding incompleteness, while reducing clinical workload, which is imagined as being a document that the clinician can review, modify, and approve as necessary (rather than taking human “out of the loop”) [13, 177, 167, 180].

An intuitive way LLMs can help with clinical report generation is as a summarization tool [35]. Given a diagnosis as input, it can use its text summarization capabilities, as discussed in previous sections, to give a clear and concise final conclusion. In this use case, LLMs do not directly contribute to improving the accuracy of the conclusion. Rather, they only act as a tool of convenience for the tedious work that otherwise would have been done by doctors.

Another popular utilization of LLMs to generate clinical reports often relies on some other type of vision-based model or manual input from a doctor as a precursor in the pipeline [181, 35, 176, 182, 46, 47]. The previous steps in the pipeline will first analyze the input medical image and feed the LLM some type of annotation. The LLM will use that information alongside some other text prompt, such as the report format, inputted by medical personnel to generate an accurate and fluent report that follows the requested format. This greatly reduces the workload on doctors [181, 183].

Most existing medical LLMs for clinical report generation focus on ChatCAD [35, 176, 46], a scheme that combines the vision-based Computer-Aided Diagnosis (CAD) with the text-based LLMs, which has been proven to improve the diagnostic performance score of the state-of-the-art report generation methods by 16.42 percent [35]. In this scheme, the CAD will generate some rudimentary text-based prompts based on the input medical diagnostic images, which will be fed into an LLM to further interpret. The LLM will then combine the inputs from CAD and other inputs, such as report format, to generate a formal report.

**Discussion** Even though using LLMs for clinical report generation or summarization has been proven more complete and more accurate than the human counterpart [165], there are still concerns with hallucination, as well as a tendency to approach inputs with a literal view instead of an assumption-based perspective often taken by human doctors. Additionally, there are also concerns that human-written reports are generally more concise than reports generated by LLMs [165].

### 4.4 Medical Education

The importance of the healthcare profession needs no explanation [48]. It is the basis of human existence. Therefore, training people for specific roles in the field is critical. Medical education can include both education for professionals, as well as education for the general public, which is arguably equally as important [184, 185, 186]. LLMs can be incorporated into the medical education system in many ways, including helping students prepare for medical exams, acting as a Socratic tutor, and answering questions [180].

Karabacak et al. [51] have proposed several benefits of incorporating LLMs into the medical education system, specifically for preparing medical students for medical exams and subsequently scenarios in the real world. They suggest that medical education can be augmented by generating scenarios, problems, and corresponding answers by an LLM. Through this system, students will be exposed to a larger variety of problems than what is in their textbook. Since LLMs can generate novel content, it will ensure that students will always have new problems to practice on [51]. LLMs can also generate feedback on the students’ responses to practice problems. This will ensure access to evaluation,

allowing students to know their areas of weakness in real time. Inherently, all of this will better prepare the medical students for the real world since they would have been exposed to more scenarios than before [187].

Another use of LLMs in the medical field is providing information to the public. Medical dialogues are often complex and difficult to understand for the average patient. By understanding the audience, LLMs can tune the textual output of prompts to use varying degrees of medical terminology. For the average person, this will make accessing and understanding medical information much less intimidating, and for the medical professional, this can ensure they have access to the most credible information [51].

**Discussion** Some potential downsides of using LLMs in medical education are the current lack of ethical training and the bias that may come from training datasets, causing some groups to be underrepresented [48]. In addition, the misinformation problem due to the many issues, such as hallucination in LLM, will present a challenge in utilizing this technology for medical education.

#### 4.5 Medical Robotics

Medical robots can be used in many facets of medicine, including during surgery [50], transporting patients, assisting nurses [188], medical rehabilitation [189], and many other use cases in the pipelines. Medical robots are used to combat the shortage of medical staff and perform tasks beyond the human's physical capabilities.

Robots require environmental information to function. The case of medical robots requires sensors to acquire input data, analyze that data, perform route planning, as well as execute the planned route to perform the required action. Therefore, route planning is a crucial stage in robotic execution. Graph-based Robotic Instruction Decomposer [49] was proposed as a way to utilize LLMs in route planning. This scheme uses scene graphs instead of image recognition to intake environment information and plan tasks in each stage for instruction. It can also predict upcoming tasks and plan pre-defined robotic movements in the scene graph. LLMs will then take the instruction, scene graph, and robot graph as inputs to output the planned route in text form. Experiments have shown this method outperforms GPT-4 by over 25.4% in simultaneously predicting correct action and object, and 43.6% in correctly predicting instruction tasks [49].

The proposed use of LLMs in medical robotics can also improve human-computer interaction. By improving the interactivity of robots, they may recognize human emotions and requests through natural language inputs. This allows patient communication with robots to be less intimidating and more user-friendly [180].

**Discussion** Some challenges with implementing medical robotics are quite similar to those when implementing collaborative robots (cobots), as both cases involve robots operating alongside humans, which requires trust in the robots to always do the right thing [190]. Dissimilar to cobots, by implementing LLM into the algorithm for route planning and robotic motion, there is more of a concern with the effects of bias and hallucination, causing an error in judgment. Unlike cobots, traditional robots have the ability to inhibit much more damage in cases of misjudgment. With an accuracy score of less than 50 percent, it is clearly still impossible for medical robotics powered through LLMs to be implemented in the real world at its current stage [190].

#### 4.6 Medical Language Translation

There are two main areas of medical language translation. One is the translation of medical terminology from one language to another [191, 192, 193]. The other is the translation of professional medical dialogue into expressions that are easy to understand by non-professional personnel [51]. Both cases are important as they both make communication more convenient, whether through different languages or between different groups of people.

The translation of medical terms from one language to another can facilitate global collaboration in both research and the application of medical techniques. Language is often one big barrier to global collaboration, and with the help of LLM, this barrier can be largely reduced. Machine translation has been proven to be 7 percent more accurate than traditional services [51]. Language translation will

also improve accuracy in education resources and research articles translation. This will help make knowledge more accessible worldwide [187].

The second use case improves medical education because LLMs can identify the skill level of the student and cater the same knowledge to that student using terminology and structures they will understand. On the other hand, it will also help patients, especially the elderly and the less knowledgeable, to understand professional medical speech [51].

**Discussion** One ethical consideration of using LLM to perform translation is the potential for discriminatory verbiage to be inserted inadvertently into the output. Because of the nature of the pipeline, this is difficult to catch and may cause miscommunications and even legal consequences. Also, potential misinformation caused by translation errors may cause patients to be confused and, in the worst case, take the wrong medical advice and execute it, inflicting harm to themselves [51].

#### 4.7 Mental Health Support

Mental health support involves both diagnosis and treatment. Depression, a common mental health problem, is treated through a variety of therapies, including cognitive behavior therapy, interpersonal psychotherapy, psychodynamic therapy, etc. [194]. Many of these techniques are primarily dominated by patient-doctor conversations. There have been various research articles on the effects of incorporating chatbots into the treatment plan [52, 195].

Chatbots powered by LLMs can massively increase the accessibility to mental health treatment resources [52]. Psychological consulting and subsequent treatments can be cost-prohibitive for many, and the ability for chatbots to serve as conversation partners and companions will significantly lower the barrier to entry for patients with financial or physical constraints [196]. The level of self-disclosure has a heavy impact on the effectiveness of mental health diagnosis and treatment. The more the patient is willing to share, the more accurate the diagnosis and, therefore, the more accurate the treatment plan. Studies have proven that the willingness to discuss mental health-related topics with a robot is high, which proves that alongside the convenience and lower financial stakes, mental health support by chatbots has the potential to be more effective than human counterparts in many scenarios [197, 198].

**Discussion** One challenge that may be difficult to overcome in the near term solely with LLMs is the difference in communication techniques between written and spoken communication. Hill et al. [199] found that respondents answered questions differently when asked to write the answer down instead of verbally expressing their answers. This may be a barrier that LLMs have to break in order to mimic a therapist to a higher degree [199]. Future studies could include longer-term studies to analyze how social penetration over time affects information disclosure [196].

