DOWNLOAD PDF COMPUTER-ASSISTED MODELING OF RECEPTOR-LIGAND INTERACTIONS

Chapter 1 : Robert Rein (Author of Computer-Assisted Modeling of Receptor-Ligand Interactions)

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Drug targets[edit] A biomolecular target most commonly a protein or nucleic acid is a key molecule involved in a particular metabolic or signaling pathway that is associated with a specific disease condition or pathology or to the infectivity or survival of a microbial pathogen. Potential drug targets are not necessarily disease causing but must by definition be disease modifying. Small molecules for example receptor agonists , antagonists , inverse agonists , or modulators ; enzyme activators or inhibitors ; or ion channel openers or blockers [11] will be designed that are complementary to the binding site of target. Most commonly, drugs are organic small molecules produced through chemical synthesis, but biopolymer-based drugs also known as biopharmaceuticals produced through biological processes are becoming increasingly more common. In order for a biomolecule to be selected as a drug target, two essential pieces of information are required. The first is evidence that modulation of the target will be disease modifying. This knowledge may come from, for example, disease linkage studies that show an association between mutations in the biological target and certain disease states. This means that it is capable of binding to a small molecule and that its activity can be modulated by the small molecule. The purified protein is then used to establish a screening assay. In addition, the three-dimensional structure of the target may be determined. The search for small molecules that bind to the target is begun by screening libraries of potential drug compounds. This may be done by using the screening assay a "wet screen". In addition, if the structure of the target is available, a virtual screen may be performed of candidate drugs. Ideally the candidate drug compounds should be " drug-like ", that is they should possess properties that are predicted to lead to oral bioavailability , adequate chemical and metabolic stability, and minimal toxic effects. Molecular mechanics or molecular dynamics is most often used to estimate the strength of the intermolecular interaction between the small molecule and its biological target. These methods are also used to predict the conformation of the small molecule and to model conformational changes in the target that may occur when the small molecule binds to it. Also, knowledge-based scoring function may be used to provide binding affinity estimates. These methods use linear regression , machine learning , neural nets [25] [26] or other statistical techniques to derive predictive binding affinity equations by fitting experimental affinities to computationally derived interaction energies between the small molecule and the target. The reality is that present computational methods are imperfect and provide, at best, only qualitatively accurate estimates of affinity. In practice it still takes several iterations of design, synthesis, and testing before an optimal drug is discovered. Computational methods have accelerated discovery by reducing the number of iterations required and have often provided novel structures. For structure-based drug design, several post-screening analyses focusing on protein-ligand interaction have been developed for improving enrichment and effectively mining potential candidates: Selecting candidates by voting of multiple scoring functions May lose the relationship between protein-ligand structural information and scoring criterion Represent and cluster candidates according to protein-ligand 3D information Needs meaningful representation of protein-ligand interactions. Types[edit] Drug discovery cycle highlighting both ligand-based indirect and structure-based direct drug design strategies. There are two major types of drug design. The first is referred to as ligand-based drug design and the second, structure-based drug design. These other molecules may be used to derive a pharmacophore model that defines the minimum necessary structural characteristics a molecule must possess in order to bind to the target. Alternatively, a quantitative structure-activity relationship QSAR , in which a correlation between calculated properties of molecules and their experimentally determined biological activity, may be derived. These QSAR relationships in turn may be used to predict the activity of new analogs. Using the structure of the biological target, candidate drugs that are predicted to bind with high affinity and selectivity to the target may be designed using interactive graphics and the intuition of a medicinal

chemist. Alternatively various automated computational procedures may be used to suggest new drug candidates. This method is known as virtual screening. A second category is de novo design of new ligands. In this method, ligand molecules are built up within the constraints of the binding pocket by assembling small pieces in a stepwise manner. These pieces can be either individual atoms or molecular fragments. The key advantage of such a method is that novel structures, not contained in any database, can be suggested. However, there may be unoccupied allosteric binding sites that may be of interest. Furthermore, it may be that only apoprotein protein without ligand structures are available and the reliable identification of unoccupied sites that have the potential to bind ligands with high affinity is non-trivial. In brief, binding site identification usually relies on identification of concave surfaces on the protein that can accommodate drug sized molecules that also possess appropriate "hot spots" hydrophobic surfaces, hydrogen bonding sites, etc. Scoring functions for docking Structure-based drug design attempts to use the structure of proteins as a basis for designing new ligands by applying the principles of molecular recognition. Selective high affinity binding to the target is generally desirable since it leads to more efficacious drugs with fewer side effects. Thus, one of the most important principles for designing or obtaining potential new ligands is to predict the binding affinity of a certain ligand to its target and known antitargets and use the predicted affinity as a criterion for selection.

