### **Biomedical Foundation Model: A Survey**

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#### Abstract

Foundation models, first introduced in 2021, are large-scale pre-trained models (e.g., large language models (LLMs) and vision-language models (VLMs)) that learn from extensive unlabeled datasets through unsupervised methods, enabling them to excel in diverse downstream tasks. These models, like GPT, can be adapted to various applications such as question answering and visual understanding, outperforming task-specific AI models and earning their name due to broad applicability across fields. The development of biomedical foundation models marks a significant milestone in leveraging artificial intelligence (AI) to understand complex biological phenomena and advance medical research and practice. This survey explores the potential of foundation models across diverse domains within biomedical fields, including computational biology, drug discovery and development, clinical informatics, medical imaging, and public health. The purpose of this survey is to inspire ongoing research in the application of foundation models to health science.

#### 1 Introduction

The term 'foundation model' was first introduced in 2021 [1]. It generally refers to large language models (LLMs) and vision language models (VLMs) that are pre-trained in large-scale datasets, usually through unsupervised methods, which equip them to handle diverse downstream tasks. By learning from vast amounts of unlabeled data, 'foundation models' have developed strong capacities to map inputs into latent embedding space. Consequently, they can be seamlessly adapted to a wide range of tasks, consistently outperforming task-specific AI models [2, 3]. For example, GPT [4], pre-trained on massive language and visual data, and achieves outstanding performance in numerous tasks such as question answering, information retrieval, and

visual understanding. Given their transformative potential and broad applicability across related fields, these models are commonly referred to as 'foundation models'.

The emergence and development of foundation models can be attributed to several key factors. 1) **Massive unlabeled data**: Vast amounts of data are available, but supervised training is impractical due to prohibitive labeling costs [1]. 2) **Increased AI model size**: The architectures of the AI model have evolved to become increasingly larger, but the limited availability of labeled data constrains their ability to fully exploit this enhanced capacity [5]. 3) **Scaling law of generalizability**: Through large-scale model training, researchers have found that model performance improves predictably with increases in model size, dataset size, and computational resources [6]. 4) **Cost-efficient for downstream tasks**: After pre-training, efficient fine-tuning with limited labeled data achieves superior performance compared to task-specific AI models.

The success of popular foundation models such as GPT and Claude in natural language and image processing makes it intuitive to apply and redesign them to healthcare. The application of foundation models in healthcare spans several sub-fields. First, the outstanding natural language processing capabilities of foundation models have the potential to advance computational biology. DNA, RNA and protein sequences can be seen as a form of natural language, and these models can learn the patterns in the sequences, enabling deeper insights into genomics. Second, drug discovery and development utilizes foundation models to accelerate target identification, optimize molecular design, and predict molecular interactions and properties, ultimately reducing the time and cost of developing new drugs [7]. Third, in the field of clinical informatics, foundation models can efficiently process millions, or even billions, of clinical and patient data points, whether structured or unstructured. They can extract patterns from patients' symptoms to better assess conditions and enable personalized treatment plans. Fourth, medical imaging analysis can employ foundation models for tasks such as image segmentation, anomaly detection, and diagnostic predictions across modalities such as MRI and CT [8], improving diagnostic accuracy and workflow efficiency. Finally, public health benefits from foundation models in analyzing large datasets for disease surveillance, epidemiological modeling, and misinformation detection, contributing to more effective public health interventions. Therefore, the opportunities for biomedical foundation models to enhance the work of clinicians, researchers, and patients are steadily increasing.

This survey aims to review existing research on foundation models in biomedical areas, summarize their development progress, identify recent challenges of biomedical foundation models to inspire potential research directions, and provide a foundation for researchers to advance their applications in health sciences. Specifically, we will discuss the foundation models in multiple biomedical fields including computational biology, drug discovery and development, clinical informatics, medical imaging, and public health (**Figure 1**).

#### 2 Computational Biology

The central dogma of molecular biology provides a foundational framework describing the flow of genetic information within living organisms [9] (Fig. 2). Genomic information is encoded in DNA, transcribed into RNA, and subsequently translated into protein. This process converts the four-letter nucleotide code of DNA into the twenty-amino-acid code of proteins, which fold into three-dimensional structures to carry out diverse cellular functions. Understanding the central dogma is critical to advance knowledge in genetics, medicine, biotechnology, and evolutionary biology. It also serves as the cornerstone for innovations in genetic engineering, gene therapy, and drug development. Consequently, topics such as 3D chromatin genetic information, RNA-driven gene expression profiles, and protein structures underpinning cellular functions are central to computational biology. This section explores the application of foundation models to these domains, encompassing genome information, RNA-based gene expression profiles, and the study of protein structure and function.

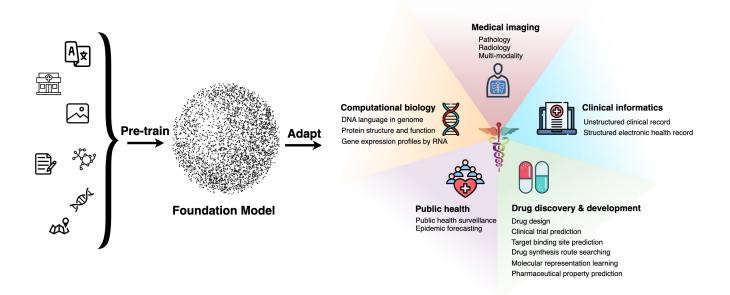


Figure 1: Overview of the foundation models in different biomedical fields. The foundation model is first pre-trained with massive unlabeled data in a self-supervised fashion. Then, it can be easily adapted for various downstream applications, including computational biology, drug discovery, public health, medical imaging, and clinical informatics.

**Genome Information** The genetic code for protein synthesis is universal but the regulatory code that governs the timing and manner of gene expression varies among different cell types and organisms [10]. This regulatory code is primarily found in the non-coding DNA regions, which constitute about 98% of the genome and include key functional elements like enhancers, promoters, and insulators. These elements regulate gene expression and repression activity, making the study of non-coding DNA crucial for understanding gene regulation, development, disease, and evolution. Recognizing the significant potential and impact of DNA, foundation models have been developed to enhance our understanding of the language of DNA. BigBird [11] pioneered in DNA sequence encodings by developing transformers for longer sequences. Following this work, a series of DNA language model has been developed and presented strong capacity for various downstream tasks, including RNA expression, enhancer activity prediction. Other recent studies are included in Table 1. To fairly compare different models. In parallel with studies on 1D DNA sequences, HicFoundation [13] was recently proposed to study 3D DNA and its functional implications. Together, these foundation models can contribute to understanding the impact of genome sequence and architecture on gene regulation and expression.

**Gene Expression Profiles by RNA** Gene expression profiles [14], valuable for understanding the dynamic activity of genes, serve as a direct reflection of gene activity. By quantifying and comparing the abundance of RNA molecules across different samples or conditions, gene expression profiling enables the identification of genes that are turned on or off, differentially expressed, or involved in specific biological processes. Traditional bulk RNA sequencing provides an average gene expression profile, masking cellular heterogeneity and potentially obscuring important information. In contrast, single-cell RNA sequencing (scRNA-seq) provides detailed insights into cellular diversity and variability by analyzing expression at the individual cell level. SCimilarity [15] is one of the most representative foundation models for single-cell profiles, enabling the comparison of transcriptionally similar cells in diverse single-cell RNA sequencing datasets. Other related

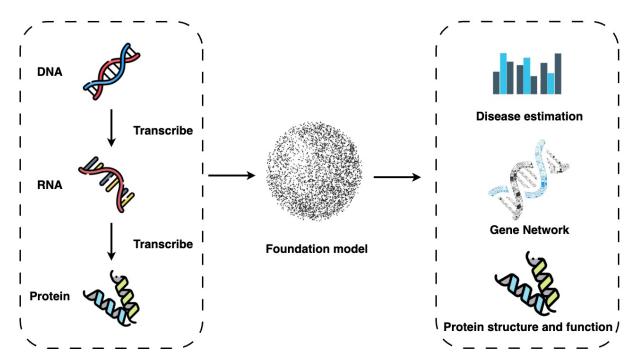


Figure 2: Overview of the application of foundation model in computational biology. Through the representation learning of DNA/RNA/Protein data in various forms, the foundation models can be applied to various downstream analysis, including disease estimation, gene network, protein structures and functions.

foundation models are listed in Table 2. The gene and cell embeddings derived from these foundation models have significantly advanced our understanding of gene expression dynamics across diverse cell types, holding immense potential to elucidate the molecular underpinnings of development, disease, and therapeutic responses.

