Prediction of G-protein Coupled Receptors using Deep Learning: A Review

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Keywords: G-protein coupled receptors, glutamate, G proteins, signalling, amino acid composition, guanosine triphosphate (GTP), guanosine diphosphate (GDP).

Abstract: The biggest super classes of the membrane proteins are G-protein coupled receptors as well as GPCRs are very significant for drug design goals. GPCRs are sometimes known as heptahelical receptor as well as seven-transmembrane receptor. GPCRs are accountable for several physicochemical and biological activities like cellular growth, neurotransmission, smell as well as vision. This paper presents a review related to current approaches to predict GPCRs. Extensive research on GPCRs have progressed to novel discoveries that open undiscovered and promising drug design opportunities and efficient drug-targeting G-protein coupled receptors therapies. This paper concentrates primarily on the process of deep learning to estimate GPCRs.

1 INTRODUCTION

GPCRs are often addressed to the heptahelical receptor or even the seven-transmembrane receptor. A protein found in the cell membrane which also binds extracellular substances as well as communicates information to an intracellular molecule named as a G protein. In cell membranes of a large variety of species, like animals, crops, microorganisms as well as invertebrates, GPCRs are present in cell membranes of a large variety of species, like animals, crops, microorganisms as well as invertebrates(Dorsam, 2007). There are various forms of G Protein-coupled receptor about 1,000 forms are identified by the human genome only. Robert J. Lefkowitz, an American molecular biologist, showed the presence of GPCRs in the year 1970s (Strader, 1994).

A wide class of proteins containing as even transmembrane helical structural motif are GPCRs (Karnik, 2003). G protein-coupled receptors are huge number of related proteins which sense molecules out of cell as well as initiate cellular reactions. Coupling with G proteins GPCRs mostly travel throughout the cell membrane seven times. There seem to be two major pathways of signal transduction concerning GPCRs one pathway is cAMP signal and another one pathway is phosphatidylinositol signal pathway (Gilman, 1987). When a ligand binds to the GPCRs, it induces conformational alterations in the G Protein-coupled receptors that enable this one to serve as a transfer mechanism for guanine nucleotides. GPCRs are a big drug priority and about 34% of all licensed drugs from the FDA target 108 elements of this group (Hauser, 2018). Another rapidly emerging field of pharmaceutical science is the long-discovered relationship among G Protein-coupled receptors and several endogenous as well as exogenous compounds (Trzaskowski, 2012).G Protein-coupled receptors convey extracellular signals through membrane in plasma of intracellular effectors through use of heterotrimeric G proteins (Pierce, 2002). GPCRs initiate drastic conformation alterations disclosing intracellular sites which also communicate with it as well as activate G proteins. G proteins correspond to GTPase group which consist of three subunits, α, β as well as γ, from which β subunits as well as γ comprise the βγ-subunits (Cabrera-Vera, 2003). This induces GDP dissociation bound to a subunit of the Gα as well as its substitution to the GTP. Gα-GTP along with Gβγ subunit control downstream effectors (See Figure: 1) (Harhammer, 1996).

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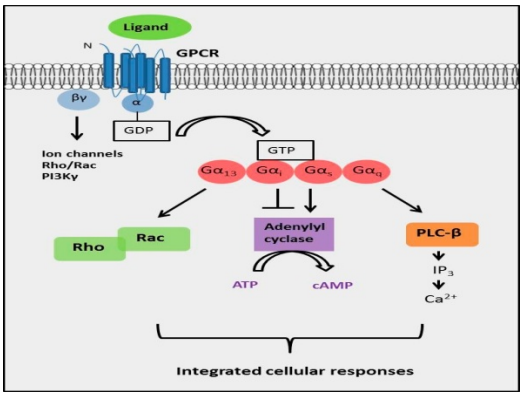

Figure1: G Signal of GPCRs through heterotrimeric G proteins (Lynch, 2016).

2 RELATED WORKS

In paper (Bhasin, 2004), author used a SVM based method, GPCRpred, for determination of G-protein coupled receptor families as well as subfamilies from dipeptide composition of proteins. When tested with the help of 5-fold cross-validation, system categorized GPCRs versus non-GPCRs with 99.5% accuracy. In addition, the model can estimate 5 main groups of GPCRs with an aggregate MCC of 0.81 as well as efficiency of 97.5%. In paper (Liao, 2016), the authors used physical-chemical properties, coming from SVM-Prot, reflecting the G-protein coupled receptors. They used random forest classification technique to differentiate them from all other sequences of proteins. In this work the average classification accuracy was 91.61% as well as 0.9282 was the average AUC.

G-protein-coupled receptors are main group of receptors for the cell surface as well as one of the most active sites of therapeutic drugs. Many of the G-protein-coupled receptors functions are uncertain along with identifying their ligands as well as signal transduction pathways are time intensive and costly. It prompts everyone meting a crucial problem: how to develop an integrated method for the classification of receptors coupled with G-proteins family to assist in classification of medicines as well as speed up the medicine research process. It is hard to estimate the categorisation of G-protein-coupled receptors by means of traditional sequence alignment strategies due to their extremely divergent nature. The covariant discriminant predictor was implemented to estimate the families of G-protein-coupled receptors in order to deal with such a scenario (Chou, 2005). In paper (Rosenbaum, 2009), the authors illustrated latest structural research of high-resolution findings have been given into the molecular pathways of activation as well as constitutive function of G-protein coupled receptors. Many of the physiological reactions to hormones, neurotransmitters and stimulants in the atmosphere are mediated by GPCRs and as therapeutic goals, they have tremendous potential for a wide range of infections. Our sense of hearing, our scent, our taste, and our discomfort are mediated by GPCRs. They are active in mechanisms of cell identification as well as interaction, and have thus developed as an influential superfamily for drug goals. Unfortunately, for only one GPCR, the atomic-level structure is open, making it hard to use structure-based skills to solve medicines as well as mutation research. They have currently developed approaches of first principles for forecasting GPCR structure and forecasting the sites of ligand binding and relative binding allegiances (Vaidehi, 2002).