Chapter 2 : Mutagenesis and Modeling of the Neurotensin Receptor NTR1

*Computer-Assisted Modelling of Receptor-Ligand Interactions: Theoretical Aspects and Applications to Drug Design (Progress in clinical and biological research) [Robert Rein, Amram Golombek] on calendrierdelascience.com *FREE* shipping on qualifying offers.*

These interactions between amino acids and nucleotides are highly specific and any aberrance at the binding site can render the interaction completely incompetent. In this study, we h In this study, we have three aims focusing on DNA-binding residues on the protein surface: We use a support vector machines SVM based approach to harness the features of the DNA-binding residues to distinguish them from non-binding residues. We located such cationic patches on the protein surface. Delphi v4 [30,31] was used for all electrostatic calculations in this study. This tool solves the non-linear Poissonâ€"Boltzmann equation usi The position of QB in the photosynthetic reaction center depends on pH: Matthias Ullmann - J , " ABSTRACT Electrostatics-based calculations have been performed to examine the proton uptake upon reduction of the terminal electron acceptor QB in the photosynthetic reaction center of Rhodobacter sphaeroides as a function of pH and the associated conformational equilibrium. Two crystal structures o Two crystal structures of the reaction center were considered: In the two structures, the QB was found in two different positions, proximal or distal to the nonheme iron. Because QB was found mainly in the distal position in the dark and only in the proximal position under illumination, the two positions have been attributed mostly to the oxidized and the reduced forms of QB, respectively. We calculated the proton uptake upon QB reduction by four different models. In the first model, QB is allowed to equilibrate between the two positions with either oxidation state. This equilibrium was allowed to vary with pH. In the other three models the distribution of QB between the proximal position and the distal position was pH-independent, with QB occupying only the distal position or only the proximal position or populating the two positions with a fixed ratio. Only the first model, which includes the pH-dependent conformational equilibrium, reproduces both the experimentally measured pH dependence of the proton uptake and the crystallographically observed conformational equilibrium at pH 8. From this model, we find that QB occupies only the distal position below pH 6. Between these pH values both positions are partially occupied. The reduced QB has a higher occupancy in the proximal position than the oxidized QB. In summary, the present results indicate that the conformational equilibrium of QB depends not only on the redox state of QB, but also on the pH value of the solution. Show Context Citation Context This approach allows the computation of the electrostatic potential at any point inside and outside the protein.

Chapter 3 : Drug design - Wikipedia

Computer modeling was used in this study to analyze binding affinity of a series of Î´-opioid selective enkephalin analogues to the model of Î´-opioid receptor, published in PDB (id: 1OZC). MolDoc.