**Protein Structure and Protein Design** Predicting protein 3D structures and functions plays critical roles in advancing our understanding of biological processes [16], and their three-dimensional structure determines how they perform specific functions, such as catalyzing reactions, transmitting signals and etc. Accurate predictions can reveal the molecular basis of diseases and further guide drug discovery. In recent years, computational approaches have provided an efficient and scalable way to fill gaps in structural knowledge and uncover the complexities of life at the molecular level. AlphaFoldz [17], a large model with high accuracy on predictions, significantly accelerating research in understanding protein functions and interaction. Moreover, building on these advancements on protein structure prediction, protein design has emerged as a complementary discipline, where researchers create or engineer proteins with specific functions or properties. Protein design enables the creation of novel enzymes, therapeutic molecules, and drugs, bringing about new possibilities in medicine, biotechnology, and synthetic biology, offering solutions to disease treatment and sustainable industrial processes. Recent advances, including large models and foundation models for protein structure prediction and protein design, are summarized in Table 3.

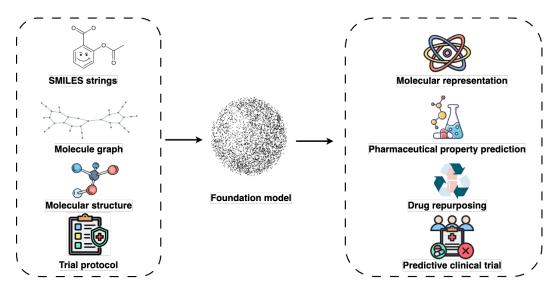


Figure 3: Overview of the application of foundation model in drug discovery and development.

# 3 Drug Discovery and Development

The development of novel drugs is crucial for global health (**Figure. 3**). The goal of drug discovery and development is to develop new drugs to treat certain human diseases. First, (early-stage) drug discovery identifies drug molecules (design or reuse) with desirable pharmaceutical properties (e.g. absorption, excretion, etc.). Then, (late-stage) drug development tests these molecules for safety and efficacy through animal models and clinical trials. Following successful trials, drugs undergo regulatory review by bodies such as the US FDA before being approved for clinical use. This section will discuss some fundamental problems in drug discovery and development. Early-stage drug discovery focuses on drug molecule structure, which involves AI-solvable tasks such as molecular representation learning, pharmaceutical property prediction, drug repurposing, and drug molecular design. AI also has a large potential to revolutionize late-stage drug development, especially in building predictive clinical trial models to guide clinical trial experts.

**Molecular Representation Learning** In contrast to pretraining procedures for LLMs, developing foundational models for healthcare requires a focus on learning representations for drug molecules. Molecular knowledge resides within three different modalities of information sources: molecular structures, biomedical documents, and knowledge bases. This section reviews self-supervised pre-training methodologies for molecule representation learning and discusses integrating drug molecules and healthcare pre-training to improve downstream tasks such as drug recommendation and disease trajectory prediction [18]. A list of recent work can be found in Table 4.

**Pharmaceutical Property Prediction** Molecular property prediction aims to learn a model that maps molecular structure to its pharmaceutical properties, which is the essential step for new drug discovery. Specifically, drug ADMET properties (Absorption, Distribution, Metabolism, Excretion, and Toxicity) refer to the characteristics of a drug that determine its absorption, distribution within the body, metabolism in the body, excretion from the body, and potential toxicity or adverse effects. Assessing and understanding ADMET properties helps predict how a drug will behave in the body, identify potential risks and interactions, optimize dosing regimens, and ensure patient safety and efficacy. Various experimental and computational approaches are employed to study and evaluate these properties during the drug development process. Pre-training approaches have been widely applied in pharmaceutical property prediction. For example, ChemBERTa, a

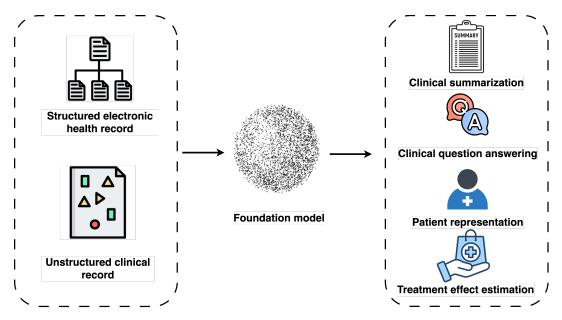


Figure 4: Overview of the application of foundation model in clinical informatics. The foundation model is pre-trained using structured electronic health record (EHR) data and unstructured clinical record (UCR) data and then adapted for various clinical analyses, including patient representation, causal inference, clinical summarization, and question answering.

BERT-based architecture, is pretrained on 77M unlabeled SMILES strings from PubChem and then fine-tuned on smaller labeled data for property prediction [19]. A review of recent studies on pharmaceutical property prediction can be found in Table 5.

**Drug Repurposing** Drug repurposing, also known as drug reuse or drug repositioning, refers to the process of finding new medical uses for drugs. It is becoming favorable compared to the development of entirely new drugs for the following reasons: lower cost, shorter development time, and lower risk [20]. Zhu et al. [21] demonstrate that the nature of graph neural networks (GNNs) makes them the ideal architecture for discovering drug uses, which led to more research using GNNs. A list of recent work can be found in Table 6.

**Predictive Clinical Trial** Clinical trials, also known as drug development, aim to evaluate the safety and efficacy of drug treatments for specific diseases in humans. However, conducting clinical trials is notoriously known to be time-consuming, labour-intensive, and expensive. On average, the process takes 7-11 years, costs around 2 billion dollars, and has a low approval rate of approximately 15% [22, 23]. Given these prerequisites, integrating machine learning into the clinical trial process has the potential to reduce manual labour and significantly enhance scalability for drug development. For example, [24] designs a hierarchical interaction network (HINT) that is pre-trained on multimodal drug data and simulates clinical trial components to predict the outcome of the trial. Some foundation models to predictive clinical trial models can be found in Table 7.

### **4** Clinical Informatics

Clinical informatics data contain a wide range of information about the medical history, treatments, and health-related activities of a patient. These records are crucial for healthcare professionals to provide effective care and manage patient health. There are several fundamental AI-solvable tasks in clinical informatics, which

can be categorized into two classes based on data types: (1) text-based problems such as clinical summarization and clinical question answering (QA) and (2) health records-based problems such as patient representation (e.g., patient similarity) and treatment effect estimation, as illustrated in Figure 4. Specifically, natural language is the most commonly used interaction method between doctors and patients, so clinical summarization and QA alleviate doctors' workload and facilitate patient care. On the other hand, health record-based tasks help doctors diagnose by providing more insights.

**Clinical Summarization** Automatic text summarization is the process of creating concise and coherent summaries of individual or multiple documents, aiming to save time in obtaining crucial information. The existing methods in this field can be broadly categorized into two types: extractive summarization methods and abstractive summarization methods, where extractive summarization select and extract key sentences or phrases directly from the source text to create a summary, preserving the original wording; abstractive summarization generates a summary by understanding the text's meaning and creating new sentences that capture the essential information, similar to how humans summarize. KeBioSum[25] is a highlighted work in this field; it applies adapter fusion to efficiently inject the knowledge adapters into the LLMs for fine-tuning for this task. The related studies are briefly reviewed in Table 8.