### 5 Challenges

Despite their potential, using LLMs in medicine is not without challenges. The large scale of these models requires substantial computational resources, which can pose a limitation. Additionally, these models are susceptible to “hallucination”, where they generate incorrect or misleading information [64]. Furthermore, issues surrounding patient privacy and data bias present significant hurdles that must be addressed to ensure the ethical and equitable use of LLMs in medicine [200]. Despite of these challenges, the future of LLMs in medicine and medicine remains promising [12]. With ongoing research and technological advances, we foresee solutions to these challenges and increased implementation of LLMs in a wider array of healthcare applications, fueling the potential for personalized medicine and improved patient care.

#### 5.1 Hallucination

Hallucination of LLMs refers to the phenomenon where the generated output contains inaccurate or nonfactual information. It can be categorized into intrinsic and extrinsic hallucinations [64, 53, 63]. Intrinsic hallucination refers to generating outputs logically contradicting factual information - such as LLMs generating wrong calculations of mathematical formulas [64]. Extrinsic hallucination happens when the output generated cannot be verified - typical examples include LLMs ‘faking’ citations



that do not exist or ‘dodging’ the question. When integrating LLMs into the medical domain, fluent but nonfactual LLM hallucinations can lead to the dissemination of incorrect medical information, which can cause misdiagnoses, inappropriate treatments, and harmful patient education. Given the criticality of the medical domain, it is vital to ensure the accuracy of LLM outputs.

**Potential Solutions** Current solutions to mitigate LLM hallucination can be categorized into training-time correction, generation-time correction, and retrieval-augmented correction. The first solution, training-time correction, aims to mitigate hallucination by adjusting model weights and thus reducing the probability of generating hallucinated outputs. Examples of training-time correction include factually consistent reinforcement learning [201] and contrastive learning[202]. Another solution to reduce hallucination is to add a ‘reasoning’ process to the LLM inference to ensure reliability. Methods include drawing multiple samples [54] or using a confidence score to identify hallucination before the final generation. The third approach is the retrieval-augmented correction method, which utilizes external resources to help mitigate hallucination. For example, using factual documents as prompts [203] or chain-of-retrieval prompting technique [204].

## 5.2 Lack of Evaluation Benchmarks and Metrics

With the emerging ability of general-purpose LLMs, current benchmarks and metrics often fail to evaluate LLM’s overall capabilities, especially in the medical domain. Current benchmarks such as MedQA (USMLE) [23] and MedMCQA [104] offer extensive coverage on question-answering tasks but fail to evaluate important LLM-specific metrics such as trustworthiness, helpfulness, explainability, and faithfulness [205]. The need for more domain and LLM-specific benchmarks and metrics is imperative.

**Potential Solutions** Singhal et al. [14] proposed HealthSearchQA consisting of commonly searched health queries, offering a more human-aligned benchmark for evaluating LLM’s capabilities in the medical domain. Benchmarks such as TruthfulQA [55] and HaluEval [56] evaluate more LLM-specific metrics, such as truthfulness, but fail to cover the medical domain. Future research is necessary to develop more medical and LLM-specific benchmarks and metrics.

## 5.3 Domain Data Limitations

Current datasets in the medical domain, as shown in Table 1, remain relatively small compared to datasets used to train general-purpose LLMs (Table 3). The medical knowledge domain is vast; existing datasets are limited and do not cover the entire space [14]. This results in LLMs exhibiting extraordinary performance on open benchmarks with extensive data coverage yet falling short on real-life tasks such as differential diagnosis and personalized treatment planning [15].

**Potential Solutions** Although the volume of medical and health data is large, most require extensive ethical, legal, and privacy procedures to be accessed. In addition, these data are often unlabeled, and solutions to leverage these data, such as human labeling and unsupervised learning [206], face challenges due to the lack of human expert resources and small margins of error. Current state-of-the-art approaches [14], [15], [19], prefer to fine-tune on smaller open-sourced datasets to improve models’ domain-specific performances. Another solution is to generate high-quality synthetic datasets using LLMs to broaden the knowledge coverage [207]. However, several works have discovered that training on generated datasets causes models to forget [57]. Therefore, future research is needed to validate the effectiveness of using synthetic data for LLMs in the medical field.

## 5.4 New Knowledge Adaptation

LLMs are trained on extensive data to learn knowledge. Once the LLM is trained, injecting new knowledge through re-training is expensive and inefficient. Two problems occur when a knowledge update is required (for example, a new adverse effect of a medication, or a novel disease): The first problem is how to make LLMs ‘forget’ the old knowledge - it is almost impossible to remove all ‘old knowledge’ from the training data, and the discrepancy between new and old knowledge can cause unintended association and bias [58]. The second problem is the timely addition of knowledge - how do we ensure the model is updated in real-time? These problems pose significant barriers to using

LLMs in medical fields, where accurate and timely update of up-to-date medical knowledge is crucial in real-world implementations.

**Potential Solutions** We can categorize current solutions into model editing and retrieval-augmented generation. Model editing [208] refers to altering the model’s knowledge by modifying the model’s parameters. These methods do not generalize, and their effectiveness varies across different model architectures. The second solution is retrieval-augmented generation, which provides external knowledge sources as prompts during model inference. For example, Lewis et al. [209] enabled model knowledge updates by updating the model’s external knowledge memory.

## 5.5 Behavior Alignment

Behavior alignment refers to the process of ensuring that the LLM’s behaviors align with the objectives of its task. While efforts are spent aligning LLMs with human behavior, the behavior discrepancy between general humans and medical professionals remains challenging for adopting LLMs in the medical domain. For example, ChatGPT’s answers for medical consultations are not as concise and professional as the human expert’s answers [210]. In addition, misalignment introduces unnecessary harm and ethical concerns [211] that lead to undesirable consequences in the medical domain.

**Potential Solutions** Current solutions include instruction fine-tuning, reinforcement learning from human feedback (RLHF) [212, 210], and prompt tuning [114, 110]. Instruction fine-tuning [213] refers to improving the performance of LLMs on specific tasks based on explicit instructions. For example, Ouyang et al. [210] used this technique to help LLMs generate less toxic and more suitable outputs. RLHF is a reinforcement learning technique that uses human feedback to evaluate and align the outputs of LLMs. It has proven effective in multiple tasks, such as helping LLMs become helpful chatbots [214] and decision-making agents [59]. Prompt tuning can also align LLMs to the expected output format. For example, Liu et al. [215] uses a prompting strategy, chain of hindsight, to enable the model to detect and correct its errors, which aligns the generated output with human expectations.

## 5.6 Ethical, Legal and Safety Concerns

Several works have raised concerns regarding using LLMs such as ChatGPT in the medical domain [200]. Most have a focus on ethics, accountability, and safety. For example, the scientific community has disapproved of using ChatGPT in writing biomedical research papers [216] due to ethical concerns. In addition, the accountability of using LLMs as assistants to practice medicine is challenging [101]. Moreover, Li et al. [61] and Shen et al. [62] found that prompt injection can cause the LLM to leak personal information, such as email addresses, from its training data a significant vulnerability when implementing LLM in the medical domain.

**Potential Solutions** While no solution is available, we have seen several efforts trying to understand the cause of these ethical and legal concerns. For example, Wei et al. [217] propose that prompt leaking is attributed to the mismatch of generalization between safety and capability objectives. Moreover, more efforts from the government and large corporations are spent to regularize and monitor the use of AI in various fields, including healthcare and medicine.

# 6 Future Directions

While LLMs have already significantly impacted people’s lives through chatbots and search engines powered by them, integrating LLMs into medicine is still in the infant stage. Numerous new avenues await researchers and practitioners to explore for medical LLMs to serve the general public better. These avenues include introducing new benchmarks, establishing interdisciplinary collaborations, developing multimodal LLMs, and applying LLMs to less established medicine fields.