Supplement Aims and Scope This supplement is intended to focus on ligand-receptor interactions and drug design. Biochemistry Insights aims to provide researchers working in this complex, quickly developing field with online, open access to highly relevant scholarly articles by leading international researchers. In a field where the literature is ever-expanding, researchers increasingly need access to up-to-date, high quality scholarly articles on areas of specific contemporary interest. This supplement aims to address this by presenting high-quality articles that allow readers to distinguish the signal from the noise. The editor in chief hopes that through this effort, practitioners and researchers will be aided in finding answers to some of the most complex and pressing issues of our time. Articles should focus on ligand-receptor interactions and drug design and may include the following topics: At the discretion of the guest editors other articles on other relevant topics within the scope of the supplement may be included. Protein receptors are utilized by all living organisms to sense the environment and monitor internal physiological states. By binding with ligands, receptors activate or inhibit downstream biochemical signaling pathways to make adjustments in cellular processes gene expression profile, metabolic flow, etc. Dysfunction of these signaling pathways is responsible for various human diseases like cancer, diabetes and so on. Receptor signaling can be improperly over-activated e. BCR-ABL oncogene in chronic myeloid leukemia , or impaired as a result of either lacking the ligand or mutations in the receptor complex e. Therefore, receptors are the targets of a lot of pharmaceutical agents. The study of receptors and their ligands is critical for elucidating the physiological and pathological processes they are involved in. By understanding the underlying mechanisms, we can find better ways to improve human health. In this issue, three studies about ligand-receptor interaction are presented. Various aspects of the drug discovery dynamics are covered: All of them are aimed for clinical applications. In Wu et al, a novel way for preparing a promising drug candidate Olesoxime cholestenone is described. Olesoxime has been reported to bind two proteins of the mitochondrial permeability transition pore: With its analgesic and neuro-protective effect, 2 olesoxime is a promising compound for treating multiple neuropathies: It is already known that transient receptor potential TRP channels are little antennas responsible for our sensations to temperature, pressure, taste, vision and pain. Jin took a functional approach to tackle this problem, modifying the status of TRP channels with a broad spectrum TRP channel blocker to show that this can suppress the response of nociceptive neurons to cold stimulation in dental pulp. Moreover, this study showed for the first time that in vivo electrophysiological technique can be used as an alternative and effective approach for evaluating the effects of some drugs in animal models. It could open up new therapeutic routes for an age old problem. Finally, an excellent review by Dr. EPO is widely known for its role in red blood cell production erythropoiesis. It is medically used in various anemia conditions and, unfortunately, consumed by some athletes illegally for performance enhancing. In addition, EPO also has a non-classical role in neuro-protection. The dual roles of EPO are mediated by different receptor complexes. This is an elegant case of rational drug design at its finest using ligand receptor biology. In summary, we hope this issue on Ligand-Receptor Interactions and Drug Design gives you more thoughts on the diversity and great potential of this topic. More exciting findings are on the way. Lead Guest Editor Dr. He now works primarily in membrane trafficking and neurodegenerative diseases. Dr Zhang can be contacted at nc. Her work spans autophagy, cancer and cardiovascular disease. Song is the author or co-author of 15 published papers. She can be contacted at ude. Zhang is the author or co-author of more than 15 published papers and has presented at multiple national conferences. He specializes in biophysics. Dr Zhang can be contacted at ude. She is an expert in metabolic diseases. Dr Xiao can be contacted at ude. Authors disclose no external funding sources. Authors disclose no potential conflicts of interest. All authors have provided signed confirmation of their

compliance with ethical and legal obligations including but not limited to use of any copyrighted material, compliance with ICMJE authorship and competing interests disclosure guidelines. Bordet T, Buisson B, et al. Journal of Pharmacology and Experimental Therapeutics. Olesoxime, a cholesterol-like neuroprotectant for the potential treatment of amyotrophic lateral sclerosis. Eckmann J, Clemens LE, et al. Mitochondrial membrane fluidity is consistently increased in different models of Huntington disease: Gouarne C, Tracz J, et al. Protective role of olesoxime against wild-type alpha-synuclein-induced toxicity in human neuronally differentiated SHSY-5Y cells. Lenglet T, Lacomblez L, et al. Zanetta C, Nizzardo M, et al. Molecular therapeutic strategies for spinal muscular atrophies: TRP channels as cellular sensors. Yin K, Zimmermann K, et al. Therapeutic opportunities for targeting cold pain pathways. Leist M, Ghezzi P, et al. Derivatives of erythropoietin that are tissue protective but not erythropoietic. Erythropoietin-mediated protection in kidney transplantation:

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Chapter 4 : CiteSeerX â€” Citation Query Electrostatic Interactions in Proteins

Computer-assisted modeling of receptor-ligand interaction. Theoretical aspects and applications to drug design. Proceedings of the OHOLO Conference. Eilat.

