CLAIMS

1. A method performed by one or more computers, the method comprising:

obtaining a network input that characterizes a protein and one or more ligands;

processing the network input characterizing the protein and the one or more ligands using an embedding neural network to generate a protein – ligand embedding of the protein and the one or more ligands; and

generating, using a generative model and while the generative model is conditioned on the protein – ligand embedding, a predicted joint three-dimensional (3D) structure of the protein and the one or more ligands,

wherein the predicted joint 3D structure of the protein and the one or more ligands defines a respective predicted three-dimensional spatial location of each atom in the protein and of each atom in each of the one or more ligands.

2. The method of claim 1, wherein the embedding neural network comprises a protein embedding neural network and a ligand embedding neural network, and wherein processing the network input characterizing the protein and the one or more ligands using the embedding neural network to generate the protein – ligand embedding comprises:

processing data characterizing the protein using the protein embedding neural network to generate a protein embedding of the protein;

processing data characterizing the one or more ligands using the ligand embedding neural network to generate a ligand embedding of the one or more ligands; and

processing the protein embedding and the ligand embedding to generate the protein – ligand embedding.

3. The method of claim 2, wherein the protein embedding comprises a respective amino acid embedding of each amino acid in the protein;

wherein the ligand embedding comprises a respective atom embedding of each atom in each of the one or more ligands; and

wherein processing the protein embedding and the ligand embedding to generate the protein – ligand embedding comprises:

generating data defining a 1D sequence of amino acid embeddings and atom embeddings by concatenating: (i) the amino acid embeddings of the protein embedding, and (ii) the atom embeddings of the ligand embedding;

wherein the protein – ligand embedding is derived from the 1D sequence of

amino acid embeddings and atom embeddings.

4. The method of claim 3, wherein the processing the protein embedding and the ligand embedding to generate the protein – ligand embedding further comprises:

transforming the 1D sequence of amino acid embeddings and atom embeddings into a two-dimensional (2D) array of embeddings;

wherein the protein – ligand embedding is derived from the 2D array of embeddings.

5. The method of claim 4, wherein the 2D array of embeddings comprises a plurality of atom – atom embeddings that are each derived from a respective pair of atom embeddings of the ligand embedding.

6. The method of any one of claims 4-5, wherein the 2D array of embeddings comprises a plurality of amino acid – amino acid embeddings that are each derived from a respective pair of amino acid embeddings of the protein embedding.

7. The method of any one of claims 4-6, wherein the 2D array of embeddings comprises a plurality of amino acid – atom embeddings that are each derived from: (i) a respective atom embedding of the ligand embedding, and (ii) a respective amino acid embedding of the protein embedding.

8. The method of any one of claims 4-7, wherein transforming the 1D sequence of amino acid embeddings and atom embeddings into the 2D array of embeddings comprises:

applying an outer product operation to the 1D sequence of amino acid embeddings and atom embeddings; or

applying a 2D concatenation operation to the 1D sequence of amino acid embeddings and atom embeddings.

9. The method of any one of claims 4-8, wherein the embedding neural network further comprises a fusion neural network; and

wherein processing the protein embedding and the ligand embedding to generate the protein – ligand embedding further comprises:

processing the 2D array of embeddings using the fusion neural network to generate an updated 2D array of embeddings;

wherein the updated 2D array of embeddings defines the protein – ligand embedding.

10. The method of claim 9, wherein the fusion neural network comprises a sequence of self-attention blocks, wherein each self-attention block is configured to perform operations comprising:

applying one or more self-attention operations to an input 2D array of embeddings to update the input 2D array of embeddings.

11. The method of any preceding claim, wherein the generative model is a generative diffusion model that comprises a denoising neural network.

12. The method of claim 11, wherein generating, using the generative model and while the generative model is conditioned on the protein – ligand embedding, the predicted joint 3D structure of the protein and the one or more ligands comprises:

generating positional data defining a respective initial position of each atom in a complex comprising the protein and the one or more ligands;

denoising the positional data over a sequence of time steps using the denoising neural network and while the denoising neural network is conditioned on the protein – ligand embedding;

wherein the predicted joint 3D structure of the protein and the one or more ligands is defined by the positional data after a final time step in the sequence of time steps.

13. The method of claim 12, wherein generating positional data defining the respective initial position of each atom in the complex comprises:

sampling the respective initial position of each atom in the complex from a probability distribution over 3D space.