## 6.1 Introduction of New Benchmarks

Recent studies have underscored the shortcomings of existing benchmarks in evaluating Large Language Models (LLMs) for clinical applications [218, 219]. Traditional benchmarks, which primarily gauge accuracy in medical question-answering, inadequately capture the full spectrum of

clinical skills necessary for LLMs [14]. Criticisms have been leveled against the use of human-centric standardized medical exams for LLM evaluation, arguing that passing these tests does not necessarily reflect an LLM’s proficiency in the nuanced expertise required in real-world clinical settings [219, 14, 220]. In response, there is an emerging consensus on the need for more comprehensive benchmarks. These should include capabilities like sourcing from authoritative medical references, adapting to the evolving landscape of medical knowledge, and clearly communicating uncertainties [14]. Additionally, considering the sensitive nature of healthcare, these benchmarks should also assess factors such as fairness, ethics, and equity, which, though crucial, pose quantification challenges [14]. The aim is to create benchmarks that more effectively mirror actual clinical scenarios, thus providing a more accurate measure of LLMs’ suitability for medical advisory roles. Current LLM research in medicine has largely focused on general medicine, likely due to the greater availability of data in this area [14, 15, 101]. However, this focus has resulted in the underrepresentation of LLM applications in specialized fields like ‘rehabilitation therapy’ and ‘sports medicine’. The latter, in particular, holds significant potential, given the global health challenges posed by physical inactivity. The World Health Organization identifies physical inactivity as a major risk factor for non-communicable diseases (NCDs), impacting over a quarter of the global adult population [221]. Despite initiatives to incorporate physical activity (PA) into healthcare systems, implementation remains challenging, particularly in developing countries with limited PA education among healthcare providers [222]. LLMs could play a pivotal role in these settings by disseminating accurate PA knowledge and aiding in the creation of personalized PA programs [223]. Such applications could significantly enhance PA levels, improving global health outcomes, especially in resource-constrained environments.

## 6.2 Interdisciplinary Collaborations

Just as interdisciplinary collaborations are crucial in safety-critical areas like nuclear energy production, collaborations between the medical community and technology communities developing medical LLMs are essential to ensure AI safety and efficacy in medicine. The medical community has primarily used technology company-provided LLMs without questioning their data training. Given this sub-optimal situation, medical professionals are encouraged to actively participate in creating and deploying medical LLMs by providing relevant training data, defining the desired benefits of LLMs, and conducting tests in real-world scenarios to evaluate these benefits [219]. Such assessments would help to determine the legal and medical risks associated with LLM use in medicine and inform strategies to mitigate LLM hallucination [224].

## 6.3 Multimodal LLM Integrated with Time-Series, Visual, and Audio Data

Multimodal LLMs (MLLMs), or Large Multimodal Models (LMMs), are LLM-based models designed to perform multimodal tasks [225]. While LLMs primarily address NLP tasks, MLLMs support a broader range of tasks, such as comprehending the underlying meaning of a meme [226] and generating website codes from images [227]. This versatility suggests promising applications of MLLMs in medicine. For example, several MLLM-based frameworks integrating vision and language, i.e., MedPaLM M [228], LLaVA-Med [33], Visual Med-Alpaca [229], Med-Flamingo [230], and Qilin-Med-VL [47], have been proposed to adopt the medical image-text pairs for fine-tuning, enabling the medical LLMs to efficiently understand the input medical images, e.g., radiology images. A most recent work [231] is proposed to integrate vision, audio, and language inputs for automated diagnosis in dentistry. However, there are only very few medical LLMs that can process time series data, such as electrocardiograms (ECGs) [232] and sphygmomanometers (PPGs) [233]. These time series data are important for medical diagnosis and monitoring. Moreover, like LLMs, MLLMs are associated with data privacy and quality challenges. The multimodal nature of MLLM also introduces unique issues, including limited perception capabilities [231][227], fragile reasoning chains [234], sub-optimal instruction-following ability [234], and object hallucination [227]. Therefore, more research is needed to address these issues, ensuring a safe and effective application of MLLM in medicine.

## 6.4 Medical Agents

With the development of Large Language Models (LLMs), LLM-based agents [235, 236] have achieved significant progress in solving complex tasks (e.g. software design, molecular dynamics simulation) through human-like behaviors, such as role-playing and communication [237, 238, 239].

However, integrating these agents effectively within the medical domain remains a challenging problem. The medical field involves numerous roles [240] and decision-making processes, especially in disease diagnosis, which often requires a series of investigations like CT scans, ultrasounds, electrocardiograms, and blood tests. The idea of utilizing LLMs to model each of these roles, thereby creating collaborative medical agents, presents a promising direction. These agents could mimic the roles of radiologists, cardiologists, pathologists, etc., each specializing in interpreting specific types of medical data. For example, a radiologist agent could analyze CT scans, while a pathologist agent could focus on blood test results. The collaboration among these specialized agents could lead to a more holistic and accurate diagnosis. By leveraging the comprehensive knowledge base and contextual understanding capabilities of LLMs, these agents could not only interpret individual medical reports but also integrate these interpretations to form a cohesive medical opinion. This multi-agent approach could significantly enhance diagnostic accuracy, reduce the time taken for diagnosis, and alleviate the workload on healthcare professionals. Furthermore, incorporating feedback loops within this system can enable continuous learning and improvement. As these Medical Agents interact with real-world medical data and cases, they can refine their decision-making algorithms and adapt to emerging medical trends and novel diseases. However, this approach also raises several challenges and considerations. Ensuring the privacy and security of patient data is paramount, as these systems would handle sensitive medical information. Additionally, the reliability and accuracy of the agents' interpretations need rigorous validation to meet medical standards. Lastly, the ethical implications of AI in healthcare, especially in decision-making roles, must be carefully examined. Overall, collaborative medical agents not only promise to improve healthcare delivery but also open up new avenues for research and development in AI-assisted medical decision-making.

## 7 Conclusion

Large language models (LLMs) have made tremendous progress in natural language processing in recent years, opening up new opportunities for their application in medicine. This survey provides a comprehensive overview of existing medical LLMs, including details on model architecture, parameter size, pre-training data, fine-tuning data, evaluation benchmarks, and so on. It also summarizes their performance across diverse biomedical NLP tasks. Our analysis reveals that while LLMs have achieved promising results on benchmarks, significant gaps remain between benchmark performance and real-world clinical utility. Therefore, we further explore the potential of LLMs in various clinical applications such as diagnosis, clinical note generation, medical education, and other scenarios. However, deploying LLMs in medical settings remains challenging. We also point out the challenges faced by LLM in medical applications, such as hallucination, lack of explainability, data shortage, and evaluation limitations. As medical LLM applications are still in their infancy, to fully realize the benefits of LLMs in medicine, future research and development needs to focus on: developing new evaluation benchmarks with medical-specific metrics like trustworthiness, safety, fairness, etc; strengthening interdisciplinary collaboration between medical and AI communities; building multimodal LLMs to integrate time series, visual, and audio data; and applying LLMs to more medical sub-domains.

In summary, this survey provides a comprehensive overview of the principles, applications, and challenges of LLMs in medicine, intended to promote further research and exploration in this interdisciplinary field. With the rapid development of foundation models, the LLMs could significantly improve future clinical practice and medical discoveries for the benefit of society. However, realizing this goal safely and accountably remains a great challenge. It requires sustained interdisciplinary collaboration between clinicians and AI researchers, doctor-in-the-loop, and human-centered design. Moreover, the co-development of appropriate training data, benchmarks, metrics, and deployment strategies could enable faster and more responsible implementation of medical large language models.

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## A Appendix: Background

In this section, we describe the background from the 1) Formulation of Large Language Model, 2) General Large Language Model. The details of existing LLMs are shown in Table 3.

### A.1 Formulation of Large Language Model (LLM)

The impressive performance of LLMs can be attributed to their Transformer architecture, large-scale pre-training, and scaling laws. Please refer to [1] for details.

#### A.1.1 Language Model - Transformer

The language model Transformer is first used in machine translation [241] and is then successfully applied to achieve state-of-the-art results [242] in multiple NLP tasks. The natural strength of the Transformer lies in its *fully-attentive mechanism*, in which no recurrence is required. It is based solely on attention mechanisms and eliminates recurrence and convolutions entirely. Therefore, it not only enables a more efficient use and model of the input data [243], resulting in efficient understanding and modeling of long-text, but also can be easily and highly paralleled training [241], inducing less training and inference cost. These characteristics make the Transformer highly scalable, which makes it easy and efficient to obtain LLMs through large-scale pre-training strategy, such as the encoder-only LLM BERT [242], the encoder-decoder LLM T5 [244], and the decoder-only LLM GPT [6].

#### A.1.2 Large-scale Pre-training

The success of LLMs typically relies on the large-scale pre-training strategy. During pre-training, an LLM is trained on massive corpora of open-domain unlabeled text (e.g., CommonCrawl, Wiki, and Books [1, 4, 5]) in an unsupervised or self-supervised learning manner. The common training objectives are masked language modeling, next sentence prediction, and next token prediction.

