Generative Biology

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Abstract

The rapid pace of progress in generative artificial intelligence (AI) techniques like deep learning, reinforcement learning, and transformer neural networks is transforming the life sciences and biomedicine. This living review paper provides an updatable, comprehensive overview and analysis of the latest literature on generative biology – the application of cutting-edge generative AI methods to accelerate insights and innovation across the life sciences and healthcare. All authors are welcome to contribute to this review via pull requests.

The review synthesizes key developments in using generative models for de novo biomedical discovery, design, and decision support. It examines techniques and applications including deep learning on omics data for personalized medicine, generative chemistry for drug development, protein structure prediction for molecular engineering, image synthesis for pathology, language models for clinical decision support, robotic simulation for prosthetics, and generative networks for cell programming.

The review highlights representative studies and benchmarks in each area while contextualizing progress, limitations, emerging best practices, and directions for future work. It also discusses social and ethical challenges raised by generative biology applications, such as compounding bias, system opacity, and dual-use risks, alongside proposed solutions.

As a living review, this paper will be continually updated as the field rapidly advances to provide researchers and practitioners with an up-to-date reference on the state of the art in employing generative AI to accelerate biomedicine for the collective good.

Executive Summary

The goal with be a 2 page TL;DR of the review after v1 is complete. Need more content.

Introduction

This is the start of the Generative Biology living review!

Recent Advances in Generative AI

Introduction

Brief background on rise of generative models like GPT-3, DALL-E, AlphaFold, etc. Summary of scope and goals of chapter focused on key advances in last 1-2 years.

Transformer-Based Language Models

GPT-3 and Foundation Models

- Overview of GPT-3 architecture and self-supervised training on massive text corpus
- Discussion of GPT-3 capabilities and limits, including few-shot learning
- Concept of foundation models as basis for many downstream applications

Other Notable Models

- Summary of other major transformer language models like Google's PaLM, DeepMind's Gopher, Meta's OPT, Anthropic's Claude etc.
- Comparison of model sizes, architectures, training approaches
- Benchmarking of models on various NLP tasks

Multimodal Generative Models

DALL-E 2 and Text-to-Image Generation

- Explain DALL-E 2 architecture and training methodology
- Discuss capabilities in text-to-image generation
- Issues around bias, appropriate use cases

Other Multimodal Models

- Overview of models like Imagen, Parti, Flamingo for text-to-image
- Discussion of video generation models like Googles Imagen Video
- Models for text to 3D shapes, text to music etc.

Outlook

- Key challenges and limitations of current generative models

- Likely future advances building on these models
- Broader societal impact of widely available generative models

Advances in Generative AI for Proteins

Introduction

- Background on proteins as key molecular machines in biology
- Promise of generative AI to accelerate protein discovery and engineering
- Overview of scope covering recent advances in last 1-2 years

Structure Prediction

- AlphaFold2 as a breakthrough method for structure prediction
- Novel model architecture and training methodology
- Examples of new biological insights from predicted structures

Function Prediction

- Using predicted structures to infer protein functions
- Structure-based identification of catalytic and binding sites
- Case studies of novel enzyme functions discovered

Designing Novel Proteins

- Generative models for designing functional protein sequences
- Leveraging structural constraints for optimized protein engineering
- Applications in industrial enzymes, therapeutics, biomaterials

Interaction Prediction

- Modeling protein-protein interactions with graph networks
- Structure-based prediction of protein-drug bindings
- Applications in drug discovery and toxicity screening

Outlook

- Challenges and next steps in improving accuracy
- Hybrid physics- and data-driven approaches
- Ethical considerations in synthetic protein design

Advances in Generative AI for RNA

Introduction

- Background on key roles of RNA in biology
- Promise of generative models to advance RNA research
- Scope focused on latest advances in RNA prediction and design

Structure Prediction

- Transformer-based prediction of RNA folding
- Novel architectures for incorporating chemical constraints
- Improved accuracy on complex structures like ribosomes

Function Prediction

- Inferring RNA functions from sequence and structure
- Identifying motifs, domains, and atomic binding sites
- Applications in understanding long noncoding RNAs

Interaction Prediction

- Graph neural networks for RNA-protein interactions
- Structure-augmented modeling of splice sites
- Predicting RNA base editing targets

Design of RNA Therapeutics

- Generative models for optimizing siRNA, antisense design
- Reinforcement learning for chemical modification patterns
- Progress in computational RNA-targeted drug design

Outlook

- Key challenges in prediction of long RNA structures
- Design of RNA for self-assembly and scaffolding
- Ethical use of synthetic RNA technologies

Advances in Generative AI for DNA

Introduction

- Background on role of DNA as carrier of genetic information
- Promise of generative models to advance DNA research
- Scope focused on latest advances in DNA prediction and design

Sequence Modeling

- Transformer architectures for modeling DNA sequences
- Pretraining on large genomic datasets
- Applications in variant calling and annotation

Regulation Prediction

- Graph neural networks for modeling 3D genome architecture
- Predicting enhancer-promoter interactions and expression
- Design of synthetic promoters and enhancers

Genome Editing

- Generative models for CRISPR guide design
- Contextual prediction of on-target editing efficacy
- Modeling of off-target effects during optimization

DNA Data Generation

- Variational autoencoders for realistic DNA sequences
- Generating paired genomic-transcriptomic data
- Applications in training genome interpretation models

Outlook

- Challenges in predicting long-range chromatin interactions
- Responsible design of synthetic genomes
- Ethical considerations for human genome editing

Generative AI and the Biosecurity Landscape

Introduction

- Background on biosecurity threats from natural, accidental, and intentional pathogens
- Rise of generative AI as a dual use technology for biodefense and misuse

Enhanced Risks

- Automated bioweapon design with generative models
- Relatively low computing needs to generate dangerous agents
- Challenges detecting artificially generated sequences/organisms

Enhanced Response Capabilities

- Generative models for vaccine and therapeutic design
- High-throughput testing of countermeasures with synthetic data
- AI for early detection of emergent pathogens and outbreaks

Recommendations

- Increased oversight for generative model development/release
- Expanding biosecurity legislation and regulations
- Fostering open research and global cooperation

Outlook

- Trajectory toward increasingly powerful generative biological capabilities
- Need for preventative ethics research and guidance
- Maintaining public trust and avoiding overreaction

Conclusion

- Balancing generative AI's benefits and risks in biology
- Importance of thoughtful governance and responsible innovation
- Staying ahead of the curve on biosecurity

Generative AI for Autonomous Experimentation

Introduction

- Promise of generative models to accelerate scientific discovery
- Rise of autonomous labs and robotics for automated experimentation
- Overview of generative AI's role in self-driving research

Closed-Loop Systems

- Integrating computational hypothesis generation with robotic wet lab testing
- Reinforcement learning pipelines for autonomous optimization
- Case studies in materials science, drug discovery

Automated Experiment Design

- Using generative models to design novel compounds, genes
- Leveraging simulations to predict experimental outcomes
- Robotic execution of designed experiments

Adaptive Sampling

- Active learning to iteratively select most informative experiments
- Bayesian optimization powered by neural networks
- Applications in probing molecular design spaces

Real-Time Learning

- Deploying models on lab edge devices
- Online learning from experimental data streams
- Improving models and experiment plans on-the-fly

Outlook

- Key challenges around model accuracy and integration
- The future of data-driven, self-driving laboratories
- Risks of full automation and need for human oversight

Conclusion

- Generative AI as a powerful tool for autonomous experimentation

- Accelerating discovery alongside human researchers
- Responsible implementation will maximize benefit

References