**Clinical Question Answering (QA)** Clinical QA aims to extract or generate natural language answers for given questions. It is commonly formulated as a machine reading comprehension problem, where the objective is to predict the text span containing the answers from given questions and passages. The Med-PaLM model [26, 27] stands out among the clinical QA foundation models, as it was the first model to pass the US Medical Licensing Examination. The related works are reviewed in Table 9.

**Patient Representation** The embedding of structured electronic health record (EHR) data has emerged as a pivotal advancement, revolutionizing the way patient information is processed and used. EHR embedding involves encoding various components of patient records, including diagnosis codes, medications, and vital signs, into a structured and numerical format. This process encapsulates a patient's medical history, diagnoses, treatments, medications, laboratory results, and other health-related information in a unified representation. The significance of patient representation lies in its ability to distill intricate clinical records into data-driven insights. These representations serve as the foundation for informed decision-making, precise diagnosis, personalized treatment plans, and comprehensive healthcare management. BEHRT [28] is a pioneer model that adapts the concept of BERT to build a neural sequence trajectory model to encode patient data. Related works are summarized in Table 10.

**Treatment Effect Estimation** Treatment effect estimation (TEE) from observational data is meaningful and practical in healthcare. It enables prescribing the right treatments to individuals based on their health statuses. One common approach to TEE is randomized controlled trials (RCTs), which are conducted by randomly assigning patients to two groups, treating them differently and comparing them in terms of a measured outcome. However, conducting RCTs is very expensive and time-consuming. A promising alternative is to estimate the treatment effect by learning from observational data. A representative foundation model work would be TransTEE [29], which explores the use of transformer architectures for estimating heterogeneous treatment effects, integrating all treatments and covariates. The related works are summarized in Table 10.

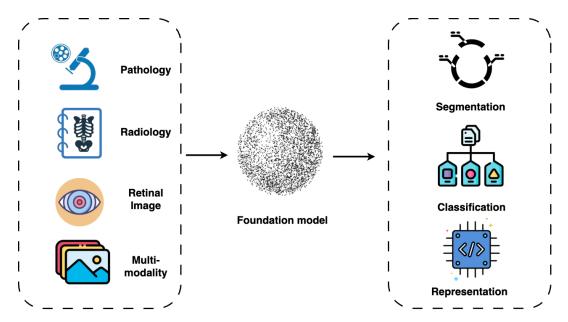


Figure 5: Overview of the application of foundation model in medical imaging.

# 5 Medical Imaging

Medical imaging encompasses a wide array of technologies, each meticulously designed to visualize distinct aspects of the human body. These technologies are instrumental in diagnosing and monitoring a variety of medical conditions, as well as assessing the efficacy of prescribed treatments. Depending on the specific modality employed, medical imaging can reveal diverse insights, ranging from identifying potential injuries or diseases to gauging the progression or regression of a condition in response to therapeutic interventions [30, 31]. The biggest challenge in training medical imaging models is data. The medical visual examination involves different types of images, such as radiology and pathology. Most data is private so it is difficult to collect various datasets at a large scale to train a general foundation model.

**Pathology** Pathology plays a central role in clinical medicine for tissue-based diagnosis and in understanding the causes and nature of the disease. Although molecular and omics-based data enhance histological assessments, the study of microscopic changes in tissue structure remains a critical part of pathology [32]. Therefore, most computational pathology work focuses on whole slide image (WSI) analysis, which includes tasks such as cell segmentation and tumor detection. Sometimes, the study of pathology is also linked to genomics where foundation models can be applied to analyze genomic data to identify mutations, gene expression patterns, and their correlation with pathological features. Considerable efforts have been made toward the development of foundation models in pathology, with PLIP [33] representing a notable contribution. PLIP introduced OpenPath, a large-scale pathology dataset, and leveraged it to pre-train a foundation model, providing resources and insights for future studies. Following this, other impactful researches are presented in Table 11.

**Radiology** Radiology is a medical specialty that uses imaging techniques such as X-rays, CT scans, and MRI to diagnose and treat disease. In daily radiology practice, radiologists interpret these medical images comprehensively in a short period. However, with the increasing availability of radiological techniques, the volume of images is growing rapidly and so is the workload of radiologists. The abundance of available images makes it a perfect training resource for foundation models. Being the pioneering work to employ the powerful

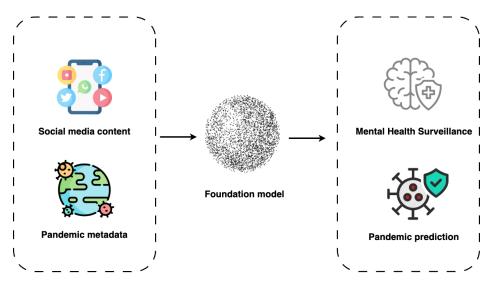


Figure 6: Overview of the application of foundation model in public health.

CLIP model in radiological images, MedCLIP [34, 35] successfully showcases the plausibility and capabilities of foundation models in this field. Foundation models in radiology are summarized in Table 12.

**Retinal Images** Optical coherence tomography (OCT) and Colour fundus photography (CFP) are the most common retinal images in ophthalmology, and their number accumulates rapidly in clinical practice [36]. The involvement of foundation models has been shown to be a game changer in retinal diseases. For instance, DeepDR Plus [37] fills the gap for the lack of individualized risk monitoring and accurate prediction of the progression of diabetic retinopathy. Another highlight would be RETFound [36], a foundation model that pre-trained a large-scale retinal image dataset and can be adapted to a broad range of retinal disease detection tasks. Some related works are briefly reviewed in Table 13.

**Multi-modality** Attempts have been made to develop foundation models specified for various modalities so it would be intuitive to develop models that span multi-modality. Different modalities have images of different granularity, but this will not pose a significant challenge for foundation models, provided that the training data is adequate. For example, Med-Flamingo [38] showcases the adaptation of CLIP-based architectures (unifying text and image modalities) to the development of generalist foundation models for medical imaging, which enhances the flexibility of medical imaging models (e.g., producing text description of medical images). Related works are summarized in Table 14.

#### 6 Public Health

Public health focuses on maintaining and improving community health and safety. Its importance has increased due to recent infectious disease outbreaks like COVID-19 and the H1N1 pandemic. Rapid dissemination of accurate information to decision-makers is crucial for controlling these outbreaks [39]. However, generating or predicting population-level information is challenging due to factors like modeling disease propagation [40], human mobility [41], socio-cultural elements [42], and human behavior nuances [43]. Efforts to improve public health can be broadly categorized into two areas: public health surveillance through novel data sources and spatiotemporal modeling for epidemic forecasting.

**Public health surveillance through multimodal and heterogeneous data** Traditional public health surveillance is often limited by the complexities of data collection from diverse stakeholders with varying levels of technological adoption [44]. In contrast, digital public health surveillance addresses these limitations by improving sensitivity, resolution, and timeliness [45]. Large and foundation models have been used in several tasks in public health surveillance. For example, key applications include analyzing social media content to assess mental health surveillance, virus-spreading information, and misinformation detection. PsychBERT [46] is the early work that pre-trained using biomedical literature on mental health and social media data. Related works are summarized in Table 15. These models also help identify mental health-related content and detect misinformation about public health.

**Epidemic Forecasting** Epidemic prediction typically relies on three types of predictions [47]: (1) predictions with real value, which anticipate parameters such as incidence or intensity peak during an epidemic season; (2) events predictions, which include estimates of onset and peak times; (3) epidemiological indicators, such as reproduction number, final size of the epidemic and attack rate predictions. [48, 49] proposed time series-based epidemic foundation models for influenza-like illness (ILI) analysis (e.g., epidemic time series forecasting).