- *Masked language modeling* is a training objective where a portion of the input text is masked, and the model is tasked with predicting the masked words based on the remaining unmasked context. This encourages the model to learn contextual representations, capturing the semantic and syntactic relationships between words [242].
- In *Next sentence prediction* training, the model is given two sentences and tasked with predicting whether the second sentence logically follows the first. This helps the model learn the relationships between sentences and improves its ability to capture the overall coherence of the text [242].
- *Next token prediction* is another common training objective, where the model is required to predict the next token in a sequence given the previous tokens. In this way, it helps the model to understand the given context and reason for the next token, developing predictive capabilities [6]. This training objective has been commonly used in existing popular LLMs, e.g., GPT-series models [7, 8], PaLM [3], LLaMA [4], and LLaMA-2 [5].

After pre-training, the LLMs have learned rich general language representations that can be leveraged for various downstream tasks. To achieve strong downstream performances, the LLMs can be further fine-tuned (i.e., trained) on a smaller, task-specific dataset. This allows the model to adapt its general language representations to the specific requirements of the target task. The combination of large-scale pre-training and fine-tuning has proven to be highly effective in achieving state-of-the-art performance. In addition, large-scale pre-training allows LLMs to learn a wide range of linguistic knowledge and a broad understanding of language patterns and concepts. It enables LLMs to perform well on “zero-shot” and “few-shot” learning scenarios. In these scenarios, they can accurately perform the downstream tasks without human-labeled data for training. It is important for many low-resource application scenarios, e.g., low-resource language scenarios and medical scenarios, where a large amount of labeled data for training is usually unavailable.

#### A.1.3 Scaling Laws

LLMs are essentially scaled-up versions of Transformer architecture [241] with increased numbers of transformer layers, model parameters, and the volume of pre-training data. The “scaling laws”

Table 3: Summary of existing general-domain (large) language models, their underlying structures, numbers of parameters, and datasets used for model training.

Domains	Model Structures	Models	# Params	Pre-train Data Scale
General-domain (Large) Language Models (Sec. A.2)	Encoder-only	BERT [242]	110M/340M	3.3B tokens
		ERNIE [247]	110M	173M sentences
		ALBERT[248]	12M/18M/60M/235M	16GB
		ELECTRA [249]	14M/110M/335M	33B tokens
		RoBERTa [250, 158]	123M/355M	161GB
		DeBERTa[251]	1.5B	160GB
	Decoder-only	XLNet [250]	110M/340M	158GB
		GPT-2[6]	1.5B	40GB
		Vicuna[252]	7B/13B	LLaMA + 70K dialogues
		Alpaca[253]	7B/13B	LLaMA+ 52K IFT
		LLaMA [4]	7B/13B/33B/65B	1.4T tokens
		LLaMA-2 [5]	7B/13B/34B/70B	2T tokens
		Galactica [98]	6.7B/30.0B/120.0B	106B tokens
		GPT-3[7]	6.7B/13B/175B	300B tokens
		InstructGPT [210]	175B	-
		PaLM [3]	8B/62B/540B	780B tokens
		FLAN-PaLM [14]	540B	-
		Bard [254]	-	-
		GPT-4[8]	-	-
	Encoder-Decoder	BART [255]	140M/400M	160GB
		ChatGLM [9, 10]	6.2B	1T tokens
		T5 [157]	11B	1T tokens
		Flan-T5 [157]	3B/11B	780B tokens
		mT5 [157]	1.2B/3.7B/13B	1T tokens
		UL2 [256]	19.5B	1T tokens
		GLM [10]	130B	400B tokens

[245, 246] predict how much improvement can be expected in a model’s performance as its size increases (in terms of parameters, layers, data, or the amount of training computed). Specifically, in order to achieve optimal model performance, the scaling laws proposed by OpenAI [245] show that the budget allocation for model size should be larger than the data size, while the scaling laws proposed by Google DeepMind [246] show that both model and data sizes should be increased in equal scales. The empirical validation of scaling laws has been instrumental in developing LLMs, providing guidance for researchers and practitioners to efficiently allocate resources and anticipate the benefits of scaling their models. As a result, building upon these scaling laws, many LLMs have been proposed, advancing the development of natural language understanding and generation.

## A.2 General Large Language Models

In this section, we briefly introduce existing general LLMs [1]. As shown in Table 3, the general LLMs can be divided into three categories based on their architecture: encoder-only LLMs, encoder-decoder LLMs, and decoder-only LLMs. Please refer to [2] for details.

### A.2.1 Encoder-only LLM

Encoder-only LLMs, typically consisting of a stack of transformer encoder layers, are designed to comprehend input sequences and produce dense context-aware representations, which aim to capture the semantic and syntactic properties of the input sequence. These models typically employ a bidirectional training strategy, which allows them to integrate context from both the left and the right of a given token in the input sequence. This bi-directionality enables the models to achieve a deep understanding of the input sentences [242]. Therefore, encoder-only LLMs are particularly suitable for language understanding tasks that require a comprehensive understanding of the input text, such as sentiment analysis [257], document classification [258], named entity recognition [259], and other tasks where the full context of the input is essential for accurate predictions. The strong performance of encoder-only LLMs in language understanding tasks has attracted significant research interest, thus leading to a large number of proposed encoder-only LLMs. Representative encoder-only LLM is the BERT [242]. Other encoder-only LLMs include DeBERTa[251], ALBERT[248], and RoBERTa[260]. ELECTRA [249], ERNIE [247]. In brief, encoder-only LLMs represent a vital

development in the field of natural language processing, with their bidirectional training and deep contextual understanding setting new benchmarks for a range of downstream tasks.

### A.2.2 Decoder-only LLM

Decoder-only LLMs, which utilize a stack of transformer decoder layers, are characterized by their uni-directional (left-to-right) processing of text, enabling them to generate language in a sequential manner. Unlike encoder-only LLMs, decoder-only LLMs are not designed for bidirectional context understanding but are rather good at language generation tasks. During training, this architecture is trained unidirectionally using the next token prediction training objective to predict the next word in a sequence, given all the previous words, which aligns naturally with language generation tasks such as text completion, storytelling [7], dialogue [8], and structured generation task - code generation [261]. During inference, the decoder-only LLMs can directly generate sequences autoregressively. The prominent examples of decoder-only LLMs are the GPT (Generative Pre-Training Transformer) series developed by OpenAI [6, 7, 8] and the LLaMA (Large Language Model Meta AI) series developed by Meta [4, 5]. Both of them have been employed successfully in language generation. Especially as a result of the open-source of LLaMA, a large number of improved LLM based on LLaMA have been proposed, e.g., Alpaca [253] and Vicuna [252]. As shown in Table 3, other popular decoder-only LLMs include PaLM [3], Bard [254], and GPT-4[8].

### A.2.3 Encoder-decoder LLM

Encoder-decoder LLMs are designed to simultaneously process input sequences and generate output sequences. They typically consist of a stack of bidirectional transformer encoder layers followed by a stack of unidirectional transformer decoder layers, in which the encoder processes and understands the input sequences, acquiring context-aware representations, and the decoder aims to generate the output sequences based on the encoded representations [244]. Therefore, encoder-decoder LLMs can combine the benefits of both the encoder and the decoder, resulting in them being suitable for tasks that require both understanding input sequences and subsequently generating output sequences, such as 1) machine translation, where the encoder processes the source language text, and the decoder generates the translation in the target language [262], 2) summarization [263], where the encoder reads the full-length document and the decoder produces a concise summary, and 3) even non-language tasks, such as protein structure prediction [264]. Representative encoder-decoder LLMs include Flan-T5 [157], and ChatGLM [9, 10].

## B Appendix: Discriminative Tasks

### B.1 Question Answering

**Task Description** Question Answering (QA) [265] aims to give answers to the given queries. It aims to generate multiple-choice or free-text responses. A multiple-choice response happens when one asks the model a question with the material for answering the question included. For example, the QA for 'Is hypertension a risk factor for cardiovascular disease, yes or no?' is multiple-choice-orientated. In contrast, an open question without potential answers to choose from gives rise to a free-text response. For example, QA for 'What are the common symptoms of influenza?' is free-text-orientated.