In paper (Basith, 2018), authors concentrated primarily on the concepts of G-protein coupled receptors drug development focused on cheminformatics. They provide a complete analysis of the cheminformatics methods focused on ligands and structures, which are best demonstrated by studies of GPCRs. In addition, an effective fusion of ligand-based experience and structure-based experience, like an incorporated solution, is also addressed, which is appearing as a potential cheminformatics-based G-protein coupled receptors drug development technique. The current GPCR structural biology development offers novel visibility into ligand binding, conformational dynamics, as well as signalling results regulation. With the current techniques to multi-dimensional drug action development, these insights allow detailed classification of drugs along with their pharmacodynamic features, which can be related to the receptor structure as well as estimates of the effectiveness of preclinical drugs (Wootten, 2018). In paper (Popov, 2018), author developed a comprehensive analytical method called CompoMug, which uses Sequence-based research, structural experience as well as a developed model of machine learning to effectively forecast stabilizing mutations in GPCRs. In paper (Carpenter, 2016), author illustrated the structure of a minimal G protein, mini-Gs, which consist only from the adenylate cyclase triggering G protein Gs of the GTPase system. Mini-Gs are a thin, soluble protein that, in absence of sub-units of Gβγ, effectively combines GPCRs.

Extensive research on GPCRs have linked to novel developments that open undiscovered and

promising drug design prospects and cost effective drug-targeting GPCR therapies. This included the development of unique signaling mechanisms like ligand promiscuity occurring in cross-talks of multitarget ligands, allosteric modulation and the development of receptor homo as well as oligomers that can be analyzed effectively with the help of analytical modeling. Computer-aided approaches for drug discovery can lower the price of creating drugs by approximately 50% (Kaczor, 2016). In paper (Bartuzi, 2017), the authors concentrated on advances in docking of G protein-coupled receptors. Appropriate statistical restoration of real ligand-receptor method is known as molecular docking. In paper (Schneider, 2018), the author illustrated latest discoveries of hybrid coarse-grained membrane protein approaches. They concentrate on in-house molecular mechanics/coarse-grained approach. They demonstrate that our molecular mechanics/coarse-grained method is capable of capturing the atomistic information of ligand binding interaction.

In paper (Vaidehi, 2016), authors identified the existing structure of the analytical approaches that provide inputs into G protein-coupled receptors allosteric communication as well as explain how allosteric modulators can be constructed with this knowledge. The binding of ligands in the extracellular region to GPCRs conveys the stimulus to the intracellular region to activate coupling with effector proteins. The method of this allosteric contact appears to be mostly unexplored. In paper (Foster, 2019), author reported the pairing of cognate peptides as well as receptors. They define common features that reveal additional possible peptidergic signaling mechanisms by combining selective genomics through 313 organisms and bioinformatics over all protein sequences as well as architectures of individual class A G protein-coupled receptors. They fused 17 potential endogenous ligands with five orphan G protein-coupled receptors correlated with disorders involving developmental, nervous as well as reproductive system diseases employing three orthogonal biochemical assays.

In paper (Kobilka, 2007), the author illustrated dynamic design of G-protein coupled receptors activation structure along with functionality mainly based on spectroscopic analyses of purified human adrenergic β2 receptor. In paper (Shiraishi, 2019), author established an original peptide descriptor-incorporated SVM to estimate 22 pairs of neuropeptides G protein-coupled receptors. For a 41 p% hit rate, the predicted pair signaling assays identified 1 homologous neuropeptide and 11 Ciona-specific neuropeptides G protein-coupled receptors. In paper (Xiao, 2011), author developed a novel Predictor by combining pseudo-amino acid composition functional domainas well as the pseudo-amino acid composition low-frequency Fourier range. This novel predictor is named GPCR-2L, in which "2L" implies a two-layer predictor. GPCR-2L's total hit rate in recognizing there are almost 97.2 percent of proteins as GPCRs or non-GPCRs. In paper (Guo, 2006), author established a novel technique ACC transform based support vector machine to determine precision of coupling among G protein-coupled receptors with G-proteins. The main sequences of amino acids are converted into vectors dependent on amino acids' key physicochemical characteristics as well as the content is converted by the implementation of ACC transformation into a uniform matrix. Support vector machine is qualified and tested through jackknife testing for nonpromiscuous coupled G protein-coupled receptors as well as promiscuous coupled G protein-coupled receptors.

In paper (Chou, 2002), the author developed a rapid system based on sequences to classify their various G-protein-coupled receptors. In cellular signaling networks that control different metabolic functions like vision, odor, neurotransmission, inflammation, cellular metabolism and cell development, G-protein-coupled receptors perform a major position of significance. For perception of human physiology as well as sickness, such proteins are really significant. Several pharmaceutical study initiatives have tried to explain their composition and purpose. These are hard to crystallize, and therefore a few of them seem to not melt in traditional solvents so very less number of GPCRs structures have been identified. In paper (Wess, 1997), author outlined current evidence extracted from structural, molecular genetics, biochemical, as well as biophysical research that have cast fresh insight on these processes and seek to combine them.

3 CONCLUSIONS

The biggest super classes of the membrane proteins are G-protein coupled receptors as well as GPCRs are very significant for drug design goals. GPCRs are sometimes known as heptahelical receptor as well as seven-transmembrane receptor. GPCRs are accountable for several physicochemical and biological activities like cellular growth, neurotransmission, smell as well as vision. This paper has presented a review for current approaches

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