# 7 Conclusion

This survey focuses on the applications and challenges of foundation models in the health sciences. We reviewed the applications and challenges of foundation models in five areas: computational biology, drug development, clinical informatics, medical imaging, and public health. We hope that this survey will provide researchers and practitioners with a useful and detailed overview of foundation models in the health sciences, provide a convenient reference for relevant experts, and encourage future progress.

Looking ahead, the integration of Foundation Models within the health sciences promises to refine and accelerate existing processes and to pioneer new research and treatment methodologies. The journey toward fully realizing the potential of these models is intertwined with the continuous development of AI technologies, alongside the fostering of interdisciplinary collaborations among scientists, clinicians, and policymakers. As we navigate these challenges, the goal remains clear: to take advantage of the power of AI to improve health outcomes and pave the way for a new era of precision medicine and public health initiatives. The advancements in Foundation Models are not an end but a beginning, marking a pivotal moment in the evolving narrative of health science and artificial intelligence.

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Work	Task	Architecture	Input	Output	Note
BigBird <sup>11</sup> (2020)	Question answering (QA), document summarization, promoter region prediction & chromatin-profile prediction.	Transformer	Long se- quences (e.g., lan- guage, DNA)	Token-wise embed- dings	NA
DNA-BERT <sup>50</sup> (2021)	Prediction of pro- moters, splice sites and transcription factor binding sites	Transformer	DNA sequence	Token-wise embedding	NA
GeneBERT <sup>51</sup> (2021)	Promoter classifica- tion, transaction fac- tor binding sites pre- diction, disease risk estimation, splicing sites prediction	Transformer	Genome sequence & 2D in- teraction matrix	Gene repre- sentation	Utilizes a 1D genome sequence and a 2D matrix representing interactions between transcription factors and genomic regions.
LOGO <sup>52</sup> (2022)	Promoter identifi- cation, enhancer- promoter interac- tion prediction	Transformer	DNA sequence	token-wise embed- dings	NA
LookingGlass <sup>53</sup> (2022)	Identify novel oxi- doreductase; predict enzyme optimal tem- perature; recognize reading frames of DNA sequence frag- ments	LSTM	DNA sequence	Token-wise embed- dings	NA
VIBE <sup>54</sup> (2022)	Eukaryotic viruses detection and classification	Transformer	Metagenome sequencing data	Token-wise embedding	A hierarchical BERT model to identify eukaryotic viruses using metagenome sequencing data and classify them at the order level.

Box 1: Foundation models for DNA languages in genome.

INHERIT <sup>55</sup> (2022)	Phage identification	Transformer	Bacteriophage Genome genome representa- sequences tion		NA
Genomic Pre-trained Network (GPN) <sup>56</sup> (2022)	Genome-wide vari- ant effect predictions	CNN	Genomic sequence	Genome representa- tion	NA
DeepConsensus (2023)	<sup>57</sup> DNA sequence cor- rection	Transformer	DNA sequence	Token-wise embed- dings	DeepConsensus uses an alignment- based loss to train a gap-aware trans- former–encoder for sequence correction.
Nucleotide Transformer <sup>58</sup> (2024)	Molecular pheno- type prediction	Transformer	Nucleotide sequence	Nucleotide representa- tion	NA
HyenaDNA <sup>59</sup> (2024)	Chromatin profile prediction, species classification, reg- ulatory elements identification	Hyena	DNA sequence	Token-wise embedding	Uses Hyena (sub- quadratic) to replace quadratic attention in transformers with implicit convolutions, enabling efficient scaling (up to 500x speedup) to 1M tokens with single- nucleotide-level resolution.
GROVER (Genome Rules Obtained Via Extracted Rep- resentations) <sup>60</sup> (2024)	Genome element identification & protein–DNA binding	Transformer	DNA sequence	Token-wise embedding	Trained on DNA sequences using byte-pair encoding. GROVER defines a vocabulary of tokens through a custom next-k-mer prediction task.
DNABERT-2 <sup>61</sup> (2024)	multi-species genome classifica- tion	Transformer	DNA sequence	Token-wise embed- dings	NA

Borzoi <sup>62</sup> (2023)	DNA model	language	Enformer (convolution + rrans- former)	DNA sequence	DNA repre- sentation	Identifies key cis- regulatory patterns governing RNA expression and post-transcriptional regulation across nor- mal tissues through attribution methods.
scooby <sup>63</sup> (2024)	DNA model	language		DNA sequence	DNA repre- sentation	NA
Evo <sup>64</sup> (2024)	Prediction tasks from to genome	molecular	Hyena	DNA, RNA, protein	(DNA, RNA, protein) represen- tation or sequence	The first examples of protein-RNA and protein-DNA co-design.
HiCFoundation <sup>1</sup> (2024)	<sup>3</sup> Genome ad diction	ctivity pre-	Transformer	3D and 1D genome data	Genome representa- tion	A Hi-C-based foun- dation model for in- tegrative analysis of genome 3D architec- ture and its regulatory mechanisms. The first model that in- fers genome activity from the coarse ge- nomic contact maps provided by Hi-C.

Work	Task	Architecture	Input	Output	Note
scBERT <sup>65</sup> (2022)	RNA language model	Transformer	scRNA sequence	scRNA-seq representa- tion	Pre-train BERT on massive unla- beled scRNA-seq data and fine- tuned on cell type annotation task.
scFormer <sup>66</sup> (2022)	RNA language model	Transformer	scRNA sequence	scRNA-seq representa- tion	NA
tGPT <sup>67</sup> (2022)	RNA language model	Transformer	scRNA sequence	scRNA-seq representa- tion	NA
scFoundation <sup>68</sup> (2023)	RNA language model	Transformer	scRNA sequence	scRNA seq representa- tion	NA
Geneformer <sup>69</sup> (2023)	RNA language model	Transformer	scRNA sequence	scRNA seq representa- tion	Pre-trained on 30M single-cell transcriptomes.
scGPT <sup>70</sup> (2023)	RNA language model	Transformer	scRNA sequence	scRNA-seq representa- tion	Enhances scFormer <sup>66</sup> with gen- erative training techniques.
sc-Long <sup>71</sup> (2024)	RNA language model	Transformer	scRNA sequence	scRNA-seq representa- tion	NA
GenePT <sup>72</sup> (2024)	RNA language model	Transformer	Gene description	Gene embedding	NA
SCSimilarity <sup>15</sup> (2024)	RNA language model	MLP	scRNA-seq	cell repre- sentation	Designed for rapid queries on similar cell profiles.
Cancer- Foundation <sup>73</sup> (2024)	RNA language model	Transformer	scRNA sequence	scRNA-seq representa- tion	Trained only on malignant cells, and its downstream task evalu- ates the generalizability to bulk RNA data.

Box 2: Foundation	models for gene	expression	profiles by RNA.

Work	Task	Architecture	Input	Output	Note
AlphaFold2 <sup>17</sup> (2021)	Protein structure prediction	Transformer	Protein se- quence	Protein structure	<b>Milestone</b> work in single-chain protein structure prediction, dominating CASP.
RoseTTAFold <sup>74</sup> (2021)	Protein structure prediction	Transformer	Protein se- quence	Protein structure	Protein monomer prediction, 3- track network architecture (1D sequence level, 2D distance map level and 3D coordinate level).
AlphaFold- Multimer <sup>75</sup> (2021)	Protein structure prediction	Transformer	Protein se- quence	Protein structure	Predict structures for protein multimers.
ProtTrans <sup>76</sup> (2021)	Protein language model	Transformer	Protein se- quence	Protein rep- resentation	NA
ProBERT <sup>77</sup> (2022)	Protein represen- tation learning	Transformer	Protein se- quence	Protein rep- resentation	NA
Evolutionary Scale Modeling (ESM) <sup>78</sup> (2022)	Protein language model	Transformer	Protein se- quence	Protein rep- resentation	The ESM family of protein lan- guage models, including ESM- 1v <sup>79</sup> , ESM-1b <sup>80</sup> , and ESM-MSA <sup>81</sup> and etc.
ESM-IF1 <sup>82</sup> (2022)	Protein de- sign	GNN, Trans- former		Protein se- quence	Backbone structure to se- quence design conditioned on sequences.
OmegaFold <sup>83</sup> (2022)	Protein structure prediction	Transformer	Protein se- quence	Protein structure	Uses protein language modeling to replace MSA, less accurate but faster.
RFDiffusion <sup>84</sup> (2023)	Protein de- sign	Diffusion model	Protein structure	Protein structure	A generative diffusion model from structure to structure for protein design.
EvoDiff <sup>85</sup> (2023)	Protein de- sign	Diffusion model	Protein se- quence	Protein se- quence	Controllable sequence-level pro- tein design diffusion model.

