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Latent toxicity of alcohol

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Abstract:
Ingested alcohol revels its effect directly by impacting the central nervous system arising from solubility in water and fats. As alcohol infiltrates into cells disturbing the environmental conditions by lowering the dielectric constant and in consequence reveals significant negative impact on environment-controlled cellular processes like all self-organisation processes. Protein folding, the formation of their functional forms and the formation of biological membranes are particularly important as appearing to be environment dependent. It may be proven by the fuzzy oil drop model interpreting the folding process as significantly dependent of the external conditions. The low-degree misfolded proteins – unrecognised in normal conditions - develop dementia, life-shortening as well as atherosclerosis, diabetes and lowered cellular and humoral immunity after reaching the higher level disorganisation.

Keywords: Protein folding, alcohol, protein synthesis, self-organisation, atherosclerosis

Background:
Biological life is inextricably linked to water. The ingredients that form biological structures are either hydrophilic, *i.e.* energetically benefiting from water contact, or hydrophobic, non-polar with adverse water contact. In addition, nature also commonly uses structures, in which polar and non-polar components are strongly interlinked. Such particles introduced into water environment crash with adverse impact and forced to isolate from non-polar parts by association and packing focused on reducing water contact. Polar parts, however, are subject to exposure. Consequently, they form organised structured with specific characteristics and function. If, however, the environment is hydrophobic in nature, the organisation process is reversed. The organisation occurs spontaneously, in contact with the environment. This process is referred to as self-organisation. In our daily lives, we encounter that process at the macro level. Soap dissolution is an example. Soap consists of fatty acids ending in a polar group, usually negatively charged. The particles of soap are set on the water surface or dissolved in water to form micelles, because like-charged polar groups often repel one another, while fat acid residues bind with one another (**Figure 1**) **[1, 2]**. If the polar group is neutralised by introduction of a positive charge, then molecules closely adhere to one another and form a plate. That is how bilayer membranes are formed (**Figure 2**) **[3, 4]**. Polypeptide chains, which form proteins after folding, consist of amino acids. The folding of polypeptide chains is a peculiar process directed by the environment. Polypeptide chains consist of amino acids, mostly polar, which determines the solubility. Non-polar fragments, however, after introduction into water environment, associate and force chain folding (**Figure 3**) **[5]**. The distribution of non-polar components in the polypeptide chain is determined by evolution. That folding results in biological function. The protein synthesis process is deterministic by default (strictly determined). The input comes from the DNA and RNA matrix. The folding stage, however, is probabilistic, *i.e.* it has no matrix. It means that the formation of a correct structure is merely probable. Thus even under normal conditions, some proteins do not obtain a correct structure. Such proteins show increased tendencies to aggregate and they are removed by a specialised repair system, *i.e.* UPR (Unfolding Protein Response). Correct folding is determined by unambiguous identification of polar and non-polar components. Such conditions are assured by water with high dielectric constant. If, however, alcohol is introduced into the environment, the identifiability of those components is decreased drastically. The number of correctly folded proteins decreases, which disrupts the equilibrium in biological systems, including in particular in human body. Alcohol is easily soluble in fats and in water. The effects are usually seen with a delay. They only appear when medical intervention is required.

Materials and Methods:
Protein is a chain structure consisting of amino acids. By default, if is formed non-folded. It is referred to as the polypeptide chain. The synthesis of the polypeptide chain is strictly determined by the input from the DNA and RNA matrix. To obtain biological activity, the polypeptide chain requires folding to form the tertiary structure of the protein. That stage does not have a strictly defined matrix. The input comes from the amino acid sequence established by evolution. In turn, the environment directs the folding towards a stable protein form that is protein within a suitable energy minimum. The polypeptide chains include water-soluble and water-soluble and water-insoluble parts (**Figure 3**). The method explaining the folding process is expressed by the model referred to as fuzzy oil drop (FOD-M) **[5]**. It assumes the possibility of organisation of the component parts of the polypeptide chain obtained with active involvement of water environment. The model evaluates the degree of adjustment of the polar and non-polar parts distribution in protein body to the environment that directs the process. If its non-polar parts (amino acids) are located in a centre separated from the polar water environment by a layer of polar components (amino acids), then such arrangement meets the requirements of adjustment to the environment and ensures the solubility of the given protein to prevent association. An ideal hydrophobicity distribution in protein body expressed using the 3D Gauss function, in which the function maximum is located in the central part of the ellipsoid spanning on the protein body. The hydrophobicity level decreases away from the centre to reach the zero level on the surface. The actual hydrophobicity distribution, which may to a varied extent reflect the idealised condition, is expressed by hydrophobic interactions between amino acids. The degree of adjustment and reproduction of the idealised arrangement is very variable. That degree of deviation of the observed distribution from the idealised distribution can be evaluated using the divergence entropy measure, introduced by Kullback and Leibler **[6]**. Water environment is not the only environment, in which proteins show their activity. The numerous proteins anchored in the plasma membrane are essential in product or information transport. The plasma

