Biochemistry & Physiology: Open Access

Sandhoff, Biochem Physiol 2023, 12:4

Review Article Open Access

A Review on the Membrane Protein Biochemistry Applications

Heike Sandhoff*

Department of Biochemistry, Chemie und Biochemie der Universitat Bonn, Germany

Abstract

The predictive powerhouse of protein structure and function that is protein sequence coevolution analysis has recently matured. The prediction of membrane and disordered protein structures, protein complex architectures, and the functional effects of protein mutations have been made possible by direct methods that make use of global statistical models of sequence coevolution. These computational methods, which provide functional and structural information in an otherwise experimentally, challenging field, have been adopted by the membrane protein biochemistry and structural biology fields. In this section, we discuss the most recent applications of protein sequence coevolution analysis to the structure and function of membrane proteins, as well as the promising directions and challenges that lie ahead. Membrane protein biochemists who want to apply sequence coevolution analysis to a specific experimental system can benefit from our insights and instructions.

Keywords: Clustered protocadherin; Sequence coevolution analysis; Membrane proteins

Introduction

Methods for sequence coevolution analysis are based on the idea that evolution produces compensatory mutations. The identities of protein residues are dependent on each other in a folded protein because amino acid side chains pack tightly together. This means that mutations at one position influence evolution at other positions in a protein sequence. A phenylalanine residue that is stabilized in a protein core by nearby aliphatic residues is one such example. This stabilizing interaction would be lost if that position were randomly mutated to a polar or charged residue, which could impair protein function. To recover capability, different build-ups close by could change to a polar or charged buildup to reestablish the connection, but in an elective structure, and make up for the first opportunity transformation [1-3]. As a result, these residues are evolutionary coupled because the initial mutation altered their evolutionary trajectory. In-depth descriptions of additional compensatory evolution mechanisms have been provided. It is important to note that because the interactions are more direct, residues that are physically close together are more strongly coupled.

In point of fact, coevolving pairs exhibit the thermodynamics of the two amino acid interactions. A residue's degree of coupling to other nearby residues is also determined by its function in protein structure or function. Reluctance to substitution by highly conserved residues may be the primary factor in identifying coevolving pairs, rather than true covariation, because highly conserved residues may impose strong constraints on the evolutionary trajectory of nearby residues [4]. The ability of these techniques to successfully predict residue pairs that are close to each other in the three-dimensional structure of proteins overshadows whether these theories of coevolution are heuristic in nature. A record of coevolution is provided by a protein family's homologous sequences. A multiple sequence alignment (MSA) can be used to identify coevolving pairs or groups of residues using algorithms by assigning an evolutionary coupling score to pairs of residues. In the beginning, these evolutionary couplings were computed using two approaches: a mutual information (MI) approach, in which the joint probability of finding a specific pair of amino acids in two positions is compared to the probability of finding the amino acids in these two positions independently, and a substitution correlation approach, in which correlations in substitution matrices between pairs of positions are calculated. Although these methods are useful, their overall accuracy in predicting actual contacts is low. An excellent recent review provides a more in-depth explanation of these approaches as well as the many variations of them.

A global model of all couplings is used to eliminate transitive couplings in order to overcome the difficulty of identifying only directly coevolving pairs, which means that position A effectively coevolves with position C due to the direct coevolution of A and B and of B and C. This was one of the initial methods' limitations. Approximation methods are used because these global models have a large number of parameters that make explicit solutions impossible [5-7]. In the beginning, a Monte Carlo method was used to randomly explore parameter space, but this method requires a lot of computational power. Susceptibility propagation, mean-field approximation, and other entropy-maximization techniques have all been used since then to approximate and simplify these coupling parameters. These various statistical approaches are contrasted in a recent review. In addition, a consensus approach or machine-learning algorithms (Raptor-X) have been used to integrate multiple direct methods to enhance prediction. Pseudo-likelihood maximization and consensus methods performed best in predicting true contacts, according to studies comparing their predictions.