Box 3: Foundation mo	dels for protein struct	ure prediction (a.k.a.	protein folding) and	nd protein design.
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Chroma <sup>86</sup> (2023)	Protein de- sign	GNN, diffu- sion	Programmabl protein con- dition		Achieving programmable gener- ation with user-specified proper- ties.
ProtHyena <sup>87</sup> (2024)	Protein language model	Hyena	Protein se- quence	Protein rep- resentation	Adopts Hyena operator for effi- cient scaling.
xTrimoPGLM <sup>88</sup> (2024)	18 protein under- standing tasks	Transformer	Protein se- quence	Protein rep- resentation	NA
ESM3 <sup>89</sup> (2024)	Protein language model	Transformer	Protein sequence, structure, function	Protein sequence, structure, function	NA
Protein Gener- ator <sup>90</sup> (2024)	Protein de- sign	Transformer, diffusion	Protein se- quence	Protein sequence, structure	A RoseTTAFold-based sequence diffusion model that simulta- neously generates protein se- quences and structures.
RoseTTAFold All-Atom <sup>91</sup> (2024)	All-atom structure prediction	Transformer	All-atom se- quences, lig- ands, bonds	All-atom structure	Generalized model for all-atom prediction including protein, nucleic acid, and other small molecules.
AlphaFold3 <sup>92</sup> (2024)	All-atom structure prediction	Transformer & diffusion	All-atom se- quences, lig- ands, bonds	All-atom structure	State-of-the-art all-atom predic- tion method.
Boltz-1 <sup>93</sup> (2024)	All-atom structure prediction	Transformer & diffusion	All-atom se- quences, lig- ands, bonds	All-atom structure	AlphaFold3-level accuracy, open- source.
Chai-1 <sup>94</sup> (2024)	All-atom structure prediction	Transformer & diffusion	All-atom se- quences, lig- ands, bonds	All-atom structure	Can also predict structures with sequence only.

Work	Task	Architecture	Input	Output	Note
Wang et al. <sup>95</sup> (2021)	Molecular rep- resentation learning	GNN	Molecule, chemical reaction	Molecular embedding	Integrates chemical reaction con- straints to enhance molecular embeddings: forcing the sum of reactant embeddings equals the sum of product embeddings.
Su et al. <sup>96</sup> (2022)	Graph-text/text- graph retrieval, molecule cap- tioning, property prediction, text-based drug design	Transformer & GNN	Molecular graph, molecular diagram, text	Molecular embedding	NA
MolT5 <sup>97</sup> (2022)	Molecule cap- tioning & text-based drug design	Transformer	Molecule or text	Text or molecule	NA
Zeng et al. <sup>98</sup> (2022)	Property predic- tion & biomed- ical relation ex- traction	Transformer	Text, molecular structure	Text, molecule	Integrates molecule and text through unsupervised meta- knowledge learning.
MolKD <sup>99</sup> (2023)	Property predic- tion	Transformer	Chemical reaction, reaction yield	Molecule representa- tion	MolKD distilled knowledge from a teacher model trained on reaction data to a student model. Also, MolKD integrates reaction yield information during pre-training to measure reactant-product transformation efficiency.
CLAMP <sup>100</sup> (2023)	Property predic- tion	Transformer	Text & molecule	Text de- scription	NA
MolFM <sup>101</sup> (2023)	Property predic- tion	Transformer	Molecular graphs	Molecular representa- tion	Two-step pretraining: (1) self- supervised learning for chemi- cal structure representation; (2) multi-task learning for biological information integration.

Box 4: Foundation models for drug molecular representation learning.

MoleculeSTM (2023)	<sup>10</sup> Drug design, biological prop- erty prediction, instruction adaptation	GNN (molecule), trans- former (molecule, text)	Molecule & text	Molecule, text	NA.
InstructMol <sup>10</sup> (2023)	<sup>3</sup> Property predic- tion	Multimodal LLM	Molecule & text	Molecule or text	NA
BioT5 <sup>104</sup> (2023)	Molecule & protein prop- erty prediction, drug-target / protein-protein interaction, molecule caption- ing, text-based drug design	Transformer	SELFIES, protein, text	Text, or molecule	Uses SELFIES strings for 100% molecule validity; extracts con- textual knowledge from unstruc- tured biological literature.
BioT5+ <sup>105</sup> (2024)	Molecule-to- text, text-to- molecule	Transformer	Text, molecule	Text or molecule	Enhance BioT5 by integrating text and molecular representa- tions.
MV-Mol (multi-view molecule) <sup>106</sup> (2024)	Molecular rep- resentation learning	Multimodal fusion ar- chitecture	Molecular struc- ture, text, knowledge graph	Molecular embedding	NA
UniMoT (Unified Molecule- Text LLM) <sup>107</sup> (2024)	Molecule-to- text & text- to-molecule generation	Transformer	Molecule or text	Text or molecule	Uses a Vector Quantization- driven tokenizer and a Q-Former to bridge molecule and text modalities.

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Work	Task	Architecture	Input	Output	Note
SMILES- BERT <sup>18</sup> (2019)	Property prediction	Transformer	SMILES strings	Token-wise embedding	NA
MolE <sup>108</sup> (2022)	Property prediction	Transformer	Molecular graphs	Molecular representa- tion	DeBERTa architecture. two- step pretraining: self-supervised learning for chemical structure representation and multi-task learning for biological informa- tion integration.
ChemBERTa- 2 <sup>19</sup> (2022)	Property prediction	Transformer	SMILES strings	Token-wise embedding	Pretrain on 77M unlabeled SMILES strings from PubChem one of the largest molecular pretraining datasets to date.
BAITSAO <sup>109</sup> (2024)	Drug synergy prediction	Transformer	Drug com- bination, cell lines	Drug synergy	NA
ActFound <sup>110</sup> (2024)	Bioactivity prediction	Transformer	Molecular structure	Molecular representa- tion	Trained on 1.6M experimentally measured bioactivities from 35K in ChEMBL, ActFound designs pairwise learning and metalearning to capture relative bioactivity differences between compounds within the same assay overcoming cross-assay incompatibility.
SMILES- Mamba <sup>111</sup> (2024)	ADMET property prediction	Mamba	SMILES string	Molecular representa- tion	NA
ChemFM <sup>112</sup> (2024)	Property prediction	Transformer	Molecular structure	Molecular representa- tions	Up to 3B parameters, pre-trained on 178M molecules using self supervised causal language modeling to generate generaliz able molecular representations Supports full-parameter and parameter-efficient fine-tuning.

Box 5: Foundation model for pharmaceutical property prediction.

Graph Trans- former Foun-	 -	Molecular graph	Molecular representa-	NA
dation Model (GTFM) <sup>113</sup> (2024)			tions	

Work	Task	Architecture	Input	Output	Note
Zhu et al. <sup>21</sup> (2020)	Drug Repur- posing	GNN	Drug & dis- ease	Drug- disease association score	NA
KG- Predict <sup>114</sup> (2022)	Drug Repur- posing	GNN	Drug & dis- ease	Drug- disease association score	Combines GCN and InteractE that processes embeddings using 3D tensor convolution to capture heterogeneous interactions.
DREAMwalk (2023)	<sup>20</sup> Drug Repur- posing	GNN	Drug, gene, & disease	Drug- disease association score	NA
TxGNN <sup>115</sup> (2024)	Drug Repur- posing	GNN	Diseases, drugs, proteins, & pathways	Drug- disease association score& explanation	Designs an Explainer module via multi-hop paths in the knowl- edge graph for interpretability.
HGTDR <sup>116</sup> (2024)	Drug Repur- posing	Graph trans- former	Drug & dis- ease	Drug- disease association score	NA

Box 6: Foundation models for drug repurposing (a.k.a., drug reuse, drug repositioning).