Theory A molecule is a small chemical element that is made up of two or more atoms held together by chemical bonds. A molecule can be composed of either single kind of element e. H2 or different kinds of elements e. Molecules can be found in both living things and non living things. A drug is a small molecule that can interact, bind and control the function of biological receptors that helps to cure a disease. Receptors are proteins that interact with other biological molecules to maintain various cellular functions in body. Enzymes, hormone receptors, cell signaling receptors, neurotransmitter receptors etc. Drug designing is a process of designing a drug molecule that can interact and bind to a target. Receptors are molecules which can be seen on the surface of the cell transmits signals upon binding by a small molecule triggering a cellular process. In an unbounded state receptor, functionalities of the receptor remain silent. Hence this definition says that receptor binds specifically to a particular ligand or vice versa, but in some cases high concentrations of ligands will bind to multiple receptor sites. Drug receptors usually remain without endogenous ligand. The receptors for these drugs molecules can be enzyme, ion channel, protein, nucleic acids etc. It is used to treat malignant tumors. Receptors for endogenous regulatory ligands are hormones, neurotransmitters, autacoids, growth factors, cytokines etc. Hence the function of these receptors is to sense the ligands and initiate the response. For example, Aspirin is a small pain killer drug molecule which contains nine carbon atoms, eight hydrogen atoms and four oxygen atoms. Design of the molecules should be complementary in shape and charge to the target. Drug molecule mediates signal transmission through a molecule that is complementary which is essential for a biological process. The evolution of the receptor functions depends on the development of specific sites which are designed to bind drug molecules. Drug molecule binding capacity is important for the regulation of biological functions. Drug-receptor interactions occur through the molecular mechanics involving the conformational changes among low affinity and high affinity states. Drug molecule binding interactions changes the receptor state and receptor function. Molecular modeling includes computational techniques that are used to model a molecule. Drug designing by using these modeling techniques is referred to as computer-aided drug design. Computer based drug designing is a fast, automatic, very low cost process. It can be done either by Ligand based drug design or structure based drug design. Ligand based drug design is purely based on the model which is going to bind to the target. Defining of pharmacophoric regions are necessary for the molecule inorder to bind to the target but structure based drug design is based on the 3 dimensional structure of the target. If any target is not available, it can be created using homology modeling. Using the structure of the target, predict the drug molecules binding affinity to the target. Building a molecule using computer techniques is a very important step in drug designing. There are so many computational tools available for building a molecule. After modeling a molecule, check where the ligand gets docked onto the receptor and check whether the ligand fits for the target molecule and then go for docking studies. Docking is a method which predicts the preferred orientation of one molecule to another molecule when they are bound together to form a stable complex. Here the protein can be called as lock and the ligand can be called as key. It describes the best fit orientation of the ligand required for binding to a particular protein. To perform a docking, first one may require a protein molecule. The protein structure and ligands are the inputs for docking.

Chapter 5 : LIGAND-RECEPTOR INTERACTIONS AND DRUG DESIGN

Robert Rein is the author of Computer-Assisted Modeling of Receptor-Ligand Interactions (avg rating, 0 ratings, 0 reviews), Molecular Basis Of Cancer.

A, side view of the complex in a plane perpendicular to the cell surface. B, top view of the complex from the extracellular side of the cell surface. TMs are positioned and numbered counterclockwise. The receptor TM backbone is shown in red. The carbon skeleton of the receptor amino acids involved in SR binding is represented in white. The carbon skeleton of SR is displayed in orange. Oxygen, nitrogen, sulfur, and chlorine atoms are shown inred, blue, yellow, andgreen, respectively. The letters aâ€”d indicate the position of the adamantane, pyrazole, dimethoxyphenyl, and quinolinyl moieties in SR , respectively. The first approach entailed computer-assisted modeling of the rNTR1 according to a method that has been described for a number of GPCRs 7. One important step in the method consists in attributing to GPCRs the known tridimensional structure of bacteriorhodopsin However, this has been criticized, because bacteriorhodopsin, although a protein with seven transmembrane helices, is not a GPCR. Quite recently, the tridimensional helical packing of rhodopsin, a true GPCR, was reported 24 , We therefore used rhodopsin as a template in constructing our model of the rNTR1. The second approach involved mutagenesis of the rNTR1 to find out residues that might interact with SR This helped docking the antagonist into the receptor, which led to the model proposed in Fig. It should be pointed out that our model was constructed based on the assumption that the residues for which mutation decreases SR potency are involved in molecular interactions with the antagonist. Although there is strong evidence that this is so for Arg, the data to support the other interactions are more indirect. Some of these aspects will be further discussed below. All the residues identified here as participating to the binding of the antagonist, except Met, were found within TMs 6 and 7 or lying at the junction between these TMs and the third extracellular loop. This appears to be a common feature of peptide receptors with respect to nonpeptide antagonist binding. Furthermore, TMs 6 and 7 are often involved in the binding of the small nonpeptide ligands 5 , Another common feature of peptide GPCRs lies in the different binding epitopes found for peptide agonists and nonpeptide antagonists. Our present data conform with this property. Conversely, mutating Tyr resulted in an apparent loss of agonist binding without affecting antagonist binding. We have shown previously that deleting a portion of the N-terminal domain of the rNTR1 also strongly decreased NT binding affinity without altering SR affinity All the mutant receptors, except Arg mutants, that had decreased affinity for SR displayed high affinity NT binding withK d values ranging from 0. This demonstrates that the mutant receptors were correctly expressed at the membrane of COS M6 cells and suggests that the mutations did not grossly affect the conformation of the rNTR1. Two residues, Tyr and Arg, were found to play a key role in SR binding. The YA mutant exhibited a fold decrease in affinity for the antagonist and less than a fold decrease in agonist affinity. Interestingly, mutating Tyr, which lies close to Tyr in the third extracellular loop, had the opposite effect. These data suggest that the decreased SR affinity for the YA mutant reflects a direct interaction of Tyr with the antagonist rather than a perturbation of the receptor conformation. Indeed, a change in conformation in the vicinity of Tyr might be expected to modify the side chain orientation of the nearby Tyr residue, which is essential for NT binding and, hence, to markedly alter agonist affinity. Structure-activity studies using SR analogs bearing structural modifications of these chemical moieties should prove useful to confirm the role of Tyrin antagonist binding. Although the potency of NT was reduced by more than 4 orders of magnitude with the mutant as compared with the wild type receptor, the maximal NT stimulation was similar for both receptors, suggesting that they were expressed at comparable levels. Indeed, we have observed with the wild type rNTR1 that maximally stimulated IP production is directly related to the amount of transfected receptor. Such a loss in potency is compatible with Arg, making an ionic link with the carboxylic function of the antagonist, as proposed in our model. This proposal is further supported by the results obtained with the enantiomers SR and SR Both enantiomers differ mainly in the