14. The method of any one of claims 12-13, wherein denoising the positional data over the sequence of time steps using the denoising neural network and while the denoising neural network is conditioned on the protein – ligand embedding comprises, at each of one or more time steps in the sequence of time steps:

receiving current positional data that defines a respective current position of each atom in the complex at the time step;

generating a denoising output using the denoising neural network and while the denoising neural network is conditioned on the protein – ligand embedding; and

generating positional data that defines a respective position of each atom in the complex at a next time step using the denoising output.

15. The method of claim 14, wherein generating the denoising output using the denoising neural network and while the denoising neural network is conditioned on the protein – ligand embedding comprises:

generating a set of atom embeddings using an encoder block of the denoising neural network, wherein each atom embedding represents one or more atoms in the complex and is based at least in part on the respective current spatial position of the one or more atoms at the time step;

processing the set of atom embeddings using an update block of the denoising neural network to generate a set of updated atom embeddings; and

processing the set of updated atom embeddings to generate the denoising output.

16. The method of claim 15, wherein the set of atom embeddings includes a respective atom embedding representing each atom included in each of the one or more ligands.

17. The method of any one of claims 15-16, wherein the set of atom embeddings includes a respective atom embedding representing each atom included in each amino acid of the protein.

18. The method of claim 15-16, wherein for each amino acid in the protein, the set of atom embeddings includes a respective atom embedding that jointly represents all the atoms included in the amino acid.

19. The method of any one of claims 15-18, wherein each atom embedding in the set of atom embeddings is based on, for each of the one or more atoms represented by the atom embedding: (i) the current position of the atom at the time step, and (ii) a respective conditioning embedding for the atom that is selected from a collection of embeddings included in the protein – ligand embedding.

20. The method of claim 19, wherein for each atom embedding that represents an atom in the complex that is included in a ligand, the conditioning embedding for the atom comprises an atom – atom embedding corresponding to the atom in the protein – ligand embedding.

21. A system comprising:

one or more computers; and

one or more storage devices communicatively coupled to the one or more computers, wherein the one or more storage devices store instructions that, when executed by the one or more computers, cause the one or more computers to perform operations of the respective method of any one of claims 1-20.

22. One or more non-transitory computer storage media storing instructions that when executed by one or more computers cause the one or more computers to perform operations of the respective method of any one of claims 1-20.

23. A method of obtaining a ligand, wherein the ligand is a drug or a ligand of an industrial enzyme, the method comprising:

for each of one or more candidate ligands:

(a) performing the method of any one of claims 1-20 to determine a predicted structure of a complex comprising a target protein molecule and the candidate ligand; and

(b) evaluating an interaction of the candidate ligand with the target protein molecule dependent on the predicted structure; and

selecting one or more of the candidate ligands as the ligand dependent on a result of the evaluating.

24. A method as claimed in claim 23, wherein the target protein molecule comprises a receptor or enzyme, and wherein the ligand is an agonist or antagonist of the receptor or enzyme.

25. A method as claimed in claim 23 or 24 wherein the ligand is a drug, and the method comprises:

performing steps (a) and (b) for each of a plurality of target protein molecules; and

selecting one or more of the candidate ligands as the ligand to either i) obtain a ligand that interacts with each of the target protein molecules, or ii) obtain a ligand that interacts with only one of the target protein molecules.

26. The method of claim 23, wherein the ligand comprises an antibody or aptamer and the target protein molecule comprises an antibody or aptamer target, in particular a virus or cancer cell protein, and wherein the antibody or aptamer binds to the antibody or aptamer target to provide a therapeutic effect.

27. The method of any one of claims 23-26, wherein the ligand is a polypeptide ligand, a polynucleoside ligand, or a polynucleotide ligand.

28. A method of obtaining a diagnostic antibody or aptamer marker of a disease, the method comprising:

selecting a target protein molecule;

for each of one or more candidate antibodies or aptamers:

performing the method of any one of claims 1-20 to determine a predicted structure of a complex comprising the candidate antibody or aptamer and the target protein molecule; and

evaluating an interaction between the candidate antibody or aptamer and the target protein molecule; and

selecting one of the one or more of the candidate antibodies or aptamers as the diagnostic antibody or aptamer marker dependent on a result of the evaluating.

29. A method as claimed in any one of claims 23-28 wherein the evaluating the interaction of one of the candidate ligands comprises determining an interaction score for the candidate ligand, wherein the interaction score comprises a measure of an interaction between the candidate ligand and the target molecule.

30. A method as claimed in any one of claims 23-29 further comprising synthesizing the ligand or diagnostic antibody or aptamer marker.