Work	Task	Architecture	Input	Output	Note
HINT <sup>24</sup> (2022)	Clinical trial outcome pre- diction	GNN	Drug, dis- ease code, text	Trial outcome	NA
inClinico <sup>117</sup> (2023)	Trial out- come prediction	Transformer	Multiomics data, trial design, drug properties	Trial outcome	NA
HINT-UQ <sup>118</sup> (2024)	Trial out- come prediction	GNN	Drug, disease code, trial protocol (text)	Trial outcome	HINT-UQ quantifies uncertainty for reliable prediction using se- lective classification.
TrialDura <sup>119</sup> (2024)	Trial du- ration prediction	Transformer	Disease names, drug molecules, trial phases, & eligibility criteria	Trial dura- tion	NA
LIFTED <sup>120</sup> (2024)	Trial out- come prediction	Sparse mixture-of- expert	Drug, dis- ease, trial protocol	Trial outcome	LIFTED uses a sparse Mixture- of-Experts framework to iden- tify cross-modal patterns and provide explanations using a shared expert model and dy- namic weighting mechanism.
CTP-LLM <sup>121</sup> (2024)	Trial phase transition prediction	GPT	Trial design document	Trial phase transition	NA
TrialEnroll <sup>122</sup> (2024)		Deep cross network	Eligibility criteria	Trial enroll- ment status	NA
ClinicalAgent <sup>1</sup> (2024)	<sup>12</sup> Trial out- come prediction	GPT4	Drug, dis- ease and text	Trial outcome	GPT4-based multi-agent system that integrates LEAST-TO- MOST and ReAct reasoning.

Box 7: Foundation models for clinical trial prediction.

Work	Task	Architecture	Input	Output	Note
BioBERTSum <sup>124</sup> (2020)	Extractive summa- rization	Transformer	Clinical docu- ment	Summary	Pretrained BERT as encoder, fol- lowed by finetuning.
Sotudeh et al. <sup>125</sup> (2020)	Abstractive summa- rization	LSTM	Clinical docu- ment	Summary	NA
KeBioSum <sup>25</sup> (2022)	Clinical summa- rization	Transformer	Text	Summary and sen- tence classifi- cation result	NA
Radiology- LLaMA2 <sup>126</sup> (2023)	Clinical summa- rization	Transformer	Radiology report	Summary	NA
COVIDSum <sup>127</sup>	Clinical summa- rization	Transformer & Graph attention network	Medical articles	Summary	NA
MRC-Sum <sup>128</sup> (2023)	Clinical summa- rization	Transformer	Text	Summary and ex- tracted informa- tion	NA

Box 8: Foundation models for clinical summarization.

Work	Task	Architecture	Input	Output	Note
Yoon et al. <sup>129</sup>	Clinical QA	Transformer	Text	Extracted terms and entities, classifi- cation result	NA
BioMedBERT <sup>130</sup> (2020)	Clinical QA, named entity recog- nition (NER)	Transformer	Text & en- tity pair	QA, NER result, relation extraction result	NA
Rawat et al. <sup>131</sup> (2020)	Clinical QA	Transformer	Text	QA, struc- tured semantic representa- tion	NA
Chen et al. <sup>132</sup> (2020)	Clinical QA	Transformer	Text	QA	NA
Yan et al. <sup>133</sup> (2022)	Clinical QA	Transformer	Text & medical knowl- edge base	Intent- slot-value triplets, action-slot- value pairs, QA	NA
DAPO <sup>134</sup>	Clinical QA	Transformer	Text	Prediction scores, ranked responses	DAPO considers dialogue- specific features such as coherence, specificity, and informativeness.
ClinicalGPT <sup>135</sup>	Clinical QA	GPT	Text	Medical diagnoses, treatment recommen- dations, summary	NA

Box 9: Foundation m	odels for clinical QA	١.
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Deid-GPT <sup>136</sup> (2023)	Clinical QA	GPT	Text	De- Identified medical text	The model replaces identifiable data following HIPAA guidelines.
ChiMed- GPT <sup>137</sup> (2023)	Information extraction, QA, di- alogue genera- tion	GPT	Text	Text	Specifically for Chinese medicine.
Med-PaLM <sup>26</sup>	Clinical QA	Transformer	Text, im- age	text, image	multimodal biomedical AI model that can answer complex questions, generate reports, and classify images, developed by Google.
Med-PaLM 2 <sup>27</sup>	Clinical QA	Transformer	Text	QA and adversarial evaluation result	The first model to pass the US Medical Licensing Examination.
Pmc- LLaMA <sup>138</sup>	Clinical QA	Transformer	Text	QA, sum- mary, relation extraction, classifi- cation result, and diagnosis	NA
Me-LLaMA <sup>139</sup>	Clinical QA	Transformer	Text	QA, sum- mary, classifi- cation result	NA
MedAgents <sup>140</sup> (2023)	Clinical QA	Transformer	Image & text	QA	LLM agent, training-free, access- ing external knowledge.

BERT <sup>141</sup> concept & sentation       sentation       and F         (2021)       visit representation       sentation       seasons         Hi-BEHRT <sup>142</sup> EHR       Transformer       EHR       EHR representation         Wisit representation       sentation       sentation       seasons         Hi-BEHRT <sup>142</sup> EHR       Transformer       EHR       EHR representation         wisit representation       sentation       sentation       sentation       ture explanation	
(2020)concept & visit representationdiction and patient rep- resentationCEHR- BERT <sup>141</sup> (2021)EHR visit representationTransformer FEHR sentationEHR representationUses and F time2v seasonsHi-BEHRT <sup>142</sup> EHR concept & visit representationTransformer sentationEHR sentationEHR representationHierard time2v seasonsHi-BEHRT <sup>142</sup> EHR concept & visit representationTransformer sentationEHR sentationEHR representation ture et term do tories.ExBEHRT <sup>143</sup> EHR concept & visit representationTransformer sentationEHR sentationClinical prediction, patient rep- resentationNA prediction, and patient clusterNA prediction, patient rep- resentationM-BEHRT <sup>144</sup> EHRTransformer transformerEHRBreastNA	
BERT <sup>141</sup> (2021)concept & visit representationsentationsentationand F time2v seasonHi-BEHRT <sup>142</sup> EHR concept & visit representationTransformer eHREHR eHR entern dataEHR representationHierard ture et term dataExBEHRT <sup>143</sup> EHR concept & visit representationTransformer eHREHR eHRClinical prediction, patient rep- resentationNA prediction, patient rep- resentationM-BEHRT <sup>144</sup> EHRTransformer eHREHRBreastNA	
concept & visit repre- sentationsentationture ex term de window feature term de tories.ExBEHRT <sup>143</sup> EHR concept & visit repre- sentationTransformer EHR Feature EHR Clinical prediction, patient rep- resentation and patient clusterNAM-BEHRT <sup>144</sup> EHR FransformerTransformer EHRBreastNA	artificial time token ourier transform-base ec encoding to represen l or age-related patterns
<ul> <li>(2023) concept &amp; prediction, patient representation</li> <li>M-BEHRT<sup>144</sup> EHR Transformer EHR Breast NA</li> </ul>	hical BERT: the local fea stractor captures shor pendencies using slidin segmentation; the globa aggregator learns long pendencies over EHR his
visit repre- sentation prediction and patient representa- tions	
GT-BEHRT <sup>145</sup> EHR Graph trans- EHR Patient NA (2024) concept & former represen- visit repre- sentation clinical risk prediction	

Box 10: Foundation models for patient representation.