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membrane creates completely different conditions for the protein anchored in it. Here non-polar residues are expected to be exposed with polar residues located in the centre.

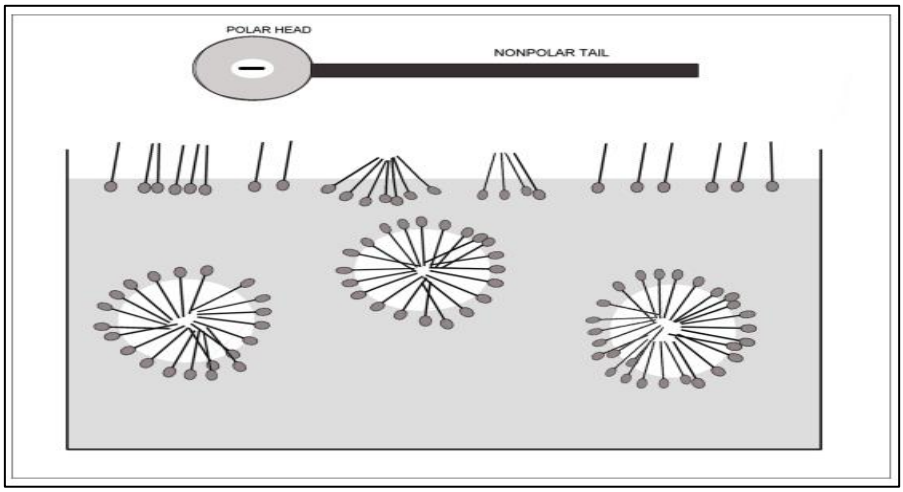

Figure 1: Self-organisation – soap molecules in water

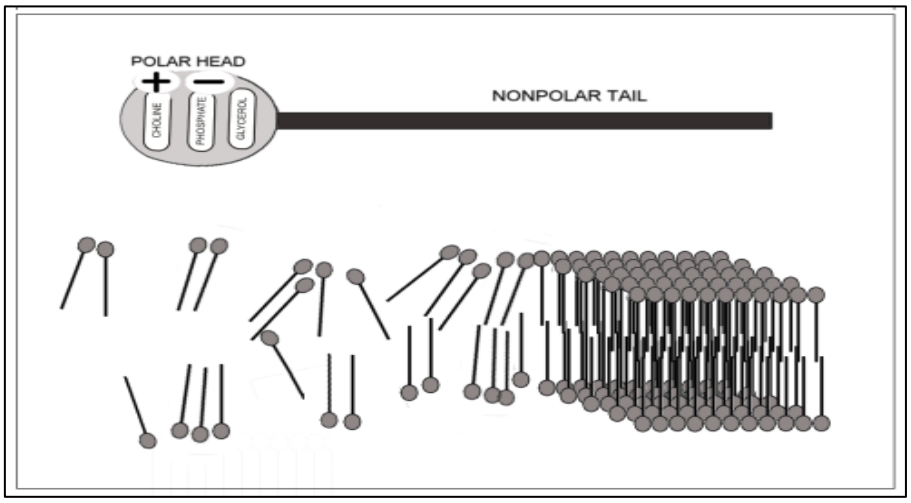

Figure 2: Self-organisation – membrane formation

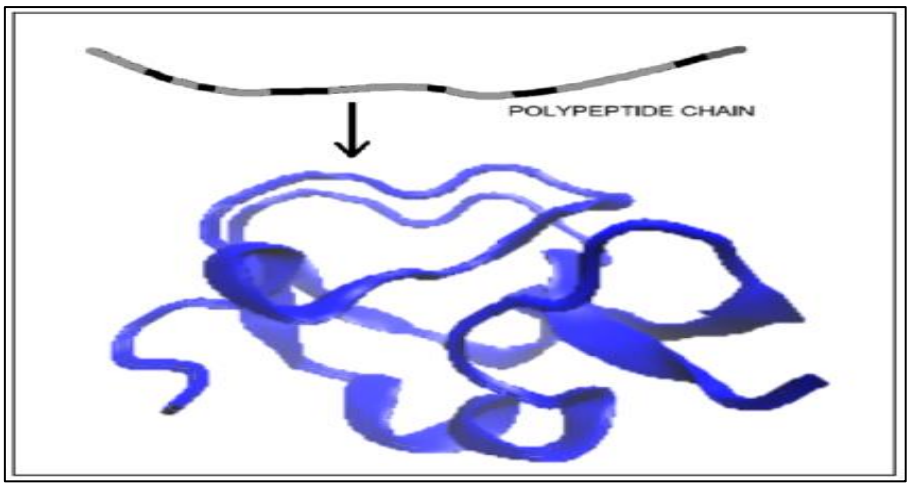

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Figure 3: Self-organisation - final step of protein synthesis – protein foldin