orientation of the COOH group borne by the asymmetric carbon, as shown by crystallographic studies The acidic function is oriented similarly for SR and the activeS isomer, SR , whereas it points in opposite direction in the much less active R compound, SR 22 , The fact that the inhibitory potency of SR was not affected by the RM mutation, in contrast to that of SR and SR , strongly argues in favor of the existence of an ionic link between Argand the carboxylic function of the antagonist. These data also point to a major role of Arg in the NT binding site. Studies are in progress to test this hypothesis. In a recent study, the binding site of NT in the rNTR1 was proposed to lie mainly in the third extracellular loop, based on computer-assisted modeling of both the receptor and the peptide ligand This suggests that the binding sites of NT and SR in the rNTR1 are close to each other and possibly overlap, which might explain the observation that SR behaves as an apparent competitive antagonist of NT binding and NT-mediated effects The NT functions associated with this receptor are as yet unknown. In our model, Phe makes hydrophobic interactions with the aliphatic adamantane moiety of the antagonist. It is possible that adding an hydroxyl group to the aromatic ring of Phe might decrease these hydrophobic interactions and account, at least in part, for antagonist selectivity. In addition, other residues yet to be identified might contribute to the affinity and selectivity of SR for the NTR1. The present model should be helpful to direct further mutagenesis studies of both the NTR1 and NTR2 and hopefully to develop new antagonists with high selectivity for each of these receptors. This in turn should greatly help in determining their respective contributions to the biological effects of NT. Section solely to indicate this fact. Received February 17, Revision received March 25,

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Chapter 6 : Receptorâ€“ligand kinetics - Wikipedia

A new methodology is presented aiming to address, in the context of 3D-QSAR studies, the effect of water molecules in receptor-ligand interactions. The methodology has been developed on a series of 47 glucose analogue inhibitors of the Glycogen Phosphorylase b, for which the structure of the receptor-ligand complex is available.