Claimsformer <sup>146</sup> (2024)	EHR concept & visit repre- sentation	Transformer	EHR	Chronic condition prediction and patient representa- tions	NA
HEART <sup>147</sup> (2024)	EHR concept & visit repre- sentation	transformer	EHR	Clinical risk prediction and patient representa- tion	Applies type-specific transforma- tions to medical entities to learn relationship-specific attention bi- ases to prioritize clinically rele- vant interactions.
HERBERT <sup>148</sup> (2024)	Risk strat- ification in chronic kidney disease	Transformer	EHR	Disease risk stratifica- tion and patient rep- resentation	NA
EHRMamba <sup>149</sup> (2024)	EHR concept & visit repre- sentation	Mamba	EHR	EHR fore- casting, clinical risk prediction, patient rep- resentation	EHRMamba uses state-space models instead of transformers for linear-time sequence mod- elling. EHRMamba can process sequences up to 3x longer.
TAME <sup>150</sup> (2021)	Patient Represen- tation	EHR	EHR	Patient rep- resentation, patient sub- typing and clinical risk prediction	NA
RAPT <sup>151</sup> (2021)	Patient Represen- tation	Transformer	EHR	Clinical pre- diction and clinical de- cision sup- port	NA
Claim-PT <sup>152</sup> (2022)	Patient represen- tation	GPT	EHR		NA

Guo et al. <sup>153</sup> (2023)	Patient Represen- tation	Transformer & GRU	EHR	Clinical risk prediction and patient representa- tion	NA
Foresight <sup>154</sup> (2024)	Patient Represen- tation	GPT	EHR	Biomedical events forecast, risk stratifi- cation and virtual trial result	NA
CEHR-GAN- BERT <sup>155</sup> (2022)	Predictive phenotyp- ing	Transformer & GAN	EHR	Patient represen- tation and predicted clinical outcomes	The generator mimics BERT- derived EHR representations; the discriminator distinguishes the generated one from the real one.
Hur et al. <sup>156</sup> (2022)	Predictive phenotyp- ing	Transformer	EHR	Patient represen- tation and predicted clinical outcomes	NA
PSN <sup>157</sup> (2022)	Patient Subpheno- typing and Similarity Measure- ment		EHR	ilarity score	PUses similarity network fusion to integrate structured EHR data with unstructured clinical narra- tives.
DAPSNet <sup>158</sup> (2023)	Patient Subpheno- typing and Similarity Measure- ment	Transformer	EHR	Drug recommen- dation	NA

ExBEHRT <sup>143</sup> (2023)	Patient Subpheno- typing and Similarity Measure- ment	Transformer	EHR	Patient group, risk score and mortal- ity risk prediction	NA
TransTEE <sup>29</sup> (2022)	Casual In- ference	Transformer	EHR	Estimated treatment effects	NA
Cure <sup>159</sup> (2022)	Casual In- ference	Transformer	Patient data	Estimated treatment effects	Encodes structured obser- vational patient data and incorporates covariate type and time into patient embeddings from unlabeled large-scale datasets.
Mascio et al. <sup>160</sup> (2020)	Clinical In- formatics Classifica- tion	Bi-LSTM or RNN or CNN	EHR	EHR repre- sentation	A comprehensive analysis of various word representation methods (e.g., Bag-of-Words, Word2Vec, GLoVe, FastText, BERT, BioBERT) and NN models.
Gao et al. <sup>161</sup> (2021)	Clinical single- label and multi- label document classifica- tion	Transformer	Clinical document	document category	NA
DDS-BERT <sup>162</sup> (2021)	diagnosis prediction	Transformer	EHR	Diagnosis	A BERT-based diagnosis predic- tion framework using EHR data from 592K patient visits. The model leverages textual clinical notes and age information, incor- porating a novel input represen- tation built from four special em- beddings and an optimized clas- sification layer.

Work	Task	Architecture	Input		Output	Note
MI-Zero <sup>163</sup> (2023)	Pathology		Image text	&	Cancer subtyping and region- of-interest identi- fication results	NA
PLIP <sup>33</sup> (2023)	Pathology	Transformer	Image text	&	Feature rep- resentation, classifi- cation result	NA
CITE <sup>164</sup> (2023)	Pathology	Transformer	Image text	&	Feature rep- resentation, classifi- cation result	NA
Virchow <sup>165</sup> (2023)	Pathology	Transformer	Image		Cancer detection result	NA
UNI <sup>166</sup> (2023)	Pathology	Transformer	Image		Segmentation mask, Cancer detection, grading, and sub- typing results	NA
PathChat <sup>167</sup> (2023)	)Pathology	Transformer	Image text	&	Prediction results, report, QA	NA
CHIEF <sup>168</sup> (2024)	Pathology	Transformer	Image text	&	Detection, classifica- tion, and prediction result	NA

## Box 11: Foundation models for pathology.

RudolfV <sup>32</sup> (2024)	Pathology	Transformer	Image text	&	Feature rep- resentation, cell segmen- tation mask, biomarker scoring, and rare disease case retrieval result	NA
PANTHER <sup>169</sup> (20	222 Athology	Transformer	Image		Feature representa- tion, cancer subtyping, survival outcome prediction	PANTHER reduces pathology whole-slide image patches into a compact set of morphological prototypes for efficient slide rep- resentation.
Jaume et al. <sup>170</sup> (2024)	Pathology	Transformer	Image text	&	Feature rep- resentation, molecular subtyping, prognostic prediction result	NA
XLIP <sup>171</sup> (2024)	Pathology	Transformer	Image text	&		XLIP's Attention-Masked Im- age Modelling module masks image features that are highly responsive to textual features. The Entity-Driven Masked Lan- guage Modelling module en- hances medical-specific features.
Prov- GigaPath <sup>172</sup> (2024)	Pathology	Transformer	Image		Feature embedding, cancer subtyping, pathomics classifica- tion	Prov-GigaPath uses a DINOv2 as a tile encoder to extract local fea- ture and a LongNet to process tens of thousands of image tiles per slide for ultra-large-context modeling.

MUSK <sup>173</sup> (2025)	Pathology	Transformer	Image & clinical report	Feature represen- tation, QA, molecular biomarker prediction, cancer pre- diction, im- munother- apy re- sponse	NA
				prediction	

Work	Task	Architecture	Input		Output	Note
CheXzero <sup>174</sup> (2022)	Radiology	Transformer	Image text	&	classification result and auxiliary prediction result	NA
RadFM <sup>175</sup> (2023)	Radiology	Transformer	Image text	&	Feature rep- resentation, classifica- tion re- sult,report, QA	NA
MedBLIP <sup>176</sup> (2024)	Radiology	Transformer	Image text	&	resentation, classifica-	MedBLIP uses a MedQFormer module to bridge the gap be tween 3D medical images to the pre-trained model.
BioVil-T <sup>177</sup> (2023)	Radiology	Transformer	Image text	&	Feature rep- resentation, classifica- tion result, temporal sentence similarity	NA
PTUnifier <sup>178</sup> (2023)	Radiology	Transformer	Image text	&	Feature rep- resentation, classifica- tion result, summa- rization, question answer	NA

Box 12: Foundation models for radiology.