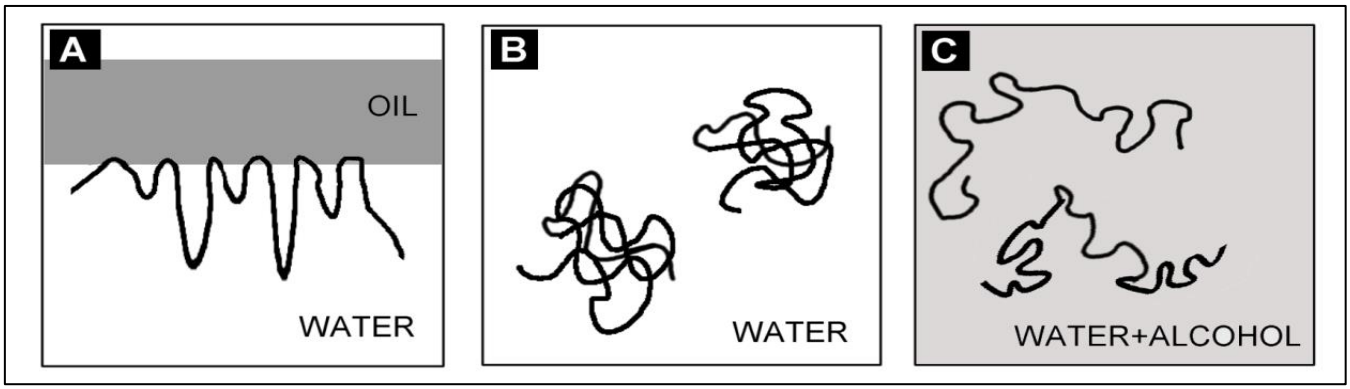

Figure 4: Role of hydrophobic fragments in structuralisation of polypeptide chain: A: hydrophobic fragments in contact with oil, polar fragments remain in water, B: hydrophobic fragments of polypeptide chain mutually assembled driving the protein folding, C: presence of alcohol disturbs the differentiation of hydrophobic/polar fragments – protein folding disturbed. The participation of non-water environment in protein folding can be assessed quantitatively using the publicly available software: HPHOB [https://hphob.sano.science].

