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Physics-Informed Generative GPT Models (PINO-GPT) for Drug Discovery

Innovation: Utilizes Fourier Neural Operators (FNOs) to model continuous 3D physical landscapes (hydrophilic/hydrophobic surfaces). Embeds physical properties directly into the molecular generation process, enhancing physical realism and relevance.

Methodology: Evolution from LSTM-based generators [2] to GPT-based transformers to current dual-FNO-enhanced PINO-GPT architectures. FNO layers process spatial physical fields, enabling generation of molecules optimized for orthosteric binding pockets. Fine-tuning enables adaptation to experimental constraints in GPCRs (e.g., agonist activity).

Results: Outperforms traditional sequence-based and diffusion-based models [3] in structure-informed drug generation tasks. Experimental validation (binding and functional assays) confirms predictive performance and real-world applicability.

Impact: Bridges computational design and wet-lab validation. Enables more interpretable, physically grounded, and experimentally aligned GenAI workflows in drug discovery.

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