Many analogues of enkephalins were synthesized by our group in addition. Basing on docking results was established that: These results reveal further steps for the computer modeling of selective encephalin analogues such as: This process is time Table 1. Ligands used in our study. Computer modeling of ligand-receptor interactions â€" enkephalin analoguesâ€¦ 2. Docking Procedure , To apply the docking procedure we postulated where Escore is a docking scoring function, Einter â€" the following assumptions: Because the in Table 2. In the absence of 4. Correlations crystallographic data, indirect methods, which In order to find relationship between sets of data include site-directed mutagenesis, chimeric studies, derived from in vitro assay and docking results, we the substituted cysteine accessibility method, and tried to predict it with a help of the Spearman affinity labeling studies, have been instrumental in correlation, using GraphPad Prism 3. As a target of our docking procedure we used measure of statistical dependence between two model of human DOR, published in PDB id: It assesses how well the relationship 1OZC , [9]. It was found that there are several key between two variables can be described using a amino acid residues which are responsible for monotonic function. If there are no repeated data ligand binding. It is occurs when each of the variables is a perfect conserved among all biogenic amine receptor monotone function of the other. The role of this residue is to bind a free Spearman, for values of rs of 0. Since the structurally correlation is very strong; between 0. Histidine His residue in helix V is correlation is too low to be meaningful [13]. It can very important for hydrogen-bond formation with be calculated by the equation: MolDoc SE algorithm [12] was used each observation on the two variables are with 10 runs for each ligand with energy calculated, and n is the number of the variables in minimization and hydrogen-bond optimization after each set. Five poses for each ligand were generated. Docking results procedure of docking was made four times with different constrains, in fact they were four different Docking program generates five pose for each amino acid residues in binding site of receptor â€" analogue. Total energy of the ligand-receptor Asp, Trp, His and Leu Computational tools Analyzing these docking results, we choose the In this study we used a model of DOR, best pose for each ligand with the lowest value of published in PDB id: Docking studies the scoring function. The data are presented in were performed using Molegro Virtual Docker, run Table 2. The range of the values obtained was on Windows operating system. Visualizations of between The lowest enkephalins, enkephalin analogues and of docking potential energy is characteristic for the complex of poses were made and analyzed on Molegro DOR with [Leu5]-enk and the highest for Molecular Viewer, and evaluation function for [Cys O2NH2 2, Met5]-enk. Computer modeling of ligand-receptor interactions â€" enkephalin analoguesâ€¦ Table 2. Ligands in ascending order of the scoring [Met5]-enk bind to the receptor pocket by function Escore obtained with docking. Complex of [Cys O2NH2 2, Leu5]-enk with DOR The data presented in Table 3 concerns the has relatively high total potential energy but it number of hydrogen bonds formed during binds very strong to the receptor pocket by three H- interaction between DOR and the ligands. Tyr interaction Trp with Tyr. Val, Tyr â€" with NH group from peptide Table 3. H-bonds and interactions between ligand and backbone, and His â€" with OH group of Tyr. It forms six H-bonds with the amino en acid residues in the receptor pocket. The bonds interactions are as follows: Interactions in the bidning pocket of DOR with: For example, correlation enkephalin T. Computer modeling of ligand-receptor interactions â€" enkephalin analoguesâ€¦ of IC50 and Escore is presented on Figure 2. This vitro assay or docking data are rather different low value shows that the correlation between Escore because the correlations between them were not and IC50 value is very low. IC50, KA and erel obtained in vitro [12]. The substitution in second position in the Obviously for this kind of investigations on encephalin structures with amino acid containing ligand â€" target interactions a novel

optimization SO2NH2 increases additionally the binding of the procedure has to be initiated in further studies. Since we obtained a set of parameters with docking The incorporation in position 2 in the encephalin or with in vitro bioassay, probably multi- molecules of Cys Bzl does not interfere on their dimensional vectors have to be introduced, such as ability to bind to DOR. So, additional interaction two-dimensional vector KA, erel or three- due to Bzl group does not appear. Total potential dimensional vector IC50, KA, erel. In the same way energies of their complexes are similar to the docking results could be presented not only with endogenous enkephalin complexes with DOR and one but with several scoring functions and the number of H-bonds formed is the same. It is able to form H-bonds docking studies, respectively, it is possible to with its OH group and different functional groups introduce a partial order, so that these sets become of ligands, such as: Analysis and comparison of groups of peptide backbone, and SO2NH2 group of maximal elements in the ordered sets could help to amino acid analogue in position 2. Calculation Basing on docking results obtained with of the parameters of in vitro experiments did not Molegro Virtual Docker it was established that all concern directly 3D structure of the receptors. All of the ligands interact by main tool. In this study we applied 3D model of forming many H-bonds with the receptor. Additional interaction between receptor and ligand appears in the case of analogues substituted with amino acid containing SO2NH2 group. This study T. Computer modeling of ligand-receptor interactions â€" enkephalin analoguesâ€¦ could not give a definitive answer if the 3D model 6 N. Bojkova, there is no correlation between values obtained in Bulg. This work was 8 N. Wood, Neuropharmacology , 21, Journal 8, Article 15 2 E. Watson, in Opioid I Herz, A. Ratner, Statistical Modeling and Analysis for 5 J. Effective Techniques for G. â€" Hughes, . . , in vitro . : - , .