**Datasets and Models** Table 2 shows the commonly used datasets in the biomedical area like MedQA (USMLE) [23], PubMedQA [105], and MedMCQA [104]. Since biomedical QA datasets are relatively small in size compared to general datasets, using pre-trained models from general datasets and then finetuning them on the biomedical data improves the performance [266, 267]. Pergola et al. [268] proposed a biomedical-specific masking method. Instead of masking tokens randomly, the model will identify biomedical-related tokens and mask them to focus more on in-domain learning. Wang et al. [269] defined the self-questioning prompting (SQP) and utilize it on the BioASQ dataset. The idea of this prompting method is to let the GPT model ask questions about the given text and then asks the GPT to answer those question to extract useful information for specific tasks. However, hallucination also threatens the quality of outputs in QA. One way is to use biomedical search systems like Almanac [270]. Another approach is to use extra datasets as an augmentation for the QA task. There are many chatbots based on LLM QA, such as Clinical Camel [18], DoctorGLM

Table 4: The performance (accuracy) on five question answering datasets. FT models are short for fine-tuned models.

Types	Models	MedQA (USMLE)	PubMedQA	MedMCQA	MMLU (Clinical Knowledge)	MMLU (Professional Medicine)
Task-specific FT Models	BERT [242]	44.6	51.6	43.0	-	-
	RoBERTa [250, 158]	43.3	52.8	-	-	-
	BioBERT [28, 68]	30.1	60.2	-	-	-
	SciBERT [30]	29.5	57.4	-	-	-
	ClinicalBERT [31]	29.1	49.1	-	-	-
	BlueBERT [69, 70, 71]	-	48.4	-	-	-
	PubMedBERT [29]	38.1	55.8	-	-	-
General LLMs	Med-PaLM-2 [15]	<b>86.5</b>	<b>81.8</b>	72.3	<b>88.3</b>	<b>95.2</b>
	FLAN-PaLM (few-shot) [14]	67.6	79.0	57.6	-	-
	GPT-4 (zero-shot) [8]	78.9	75.2	69.5	86.0	93.0
	GPT-4 (few-shot) [8]	86.1	80.4	<b>73.7</b>	86.4	93.8
	GPT-3.5 (zero-shot) [7]	50.8	71.6	50.1	69.8	70.2
	GPT-3.5 (few-shot) [7]	60.2	78.2	62.7	68.7	69.8
	Clinical Camel-13B (zero-shot) [18]	34.4	72.9	39.1	54.0	51.8
	Clinical Camel-13B (5-shot) [18]	45.2	74.8	44.8	60.4	53.3
	Clinical Camel-70B (zero-shot) [18]	53.4	74.3	47.0	69.8	71.3
	Clinical Camel-70B (5-shot) [18]	60.7	77.9	54.2	72.8	75.0
	Galactica [98]	44.4	77.6	52.9	-	-
	BioMedLM [74]	50.3	74.4	-	-	-
	BioGPT [73]	-	81.0	-	-	-
	PMC-LLaMA [22]	56.4	77.9	56.0	-	-
	Human (expert) [101, 276]	87.0	78.0	90.0	-	-

[21], ChatDoctor [19], HuaTuo [17], HuaTuoGPT [32], and MedAlpaca [16]. Except for a few [271], most chatbots are a black box the the consumers, so further studies of those chatbots are required.

**Evaluation** We use accuracy as the metric in QA. We compare the performance of task-specific (fine-tuned) BERT variations [29, 272, 23, 273], Med-PaLM-2 [15, 18], FLAN-PaLM [14], GPT-4 [274, 18], GPT-3.5 [275, 18], Clinical Camel [18], Galactica [98], BioMedLM [74], BioGPT [73], and PMC-LLaMA [22] on the datasets we introduced. Table 4 shows the detailed QA performance on five widely-used datasets. The citations in this paragraph correspond to the sources providing data on the performance of the models. We can see that significantly BERT models have worse performance than GPT models. For GPT models, the rule that the few-shot setting outperforms the zero-shot setting still holds. Among all models, Med-PaLM-2 have a relatively high accuracy. It shows that fine-tuning the LLMs on the medical data is workable and can significantly improve performance.

## B.2 Entity Extraction

**Task Definition** Entity extraction, or named entity recognition (NER) [259] aims to identify named entities mentioned in unstructured text into predefined categories such as the names of persons, organizations, locations, medical codes, time expressions, quantities, monetary values, percentages, etc. Existing task-specific fine-tuned models leverage large-scale pre-trained language representations and fine-tuning on NER datasets to achieve state-of-the-art performances. The self-attention mechanisms [241] allow for efficiently capturing complex patterns and dependencies. In the healthcare domain, medical NER aims to extract medical entities such as disease names, medication, dosage, and procedures from clinical narratives, electronic health records (EHRs), and chemicals and proteins from scientific literature. Therefore, NER can provide a solid basis for clinical decision support systems, automated patient monitoring, etc.

**Datasets and Models** Table 2 shows several commonly used biomedical NER datasets, such as NCBI Disease [124], JNLPBA [125], and BC5CDR [127]. To perform the NER task, for each input token, the existing models output a dense representation, which not only embeds the tokens but also includes its relation with other tokens in the text. Therefore, with the dense representations of

Table 5: The performance (F1-score) on four entity extraction datasets.

Types	Models	NCBI Disease	BC5CDR Disease	BC5CDR Drug/Chem.	JNLPBA
Task-specific FT Models	BERT [242]	85.63	82.41	91.16	74.94
	BioBERT [28, 68]	89.36	86.56	93.44	77.59
	SciBERT [30]	88.57	<b>90.01</b>	90.01	77.28
	PubMedBERT [29]	87.82	85.62	93.33	<b>79.10</b>
	BlueBERT [69, 70, 71]	88.04	83.69	91.19	77.71
General LLMs	ClinicalBERT [31]	86.32	83.04	90.80	78.07
	GPT-3 [7]	51.40	43.60	73.00	-
	GPT-3.5 (zero-shot) [7]	24.05	-	29.25	-
	GPT-3.5 (one-shot) [7]	12.73	-	18.03	-
	GPT-4 (zero-shot) [8]	56.73	-	74.43	-
	GPT-4 (one-shot) [8]	48.37	-	82.07	-
	ChatGPT [289]	50.49	51.77	60.30	41.25
	BARD (zero-shot) [254]	<b>96.00</b>	-	97.70	-
	BARD (5-shot) [254]	95.60	-	<b>98.30</b>	-

input tokens extracted as vectors, additional layers are applied to the last Transformer layer to fit the downstream entity extraction task. The widely-used additional layers are softmax, BiLSTM [277], CRF [278, 279], and their combinations [280, 278, 281, 279, 282, 283]. Gu et al. [284] proposed a distillation method that uses few-shot GPT-3.5 to extract the correct entities and create the training set for the student model. This method shows that GPT models can be used to label the dataset first to achieve unsupervised learning. Wang et al. [269] defined a new prompting method self-questioning prompting (SQP) for NER. Wang et al. [269] further evaluated the performances of BARD, GPT-3.5, and GPT-4 with SQP and achieved some state-of-the-art results.

**Evaluation** The entity-level F1 score is widely used to evaluate the models’ performance. Recently, there have been some works studying the performance of LLMs, i.e., GPT-3 [285, 286, 287], GPT-3.5 [288], GPT-4 [288], and ChatGPT [218], on biomedical NER tasks. The citations in this paragraph correspond to the sources providing data on the performance of the models. We summarize the performances of existing LLMs on the NER task in Table 5. It is obvious that both the encoder-only BERT-series models (e.g., BioBERT [28], SciBERT [30], PubMedBERT [29], BlueBERT [69], and ClinicalBERT [31]) significantly outperform most decoder-only LLM GPT-series models (e.g., GPT-3 [7] and GPT-4 [8]), under both the zero-shot and few-shot settings. Recently, there have been some works studying the performance of GPT-3 [285, 286, 287], GPT-3.5 [288], and GPT-4 [288, 218] on biomedical NER tasks. *It shows current GPT models still need further studies to outperform traditional task-specific fine-tuned models [287].*

### B.3 Relation Extraction

**Task Description** Similar to entity extraction, relation extraction (RE) aims to find the relation between entities in a text. It is highly related to entity extraction since identifying entities first can improve the model’s performance. A relation can be ordered or unordered. For example, in the sentence ‘I work in London’ the relation ‘workspace’ is order-sensitive and the pair (I, London) is of such a relation, but in the sentence ‘Alice and Bob are friends’ the relation ‘friend’ is not order-sensitive. In the biomedical area, relation extraction is often used to extract relations in a MedAbstract text for further applications like text summarization.