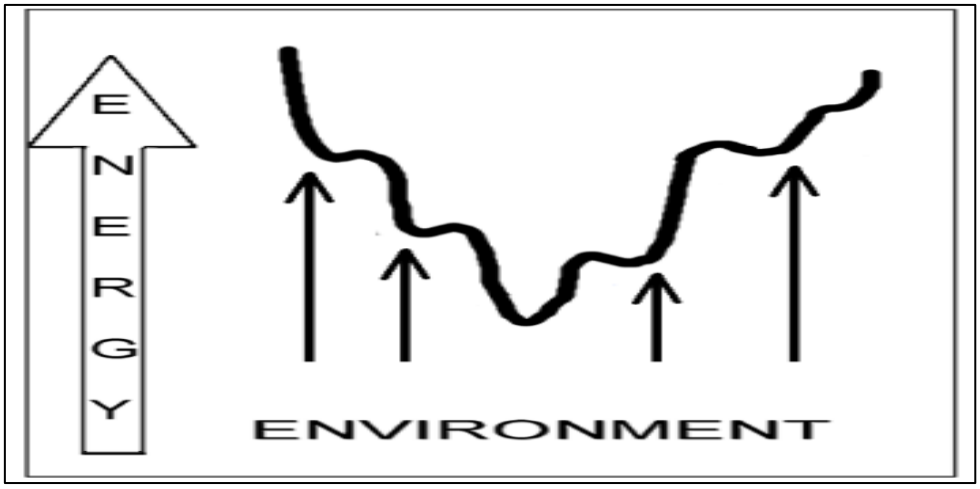

Figure 5: Funnel model – arrows show local energy minima, where polypeptide folds finds its stabilisation

The environment directing the folding process towards the adjustment of the protein structure to the hydrophobic environment is described in the form of adjustment to the inverse of the 3D Gauss function. The discussed two environments representing polar opposite conditions are not exhaustive of all possible conditions for protein folding. Thus, a function was introduced to include the share of the two mentioned functions, in which the share of the environment expressed by the inverse function is coupled with the K parameter that measures the share of the non-water environment **[5]**. The value of K=0.0 designates water environment. The phenomenon of protein structure dependency on the environment is graphically presented in **Figure 4**. Using the FOD-M model, which determines the hydrophobicity distribution in protein body, the conditions to obtain the given structure can be identified. **Figure 4** shows protein with a very high degree of hydrophobicity distribution adjustment to the idealised arrangement (K=0). All other examples represent proteins with higher K values, according to specific environmental characteristics. Every protein, to obtain its predictable structure, which also guarantees its biological function, requires an appropriate environment. Introducing environmental changes covering the entire body in the form of presence of alcohol, which may be present both in water and fats, changes its properties. The spontaneity of the protein folding process consists in aiming towards the given polypeptide chain structure by achieving the appropriate energy minimum condition (**Figure 5**). The problem, however, is that the local energy minima for the given chain are multiple (the multiple minima problem) **[7]**. Achieving the appropriate structure is connected with the achievement of the appropriate energy minimum. It is visually expressed by the so-called funnel model (**Figure 5**). The process towards the appropriate energy minimum in FOD-M model interpretation occurs with active

involvement of the environment, of which the specific characteristics are expressed by the horizontal axis (**Figure 5**) **[7]**. If that environment is disrupted by the presence of alcohol, the direction may lead to protein adjustment to a different energy minimum, resulting in an incorrect structure (**Figure 5**).

Results:

Alcohol (ethanol) is a special compound. It is easily soluble both in water and fats, affecting their final properties. Thus, the potential effects of alcohol are multiple. But alcohol is widely consumed. Introduced into the body, it reveals its presence above all by affecting the processes occurring in the central nervous system, including in particular the brain, of which the activity is to a large extent determined by the involvement of fat ingredients. Even low alcohol concentrations reveal their presence by disrupting behaviour, understanding, response and memory. The effects of alcohol on the body are twofold and depend on the concentration and percentage of ingested alcohol. High percentage alcohols (spirits) destroy tissues and their effects are quickly visible. This results in hazard awareness. The effects of frequent consumption of alcohol with low concentration (beer, wine) are wrongly considered as safe and non-toxic. The consequences of that impact are revealed with a long delay. Excessive alcohol consumption is related to multiple somatic disorders (as per WHO), up to 200 different types of disorder. Alcohol is the cause of 6% of all deaths and more than 25% of deaths in the 20-39 age group (World Health Organisation 2015 – https://www.who.int/news-room/fact-sheets/detail/alcohol). A high alcohol level initiates inflammation. It is visible in the gastrointestinal tract. The most often damaged organ is the liver. The pancreas is also exposed, with its acute inflammation being in 20-25% caused by ethanol. 32-67% of all persons addicted to alcohol show the symptoms of peripheral polyneuropathy. Introducing portions of low concentration alcohol into the body, in the form of wine or beer, is commonly, yet wrongly, considered as safe. After ingesting alcohol, its presence is very quickly recorded in exhaled air and in blood, which proves that alcohol penetration finds no barrier in the body. The involvement in biochemical processes at low ethanol level in cells is relatively small. However, some stages of metabolism are very vulnerable. These are the stages, at which environmental conditions have a particularly strong impact on the course of the given process, thus the structure formation process. This is applicable to self-organisation processes **[8-13]**. Disrupting the environment, in which self-organisation processes occur, prevents the formation of correctly organised structures. The presence of water environment, in which the characteristics of polar and non-polar particle components is the most exposed, is pre-requisite for process correctness. The presence of ethanol disrupts that differentiation and impedes correct formation of organised structures **[14–22]**. The classic example of the negative impact of alcohol in daily diet is COVID-19 mortality statistics **[23, 24]**. It was demonstrated that the highest mortality rates were recorded in countries with consistent small yet frequent presence of alcohol in daily diet. Consistent consumption of beer and wine with unnoticeable daily effects resulted in the accumulation of adverse impacts. In case of a disease hazard, *e.g.* virus invasion, the organism shows a drastically reduced defensive capacity (lit). The proteins vulnerable to the presence of alcohol also include the receptors responsible for lipid metabolism. Their deficiency or reduced activity results in the formation of cholesterol deposits in blood vessel, with all consequences in the form of atherosclerosis. One of the main metabolic risk factors of atherosclerosis is LDL-Cholesterol. The atherogenic impact depends on the increased blood cholesterol level and the time over which that level is maintained. The liver is central to the cholesterol homeostasis. In case of ethanol ingestion, that organ is perfused with blood coming from the portal vein system.