KoBO <sup>179</sup> (2023)	Radiology	Transformer & CNN & GNN	Image text	&	Feature rep- resentation, classifi- cation result, seg- mentation mask, and semantic analysis.	The KoBo framework integrates clinical knowledge to improve semantic consistency and in- troduces an unbiased, open- set knowledge representation to handle noisy samples.
ELIXR <sup>180</sup> (2023)	Radiology					
MaCO <sup>181</sup> (2024)	Radiology	Transformer	Image text	&	Classification segmen- tation, detection results	Maco incorporates a correlation weighting mechanism to refine the alignment between masked X-ray image patches and their as- sociated reports.
Clinical- BERT <sup>182</sup>	Radiology	Transformer & CNN	Image text	&	Report	Clinical-BERT employs Masked Medical Subject Headings (MeSH) Modeling where MeSH is a semantic component in radiograph reports, and Image- MeSH Matching to align visual features with MeSH terms using a two-level sparse attention mechanism.
SAMed <sup>183</sup> (2023)	Radiology	Transformer	Image &text		e	SAMed utilizes a low-rank adap- tation strategy, updating the SAM image encoder, prompt en- coder, and mask decoder using labelled medical datasets.
Xraygpt <sup>184</sup>	Radiology	Transformer	Image text	&	Report and question an- swer	NA
Chatcad <sup>185</sup> (2023)	Radiology	Transform	Image text	&	Report and advice	NA
3D-CT-GPT <sup>186</sup> (2024)	Radiology	Transformer	Image text	&	Report	NA

ZePT <sup>187</sup> (2024)	Radiology	Transformer	Image text	&	Segmentation mask and anomaly map	ZePT uses a two-stage training approach: first, learning funda- mental queries for organ seg- mentation via object-aware fea- ture grouping to capture organ- level features, and second, refin- ing advanced queries with auto- generated visual prompts for de- tecting unseen tumours.
miniGPT- Med <sup>188</sup>	Radiology	Transformer	Image text	&	Report, bounding box and QA	NA
MAIRA-2 <sup>189</sup> (2024)	Radiology	Transformer	Image text	&	Grounded and non- grounded report	NA
BrainSegFounde (2024)	er Radiology	Transformer & U-Net	Image		Segmentation mask	NA
ChEX <sup>191</sup>	Radiology	Transformer	Image text	&	Bounding box & description	Chest X-Ray Explainer (ChEX) integrates textual prompts and bounding boxes to allow the in- terpretation of specific anatomi- cal regions and pathologies.

Work	Task	Architecture	Input	Output	Note
RETFound <sup>36</sup> (2023)	Retinal Im- ages	Transformer & CNN	Image & text	Feature pre- sentation, symptom classifi- cation result.	NA
DeepDR Plus <sup>37</sup>	Retinal Im- ages	CNN	Image & metadata	Progression and risk score	DeepDR Plus is designed to pre- dict the time to diabetic retinopa- thy progression over five years using only fundus images.
KeepFIT <sup>192</sup> (2024)	Retinal Im- ages	Transformer & CNN	Image & text	Feature pre- sentation, symptom classifica- tion result, and image captioning	The model integrates Fundus Image-Text expertise through im- age similarity-guided text revi- sion and a mixed training strat- egy.
RetiZero <sup>193</sup> (2024)	Retinal Im- ages	Transformer & MAE	Image & text	Feature pre- sentation, symptom classifica- tion result, Image Retrivel	NA
RET-CLIP <sup>194</sup> (2024)	Retinal Im- ages	Transformer	Image & text	Feature pre- sentation, symptom classifi- cation results.	RET-CLIP uses a tripartite opti- mization strategy that considers both eyes, and patient-level data, aligning with real-world clinical scenarios.
FLAIR 195 (2025)	Retinal Im- ages	Transformer & CNN	Image	Symptom classifi- cation result	NA

## Box 13: Foundation models for retinal image.

Work	Task	Architecture	Input	(	Output	Note
BiomedGPT <sup>196</sup>	Multi- modality	Transformer	Image & text	1	Feature rep- resentation & QA	NA
BiomedCLIP <sup>34</sup>	Multi- modality	Transformer	Image & text	1	Feature rep- resentation & QA	NA
Med- Flamingo <sup>197</sup>	Multi- modality	Transformer	Image & text		Report & QA	NA
MedSAM <sup>198</sup>	Multi- modality	Transformer	Image		Segmentation mask	NA
SAM- Med2D <sup>199</sup>	Multi- modality	Transformer	Image		Segmentation mask	SAM-Med2D incorporates more diverse prompts: bounding boxes, points, and masks.
LVM-Med <sup>200</sup>	Multi- modality	Transformer & GNN	Image	1 5 t 0 2 2 5	Feature rep- resentation, segmenta- tion mask, detection and clas- sification results	In LVM-Med, two sets of fea- ture embeddings are produced using transformers to construct a graph neural network each rep- resenting nodes and edges with second-order graph matching al- gorithm.
AutoSAM <sup>201</sup>	Segmentation	Transformer	Image		Segmentation mask	NA
Med-SA <sup>202</sup>	Segmentation	Transformer	Image			Med-SA employs space-depth transpose to extend SAM's 2D ca- pabilities to 3D medical images and a Hyper-Prompting Adapter for prompt-conditioned adapta- tion.

Box 14: Foundation models for multimodal medical imaging.

Llava-med <sup>203</sup>	Multi- modality	Transformer	Image & text	Report & QA	LLaVA-Med first aligns with biomedical vocabulary using figure-caption pairs, then learns conversational semantics through instruction-following data, mimicking a layper- son's gradual acquisition of biomedical knowledge.
Visual Med- Alpaca <sup>204</sup>	Multi- modality	Transformer	Image & text	Classification result & QA	NA
RELU <sup>205</sup>	Multi- modality	Transformer	Image & text		The RULE framework includes a calibrated retrieval strategy to optimize factual risk and a fine- tuned preference dataset to im- prove retrieval-augmented gen- eration.
MA-SAM <sup>194</sup>	Multi- modality	Transformer	Image	Segmentation mask	MA-SAM adapts SAM's 2D back- bone to handle volumetric and temporal information. It also in- tegrates 3D adapters to extract 3D features while preserving pre- trained 2D weights through effi- cient fine-tuning.
UniMed- CLIP <sup>35</sup>	Multi- modality	Transformer	Image & text	Feature rep- resentation, classifi- cation result	NA
HuatuoGPT- Vision <sup>206</sup>	Multi- modality	Transformer	Image & text	Feature rep- resentation, QA	NA
RadEdit <sup>207</sup>	Multi- modality	Diffusion	Image & text	Synthetic datasets	RadEdit uses generative image editing to simulate dataset shifts and diagnose failure modes of biomedical vision models. The model uses multiple image masks to constrain edits and ensure con- sistency.

BiomedParse <sup>208</sup> Multi- (2024) modality Transformer Image & Segmentation NA text & se- mask, ob- mantic la- ject recog- bel nition and clinical detection result			text & se- mantic la-	mask, ob- ject recog- nition and clinical detection
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Work	Task	Architecture	e	Input	Output	Note
Luo et al. <sup>209</sup> (2021)	Virus spread- ing informa- tion	Transforme	r	Clinical notes & So- cial media posts	Symptoms	NA
COVID-19 Surveiller <sup>210</sup> (2022)	Virus spread- ing informa- tion		r	Social media posts	COVID- 19 event prediction	NA
PsychBERT <sup>46</sup> (2021)	Mental Health Surveillance	Transforme	r	Social media posts	Mental condition detection	NA
PHS-BERT <sup>211</sup> (2022)	Mental Health Surveillance	Transforme	r	Social media posts	Mental condition detection	NA
Saha et al. <sup>212</sup> (2022)	Mental Health Surveillance	Auto- Regressive Integrated Moving Average Model		Social media posts	Mental condition detection	NA
MentaLLaMA <sup>213</sup> (2024)	Mental Health Surveillance	Transforme	r	Social media posts	Mental condition detection	NA
Deka et al. <sup>214</sup> (2022)	Misinformation detection	Transforme	r	Medical ar- ticles	Classification result	NA
Vec4Cred <sup>215</sup> (2023)	Misinformation detection			Web textu- ral content	Classification result	NA
Upadhyay et al. <sup>216</sup> (2023)	Misinformation detection			Web textu- ral content	Classification result	NA

Box 15: Foundation models for public health surveillance through multimodal and heterogeneous data.