**Datasets and Models** Table 2 shows some biomedical datasets for RE, such as BC5CDR, BioRED, and DDI. In reality, most datasets indicate the potential entity for the relation instead of asking the model to find it, so RE is usually considered as a classification problem. One common technique for task-specific fine-tuned models is to use the [CLS] token or the classification token, which learns the information of all input tokens, and is further used to classify the relation. There are some works on using the [CLS] token and applying softmax in the last layer [290, 291, 292, 293]. There are also approaches that use not only the [CLS] token, but also all other token representations. It shows that using all token representations outperforms other attempts [294]. Wang et al. [269] defined the self-questioning prompting (SQP) as we discussed in Sec B.1 and utilize it in the DDI RE task.

Table 6: The performance (F1-score) on four relation extraction datasets.

Types	Models	BC5CDR	ChemProt	DDI	GAD
Task-specific FT Models	BioBERT [28, 68]	-	76.46	80.88	82.36
	SciBERT [30]	<b>79.00</b>	<b>83.64</b>	<b>84.08</b>	81.34
	PubMedBERT [29]	-	-	82.36	<b>83.96</b>
	BioGPT [73]	46.17	-	40.76	-
General LLMs	GPT-3 [7]	-	25.90	16.10	66.00
	GPT-3.5 (zero-shot) [7]	-	57.43	33.49	-
	GPT-3.5 (one-shot) [7]	-	61.91	34.40	-
	GPT-4 (zero-shot) [8]	-	66.18	63.25	-
	GPT-4 (one-shot) [8]	-	65.43	65.58	-
	ChatGPT [289]	-	34.16	51.62	52.43
	BARD (zero-shot) [254]	-	-	56.60	-
	BARD (5-shot) [254]	-	-	77.20	-

Table 7: The performance (F1-score) on four text classification datasets.

Types	Models	HoC	i2b2	MIMIC-III	OHSUMED
Task-specific FT Models	PubMedBERT [29]	82.32	-	-	-
	BioGPT [73]	<b>85.12</b>	-	<b>82.30</b>	-
General LLMs	GPT-4 (5-shot) [8]	-	<b>99.00</b>	67.40	-
	ChatGPT (0-shot) [289]	-	92.90	-	39.93
	ChatGPT (2-shot) [289]	-	92.90	-	47.05
	ChatGPT (5-shot) [289]	-	92.90	60.00	45.39
	ChatGraph [296]	-	-	-	<b>60.79</b>

**Evaluation** For evaluation, existing works use the F1-score as the metric. Since here we have a simple classification problem, the definition of terms in F1-score is conventional. In Table 6, we compare the performance of BioBERT [28, 295], SciBERT [30, 295], PubMedBERT [29, 295], BioGPT [73], GPT-3 [285, 286, 287], GPT-3.5 [288], GPT-4 [288], and ChatGPT [218] on the datasets we introduced before. It is clear that at present task-specific fine-tuned models outperform GPT models. For GPT models, even the best model (GPT-4) can’t have an F1-score of over 70%, while all task-specific fine-tuned models based on BERT can have an F1-score of about 80%. Again, for token-level tasks, zero-shot and few-shot don’t have a significant difference in performance [269].

#### B.4 Text Classification

**Task Description** Not like entity extraction or relation extraction, text classification is a sentence or text-level task. It is a classic classification problem: assigning predefined labels to a text, and it is common for a text to have multiple labels to describe it. Therefore, the task is to predict all correct labels given the input medical text. It can be used as the preprocessing of medical text simplification and summarization.

**Datasets and Models** Table 2 shows some commonly used text classification datasets, such as HoC and OHSUMED. Since it is a text-level task, the [CLS] vector is augmented when using task-specific fine-tuned (transformer-based) models. Another approach to distilling the overall information is to use the weighted sum of final attention layer outputs. There are works showing that adding a custom attention layer after the original model (BERT) improves the performance [298, 299]. McCreery et al. [300] double-fine-tuned the BERT model in the sense that they first fine-tuned the model on a general dataset and then fine-tuned it on a medical-specific dataset. There are also some works combining graph-based models with general LLMs. ChatGraph [296] used ChatGPT to extract text information and apply it to a graph-based model that outperforms GPT models. CohortGPT [301] used Chain-of-Thought prompting and knowledge graph to outperform few-shot ChatGPT and GPT-4.



Table 8: The performance (F1-score) of natural language inference.

Types	Models	MedNLI
Task-specific FT Models	BERT [297]	76.11
	ALBERT [297]	77.84
	Roberta [297]	80.14
	BioBERT [297]	81.83
	ClinicalBERT [297]	80.66
	BlueBERT [297]	83.92
	SciBERT [297]	79.43
	BlueBERT+AG [297]	<b>84.34</b>
General LLMs	GPT-3.5 [7]	82.21
	GPT-3.5-Distillation [284]	80.24
	GPT-4 [8]	85.69
	BARD (zero-shot) [254]	76.00
	BARD (5-shot) [254]	76.00

**Evaluation** For evaluation, we use the F1-score, and the definition of terms in the F1-score is conventional. Table 7 compares the performance of PubMedBERT [29], BioGPT [73], GPT-4 [34, 301], ChatGPT [296, 301], and ChatGraph [296] on four benchmark datasets. We can see that GPT models have better performance on the i2b2 dataset rather than OHSUMED dataset. It might be because its few-shot setting is not good enough. Overall, few-shot GPT outperforms zero-shot GPT models, and with more parameters, we tend to have higher F1-scores.

## B.5 Natural Language Inference

**Task Description** Natural Language Inference (NLI) is a sentence-level task. It includes two sentences: hypothesis and premise. Determining whether the hypothesis ( $H$ ) can be inferred from the premise ( $P$ ) is the task. The outcome belongs to one of the following three labels: (i) *Entailment*: the hypothesis can be inferred from the premise, or logically,  $P \implies H$ . (ii) *Contradiction*: the negation of the hypothesis can be inferred from the premise, or logically,  $P \implies \neg H$ . (iii) *Neutral*: all other cases, or logically,  $\neg((P \implies H) \vee (P \implies \neg H))$ .

**Datasets and Models** Table 2 shows some commonly used datasets, such as MedNLI [146] and BioNLI [147]. Since biomedical datasets for NLI are scarce, researchers also use some general datasets like SNLI [302] and MultiNLI [303]. In task-specific fine-tuned models, similar to RE, [CLS] vector is often added to the text to show the overall information. The difference is that now we have two sentences, so a [SEP] vector is also applied to indicate the separation of premise and hypothesis, hence the overall input will look like '[CLS], premise, [SEP], hypothesis'. For BERT-based models, a classification head is applied to the final [CLS] vector to predict the label. Kanakarajan et al. [68] first pre-trained BioBERT [28] on MIMIC-III [39] and then fine-tuned the model on MedNLI [146]. Cengiz et al. [304] used the so-called two-stage sequential transfer learning method. They trained the BioBERT model on SNLI [302] and MultiNLI [303] first then fine-tuned it on the MedNLI dataset [146]. They also used the majority vote method to combine the prediction output of different trained models. Gu et al. [284] combined GPT-3.5 and PubMedBERT using knowledge distillation. They fed GPT-3.5 original texts and asked it to distill the data, then they used the distilled data to further train the PubMedBERT model. Wang et al. [269] defined the self-questioning prompting as we discussed in Sec B.1 and utilize it in the MedNLI task.

**Evaluation** For evaluation, we report the F1-score. We compare the performance of various task-specific fine-tuned models, e.g., BioBERT, ClinicalBERT, BlueBERT, and SciBER on the benchmark MedNLI dataset [284]. We also show the performances of GPT-3.5 and GPT-3.5-Distillation (see Table 8). As we can see, BioBERT [28] has the best performance. It also demonstrates that current general LLMs still need further explorations on natural language inference.

Table 9: The performance (sample Pearson correlation coefficient) of semantic textual similarity.

