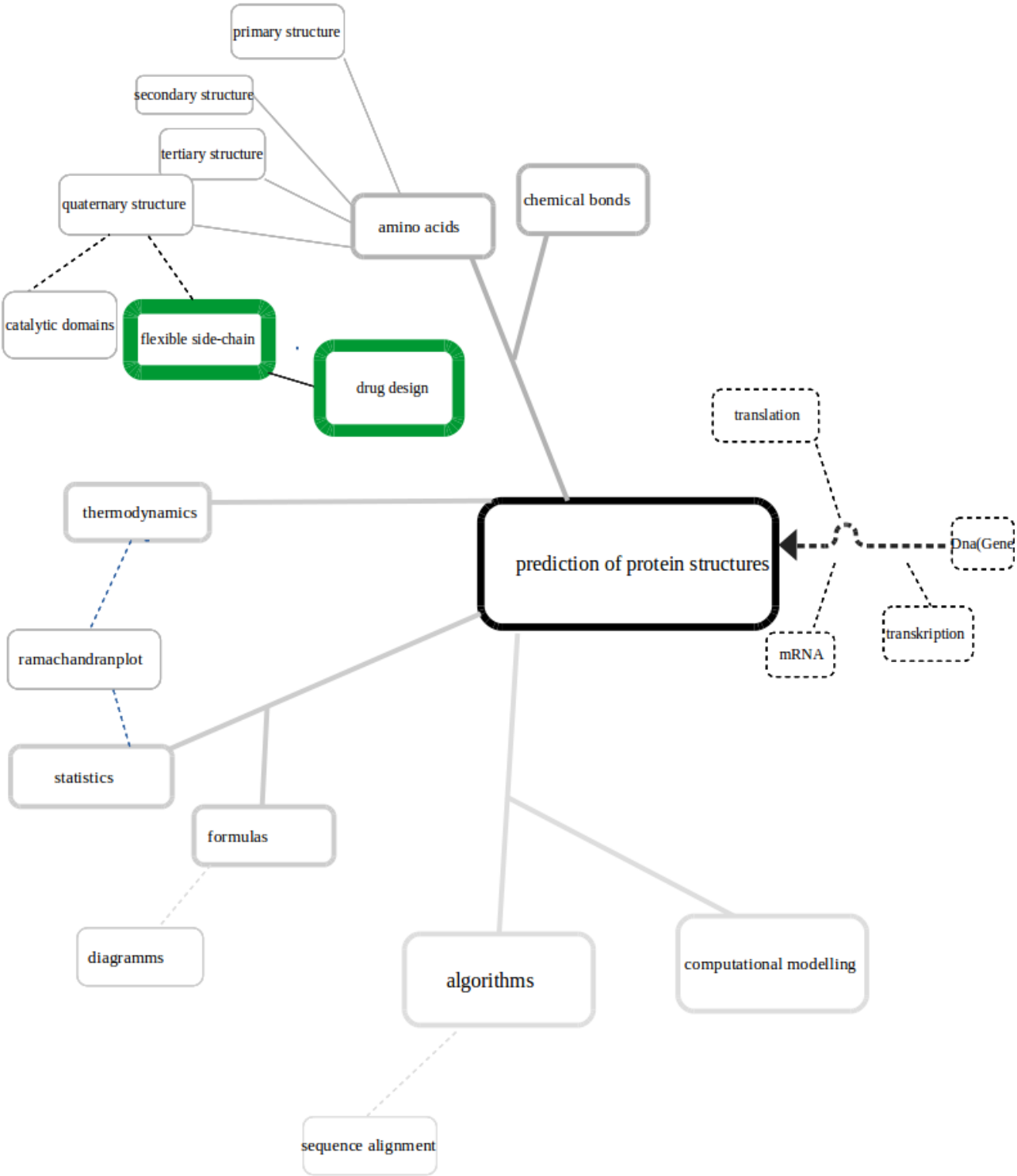
Many different approaches are needed to enable an expansion of the industry for drug design. Focusing on (membrane-)protein-ligand interactions it is of interest to know the structure of the target molecule. In the following literature review three papers are listed, that deal with the prediction of the structure of a functional (flexible) side-chain of a protein and approaches to inhibit its function.

In his article „An Exact Algorithm for Side-Chain Placement in Protein Design“ from year 2011, Stefan Canzar stated the importance of protein design in order to successfully design drugs. He presented an algorithm for the exact placement of the side-chain of a protein, given only the protein backbone. Given the two assumptions, that “the side-chains adopt only statistically dominant low-energy conformations” and “the energy of a protein is the sum of intrinsic side-chain energies and pairwise interaction energies”, Canzer states that these information are not enough to predict the side-chain placement. He suggests to rather combine two algorithms named the branch-and bound algorithm and the Lagrangian relaxation approach. However the author proposes to connect his approach to other methods developed.

An approach in order to design drugs is to examine the molecules that activate our target molecules. Paying attention to Allison E.Kennedy’s paper “Nerve growth factor inhibitor with novel-binding domain demonstrates nanomolar efficacy in both cell-based and cell-free assay systems” published in year 2017, she provides a method of molecular modeling in silicio docking of the Ligands. Kennedy provides information about the interaction between the nerve growth factor(NGF), a protein that regulates the development of neurons through activation of the Tropomyosin receptor kinase A (TrkA) a trans-membrane protein. At it has been proven that elevated levels of the NGF have a negative impact on the organism it is in interest of scientist to partially hinder the affinity of NGF to the TrkA. As a total inhibition could lead to apoptosis. A method suggested by Kennedy is to alter the structure of the NGF and inserting small structures that partially limit the flexibility the the functional loops of the NGF, using a software named Sybyl-X 2.1.1.

To provide precise and fast information about functionalities and structures of unknown proteins it can be helpful to compare a unknown protein-structure to already known structures. This is a main approach of Narayanan Eswar as presented in her article “Comparative protein structure modeling using MODELLER”. The main program used for her work is called MODELLER. It is used to compare the structures of two or more proteins providing information about their similarities, folding pattern of the unknown protein and possible functions. However Eswar states errors that may occur and categories them in five groups as suggested by Sanchez and Sali in their paper “Advances in comparative protein structure modelling” from year 1997. One of the errors listed is “Errorrs in side-chain packing” as it is “critical if they occur in regions that are involved in protein functions”.


primary structure
secondary structure
tertiary structure
quaternary structure
amino acids
chemical bonds
catalytic domains
flexible side-chain
drug design
translation
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statistics
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algorithms
computational modelling
sequence alignment