New approaches to characterizing membrane proteins are required because there are so few structures of membrane proteins compared to soluble proteins. How helpful will techniques for sequence coevolution analysis be to researchers studying membrane proteins? Despite the fact that well-known papers promise to provide high-resolution structures of proteins based solely on sequence information, sample sets frequently favour well-represented protein families [8]. By looking at some examples of how sequence coevolution analysis can be used with membrane proteins, we can see how useful it can be. From de

***Corresponding author:** Heike Sandhoff, Department of Biochemistry, Chemie und Biochemie der Universitat Bonn, Germany, E-mail: asanheike@edu.cn

Received: 1-Apr-2023, Manuscript No: bcp-23-91805, **Editor assigned:** 3 -Apr-2023, Pre QC No: bcp-23-91805 (PQ), **Reviewed:** 17-Apr-2023, QC No: bcp-23-91805, **Revised:** 21-Apr-2023, Manuscript No: bcp-23-91805 (R), **Published:** 29-Apr-2023, DOI: 10.4172/2168-9652.1000411

Citation: Sandhoff H (2023) A Review on the Membrane Protein Biochemistry Applications. Biochem Physiol 12: 411.

novo protein structure prediction to understanding conformational changes, these examples demonstrate how sequence coevolution can be used to study membrane proteins at multiple levels. We apologize for omitting any studies from this rapidly expanding field because we were unable to cover all examples. We provide guidelines for using sequence coevolution analysis effectively based on this survey.

The de novo prediction of protein structure based solely on sequence information was one of the promises made in the initial paper on protein sequence coevolution analysis. The main idea is to use the coevolving residue pairs as distance constraints for structural modeling with NMR methods or computational structure prediction software like Rosetta inferring that the paired residues should be close to each other in space in the three-dimensional structure. However, it wasn't until direct methods were developed to distinguish transitively coupled pairs from directly coupled residue pairs that the precision of predicted structural contacts became sufficient to infer protein structure. Direct strategies were before long applied to α-helical layer proteins, for certain modifications explicit for film proteins. In addition, the model structures were scored based on how well they adhered to secondary structure prediction, coevolution constraints, and models of which residues are exposed to the lipid membrane. Based on a test set of 25 known membrane protein structures, this EV Fold membrane algorithm can produce highly accurate models of -helical membrane proteins [9-10]. These models are comparable to a reasonable homology model, making them a useful starting point for a membrane protein biochemist lacking other structural information. The RMSD over C atoms for these models and their corresponding experimentally determined structure ranges from 2.8 to 5.1.

Conclusion

This review examines how studies of membrane protein structures and functions can use sequence coevolution analysis to identify functional sites in proteins, understand conformational changes, discover and characterize protein-protein interactions, and integrate with other structural approaches to reveal the structure of large membrane protein complexes. In order to encourage proper usage and increase the likelihood of successful application of this remarkable and cutting-edge method, we have provided guidelines for performing sequence coevolution analysis. When sufficient sequence information can be assembled into a high-quality MSA, we anticipate that biochemists will increasingly use sequence coevolution analysis on their own protein families of interest. We find such analyses to be extremely helpful in generating hypotheses that can be tested experimentally.

Declaration of Competing Interest

The authors declare that they have no competing financial interests

Acknowledgement

None

References

1. Carreras HA, Calderón-Segura ME, Gómez-Arroyo S, Murillo-Tovar MA, Amador-Muñoz OA (2013) Composition and mutagenicity of PAHs associated with urban airborne particles in Córdoba, Argentina. Environ Pollut 178: 403–410.
2. Ceretti E, Zani C, Zerbini I, Viola G, Moretti M, et al. (2015) Monitoring of volatile and non-volatile urban air genotoxins using bacteria, human cells and plants. Chemosphere 120: 221–229.
3. Chang CC, Chiu HF, Yang CY (2015) Fine particulate air pollution and outpatient department visits for headache in Taipei, Taiwan. J Toxicol Environ Health A 78: 506–515.
4. Chow JC, Watson JG, Mauderly JL, Costa DL, Wyzga RE, et al. (2006) Health effects of fine particulate air pollution: lines that connect. J Air Waste Manag Assoc 56: 1368–1380.
5. Galvão MF, Cabral TM, de André PA, Andrade MF, de Miranda RM (2014) Cashew nut roasting: chemical characterization of particulate matter and genotocixity analysis. Environ Res 131: 145–152.
6. Garcia SM, Domingues G, Gomes C, Silva AV, Almeida SM (2013) Impact of road traffic emissions on ambient air quality in an industrialized area. J Toxicol Environ Health A 76: 429–439.
7. Gentry-Schields J, Bartram J (2014) Human health and the water environment: using the DPSEEA framework to identify the driving forces of disease. J Sci Total Environ 469: 306–314.
8. Kaur R, Kaur J, Mahajan J, Kumar R, Arora S (2013) Oxidative stress implications, source and its prevention. Environ Sci Pollut Res Int 21: 1599–1613.
9. Krupnick AJ (2008) Challenges to managing air pollution. J Toxicol Environ Health A 71: 13–28.
10. Ma TH, Cabrera GL, Chen R, Gill BS, Sandhu SS, et al. (1994) Tradescantia micronucleus bioassay. Mutat Res 310: 221–230.