Types	Models	BIOSSES	2019 n2c2/OHNLP
Task-specific FT Models	BERT [242]	81.40	69.23
	ClinicalBERT [31]	91.23	83.20
	XLNet [250]	-	84.70
	RoBERTa [250, 158]	81.25	<b>87.78</b>
	HConv-BERT [305]	-	79.40
	BERT (CSE-concate) [306]	-	86.80
	ClinicalBERT (iterative training) [31]	-	87.00
General LLMs	BARD (zero-shot) [254]	57.60	-
	BARD (5-shot) [254]	60.10	-
	GPT-3.5 (zero-shot) [7]	87.30	-
	GPT-3.5 (5-shot) [7]	89.20	-
	GPT-4 (zero-shot) [8]	88.90	-
	GPT-4 (5-shot) [8]	<b>91.60</b>	-

## B.6 Semantic Textual Similarity

**Task Description** Semantic Textual Similarity (STS) is similar to natural language inference (NLI). While NLI is more of a qualitative task, STS is a quantitative task. It aims to give a numerical value in a range (such as  $[0, M]$ ) for any pair of sentences that indicates the degree of similarity, with the interpretation that 0 means two sentences are completely independent and  $M$  means two sentences are completely correlated or equivalent.

**Datasets and Models** As shown in Table 2, the ‘2019 n2c2/OHNLP’ [149], BIOSSES [150], and MedSTS [148] are widely-used benchmark datasets for STS. Since STS is a text-level task, [CLS] vector is naturally added to extract the overall information. Mutinda et al. [70] added a fully connected layer after the [CLS] vector as the architecture. Yang et al. [250] combined the representation of different models and added a fully connected layer. Wang et al. [305] dropped the concept of [CLS] and used the Hierarchical Convolution (HConv) layer as the added last layer. Wang et al. [269] defined the self-questioning prompting (SQP) and utilize it on the BIOSSES dataset. Xiong et al. [306] used the concatenation of character level, sentence level, and entity level representation (CSE-concate) to extract the information that is fed to the further added MLP layer. For further training on a pre-trained model, there is an understanding that the new dataset should have a similar distribution as the dataset for pre-training for better performance. The method of iterative training is introduced for this purpose [307, 71]. The method is called iterative because it does the following two steps iteratively: a) It first freezes the model and computes the outputs from the dataset, then it chooses a subset of the dataset so the outputs of the subset have a similar distribution to that of the pre-training dataset. b) After that, we further trained the model using the obtained subset.

**Evaluation** For comparison, we choose the sample Pearson correlation coefficient  $r_{xy}$ : for  $n$  pairs of data  $\{x_i, y_i\}_{i=1}^n$ , we define  $r_{xy} = \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^n (x_i - \bar{x})^2} \sqrt{\sum_{i=1}^n (y_i - \bar{y})^2}}$ . Here,  $\{x_i\}_{i=1}^n$  represents the actual similarity and  $\{y_i\}_{i=1}^n$  represents the predicted similarity. We compare the performance of BERT [70, 295], ClinicalBERT [70, 295], XLNet [250], RoBERTa [250, 295], HConv-BERT [305], BARD [269], GPT-3.5 [269], GPT-4 [269], BERT (CSE-concate) [306], and ClinicalBERT (iterative training) [71] on BIOSSES and ‘2019 n2c2/OHNLP’ datasets. As we can see, the task-specific fine-tuned model RoBERTa achieves the best results on the ‘2019 n2c2/OHNLP’ dataset. Meanwhile, although GPT-4 can achieve the highest Pearson correlation coefficient of 91.60, we can notice that, with significantly fewer model parameters, the task-specific fine-tuned model ClinicalBERT achieves a competitive result compared to GPT-4. Therefore, the current general LLMs still need further exploration and improvement on this task.

## B.7 Information Retrieval

**Task Description** Information retrieval (IR) plays an important role in the clinical area. It is the process of retrieving relevant knowledge or information related to the query from a number

Table 10: The performance ((NDCG@10) on three information retrieval datasets.

Types	Models	TREC-COVID	NFCorpus	BioASQ
Task-specific FT Models	OpenAI cpt-text-S [308, 72]	67.9	33.2	-
	OpenAI cpt-text-M [308, 72]	58.5	36.7	-
	OpenAI cpt-text-L [308, 72]	56.2	38.0	-
	OpenAI cpt-text-XL [308, 72]	64.9	<b>40.7</b>	-
	BioCPT [28, 68]	70.9	35.5	<b>55.3</b>
General LLMs	GTR-Base [309]	53.9	30.8	27.1
	GTR-Large [309]	55.7	32.9	32.0
	GTR-XL [309]	58.4	34.3	31.7
	GTR-XXL [309]	50.1	34.2	32.4
	ChatGPT [289]	76.7	35.6	-
	ChatGPT [289] + GPT-4 [8]	<b>85.5</b>	38.5	-

of unstructured data. It is used to satisfy one’s need for searching information, such as article recommendations and literature searches. IR in the biomedical domain contains many tasks. Text summarization and text simplification are two relevant tasks as we will discuss in Sec C.1 and Sec C.2. Question answering is also an important task included in IR, which we have discussed in Sec B.1. In this subsection, we will be concentrating on the query-article relevance task, which is also known as the ranking task. In particular, for a query  $q$  and a dataset of articles  $\{d_i\}_{i=1}^n$ , we aim to find the most relevant  $k$  articles  $(d_1^q, d_2^q, \dots, d_k^q)$  where the degree of relevance is defined task-specifically.

**Datasets and Models** Table 2 shows some commonly used datasets in the biomedical area like TREC-COVID [151], NFCorpus [152], and BioASQ [153]. As a more general dataset, BEIR (Benchmarking IR) [153] is often included in the training step of biomedical IR. Jin et al. [72] developed a BERT-based model BioCPT that encodes the query and articles for the ranking task. They split the method into training, inference, and evaluation steps. In the training step, they introduced query-to-document loss and document-to-query loss to train the encoders for the query and articles. In the inference step, they concatenate the encoding of the query and its best-fit article  $d_1^q$  together with  $k - 1$  non-relevant articles  $(d_2^q, d_3^q, \dots, d_k^q)$  found by maximum inner product search (MIPS) to further train the model to rank  $d_1^q$  at the top. In the evaluation step, for each input query  $q$ , the model evaluates over the whole dataset  $\{d_i\}_{i=1}^n$  to find the best  $k$  relevant articles by MIPS and used the model from the inference step to rank those  $k$  articles. Sun et al. [310] applied zero-shot ChatGPT to rank the most relevant documents without abnormal prompting. They also further used GPT-4 to re-rank the top 30 documents retrieved by ChatGPT. Abonizio et al. [311] introduced two LLM-based data augmentation methods, namely InPars and Promptagator, for IR. For InPars, they used GPT-3 and GPT-J to generate a new query for a randomly selected document. They used few-shot prompting which provides the model with good query examples or bad query examples. For Promptagator, the major difference is that a more dataset-specific prompting is applied. Ateia and Kruschwitz [312] proposed a query expansion technique that expands the current query into a more comprehensive query, which consistently improves the performance of any successive tasks. It is done purely by the GPT model with regular instructional prompting. Similarly, Wang et al. [313] used ChatGPT to generate more refined Boolean queries for systematic reviews. They showed that ChatGPT is able to generate or refine queries with higher precision.

**Evaluation** For evaluation, we use the Normalized Discounted cumulative gain at  $k$  (NDCG@ $k$ ). With the notation we defined earlier, we further denote  $\text{rel}(q, d)$  as the relevance of article  $d$  to query  $q$ . If we have the best  $k$  articles in order  $(d_1^{\text{ideal}}, d_2^{\text{ideal}}, \dots, d_k^{\text{ideal}})$  and  $k$  articles retrieved by the model  $(d_1^{\text{model}}, d_2^{\text{model}}, \dots, d_k^{\text{model}})$ . We define  $\text{NDCG}@k = \left( \sum_{i=1}^k \frac{\text{rel}(q, d_i^{\text{model}})}{\log(i+1)} \right) / \left( \sum_{i=1}^k \frac{\text{rel}(q, d_i^{\text{ideal}})}{\log(i+1)} \right)$ . We compare the performance of Google’s Generalizable T5-based dense Retrievers (GTR) [314, 72], OpenAI’s cpt-text [308, 72], BioCPT [72], ChatGPT [310], and ChatGPT+GPT-4 [310] on the datasets we introduced before. The citations in this paragraph correspond to the sources providing data on the performance of the models. From Table 10, we can see that ChatGPT and GPT-4 have the best performance. One peculiar thing is that an increase in parameters doesn’t necessarily improve the performance. GTR-XXL even has a lower NDCG@10 score than those of other GTR models.

Table 11: The performance (ROUGE-1 &amp; ROUGE-2) of the text summarization task.

Types	Models	PubMed
Task-specific FT Models	BioBERT (LSTM) [315]	35.82 & 17.15
	BioBERTSum [315]	37.45 & 17.59
	BioBERT (Pubmed + PPF) [316]	74.21 & 32.88
	BioBERT (PMC + PageRank) [316]	75.82 & 34.01
	BioBERT (Pubmed + PageRank) [316]	76.09 & 34.38
	BioBERT (Pubmed + PMC + PageRank) [316]	<b>76.34 &amp; 34.67</b>

Also, we can see that all models are not very stable facing different data, even ChatGPT+GPT-4 has only a 0.3847 score for NFCorpus.

## C Appendix: Generative Tasks

### C.1 Text Summarization

**Task Description** There are two types of text summarization: extractive and abstractive summarization. Extractive summarization aims to find the most important sentences in the text while omitting the redundant or irrelevant sentences. In contrast, abstractive summarization generates brand-new texts that summarize the given text. Therefore, the extractive approach is more related to token-level tasks while the abstractive approach is more relevant to high-level tasks (e.g. text generation).

**Datasets and Models** Table 2 shows the commonly used datasets PubMed [37] and MentSum [155]. There are also some commonly used general datasets like GigaWord [317], CL-SciSumm [318], and S2ORC [89]. For extractive summarization, the key point is to define some scoring system that scores all sentences and hence finds the most important ones. Moradi et al. [319] used a clustering-based method to summarize medical texts. They vectorize the tokens of the text by BERT and cluster the sentence vector into  $k$  clusters, then they define an informativeness score that chooses one sentence from each cluster to form a summary. Moradi et al. [316] used the graph-based model to summarize. They treated sentences as nodes and relations as edges. The relations are measured by calculating the cosine similarity of vectors representing the sentences. They then used different graph ranking algorithms to choose important sentences as a summary. Du et al. [315] used purely the transformer-based model as the scoring system. They tokenized the whole text with [CLS] and [SEP] augmented. They further augmented the corresponding sentence and token positions to each token and fed the whole vector into the model. A sigmoid layer is added to the model so the output is between zero and one, and the output is considered the score for each sentence. Since the transformer automatically extracts relations of one sentence to others, Du et al. don’t need to design a score manually. Chen et al. [320] also relied only on the model to score the sentences. The difference is that they used AlphaBERT and the training is split into pre-training and fine-tuning. McNerney et al. [321] combined the summarization model with a query to output more specific summaries. Pang et al. [322] proposed a principled inference framework with top-down and bottom-up inference techniques to improve summarization models. There are also works about summarizing more than one text at a time. Those works mainly relied on graph-based or transformer-based models to extract relations between different texts [323]. Zhang et al. [324] applied one-shot GPT-3.5, using dialogues and summaries from the same category as prompts to generate abstractive summarization. More studies are needed to qualitatively analyze the performance of GPT models on biomedical text summarization [325].

**Evaluation** For performance comparison, we use the standard Recall-Oriented Understudy for Gisting Evaluation (ROUGE) [326]. We compare the performance of BioBERT variations with different training sets [316], rankings (PageRank and PPF) [316], and added last layers [315] on PubMed (please see Table 11). The citations in this paragraph correspond to the sources providing data on the performance of the models. We can see that models fine-tuned on Pubmed or PMC data have better performance. The ranking strategy doesn’t create significant differences in the models. Overall, by inspecting the ROUGE-2 scores, current BERT models are far below the expectation of true text summarization.

Table 12: The performance (BLEU) of the text simplification task on the MultiCochrane (English) dataset.

Model	MultiCochrane
GPT-3 (zero-shot) [7]	2.38
Flan-T5 (zero-shot) [157]	8.12
mT5 [157]	<b>8.82</b>
Flan-T5 (fine-tuned) [157]	8.70

Table 13: The performance (accuracy) of the text simplification task on the AutoMeTS dataset.

Model	AutoMeTS
BERT [242]	62.40
RoBERTa [250, 158]	53.28
XLNet [250]	46.20
GPT-2 [6]	49.00
BERT [242] + RoBERTa [250, 158] + XLNet [250] + GPT-2 [6] [18]	<b>64.52</b>

## C.2 Text Simplification

**Task Description** One may confuse text simplification with text summarization [327]. While text summarization concentrates on giving shortened text while maintaining most of the original text meanings, text simplification focuses more on the readability part, hence there is no extractive approach for text simplification. The task is to generate a new text that recovers almost all the information of the original text while improving its readability. In particular, complicated or opaque words will be replaced; complex syntactic structures will be improved; and rare concepts will be explained [327]. For example, a complex sentence like ‘Lowered glucose levels result both in the reduced release of insulin from the beta cells and in the reverse conversion of glycogen to glucose when glucose levels fall’ can be simplified into ‘This insulin tells the cells to take up glucose from the blood’. It is possible in extreme cases, text simplification may increase the length of a text for readability improvement. Text simplification has potential in biomedical education since one major characteristic of medical education is its opaque vocabulary [166, 328].

**Datasets and Models** Table 2 shows the commonly used text simplification datasets. Patel et al. [329] used NER to identify the medical terms. Lexical substitution is then applied to reduce the complexity of the text. Jeblick et al. [330] tested the performance of ChatGPT on simplifying self-collected radiology reports. They tried different prompting texts and found out that the prompt ‘Explain this medical report to a child using simple language’ performs the best. However, by evaluating from a) factual correctness, b) completeness, and c) harmfulness, they concluded that GPT models may generate harmful texts which is unacceptable in the medical domain. Joseph et al. [157] evaluated the performance of zero-shot GPT-3 and Flan-T5 on MultiCochrane. They also fine-tuned mT5 [331] and Flan-T5 on this dataset. Yang et al. introduced a data augmentation method for text simplification based on LLMs. For a text without its simplified counterpart, they used GPT-3 to generate multiple choices for simplified text and further trained a BERT model as the score to choose the best one as the simplification. Van et al. [158] transferred the simplification task into a prediction task. They assume they have the original text  $(d_1, d_2, \dots, d_n)$  and a unfinished simplified text  $(s_1, s_2, \dots, s_i)$ . The task is to predict the next token  $s_{i+1}$ . In particular, at each time, the model receive  $(d_1, d_2, \dots, d_n, s_1, s_2, \dots, s_i)$  as input and predict  $s_{i+1}$ . They used different models like BERT, RoBERTa, XLNet, and GPT-2. They also tried to combine the predicted token  $s_{i+1}$  of all four models to outperform any of them.

**Evaluation** For evaluation, we use the bilingual evaluation understudy (BLEU) [332]. We compare the performance of GPT-3 [157], Flan-T5 [157], and mT5 [157] on MultiCochrane (English) [157] (please see Table 12). For AutoMeTS dataset [158], we use the accuracy of the next token  $s_{i+1}$  as we discussed at the end of Sec C.2 and we compare the performance of BERT, RoBERTa [158], XLNet [158], GPT-2 [158], and their combination [158] (please see Table 13). The citations in this paragraph correspond to the sources providing data on the performance of the models. For MultiCochrane, T5 models have much better performance. For AutoMeTS, a combination of different models actually outperforms any of them, but overall, none of those models have a high accuracy or BLEU score.

## C.3 Text Generation

**Task Description** Text generation is obviously a broad task. It includes or is related to many more specific tasks like question answering (Sec B.1) and text summarization (Sec C.1). In this subsection,

we concentrate on data-to-text tasks with open answers rather than well-defined answers, which involves taking structured data (e.g. a table) and producing text that describes this data as output. For example, generating patient clinic letters, radiology reports, and medical notes [333].

**Datasets, Models, and Discussion** Yermakov et al. [334] introduced a new dataset BioLeaflets and evaluated multiple LLMs' performance on the data-to-text generation task. They found that T5 [244] and BARD [254] are more powerful in this task. However, multiple questions remain. Current LLMs may generate texts with typos, hallucinations, and repetitious words. Also, LLMs are not mature enough to produce coherent long text so far. Ranjit et al. [335] studied the task of generating reports for chest X-ray images. They also found and discussed the hallucinations that occurred in the GPT-generated texts. There are also concerns about using model-generated pseudo-text for attacking since humans without expert knowledge cannot easily see the factual errors in the generated texts. Rodriguez et al. [336] works on preventing attacks in the biomedical domain.