Discussion:

Proteins are a key biological component responsible for function. Proteins are continuously synthesised and systematically degraded. Protein synthesis is a complex process. Its initial stages are strictly defined by input (deterministic). The input comes from the DNA and RNA matrix. The polypeptide chain, however, only becomes active, when folded and formed into tertiary structure. The folding is driven by chain interactions with water or hydrophobic environment of the membrane for membrane proteins. Water-soluble proteins are driven by the association of the non-polar components present in the polypeptide chain, of which the contact with water is energetically adverse. The folding is directed through evolution by an appropriate distribution of non-polar parts in the polypeptide chain. That stage in the protein synthesis process is particularly vulnerable to environmental conditions. Osteoporosis and osteoarthritis as significantly lower production of bone components is recognised as week efficiency of proper production of certain proteins **[25].** Small percentage of Alzheimer's disease related to mutations, which obviously lead to misfolding proves that environment-dependent folding influence the misfolding processes supporting the amyloid fibrils formation **[26, 27]**. The inflammation and neuroimmune dysregulation is treated as consequence lower efficiency of regulation processes responsible for homeostasis **[28]**. The dis-regulation related to basic physiological processes is observed in form of sleep disorder **[29-31].** The misfolded proteins losing their activity make also their degradation limited what significantly influences the homeostatis disorder **[32, 33].** Misfolded proteins fail to undergo the degradation process **[34]**. The experimental observations suggests the universality and global interference of misfolding effects which may the consequence of external force field chages caused also by the presence of alcohol

Conclusion:

A folded protein, already within the appropriate energy minimum, is relatively resistant to environmental effects. The folding itself, however, based on self-organisation principles, is extremely vulnerable as it is only subject to the principles of probability to achieve its objective. Each product formation process is more vulnerable to the environment than the end

product. The introduction of alcohol into water significantly disrupts the folding process and disorganises the conditioning system by decreasing the differentiation of polar and non-polar parts. Incorrect protein folding or deficiency of the biologically required count disrupts the equilibrium in biological systems, which enables the initiation of pathological processes. Each, even minor, amount of alcohol consumed leaves an initially unnoticeable mark. The effects only manifest when the disorder is already advanced.

Data accessibility:
Three tools available in open access systems allow the results described to be obtained in relation to: Assessing the type of ordering of hydrophobicity distribution in a protein body: https://hphob.sano.science/

Author contributions:
All Authors of equal contribution.

Informed consent statement:
Not applicable.

Data availability statement:
Not applicable. The tools allowing simulation of discussed issues are available in open access. Addresses are given.

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References:
[1] Kung HC & Goddard ED. *J. Colloid Interface Science*. 1969 **29**:242. [PMID: 5776568]
[2] Seddon AM *et al. Biochim Biophys Acta*. 2004 **1666**:105. [PMID: 15519311]
[3] Stieger B *et al. Biochim Biophys Acta Mol Basis* Dis. 2021 **1867**:166079. [PMID: 33476785]
[4] Fernandis AZ & Wenk MR. *Curr Opin Lipidol*. 2007 **18**:121. [PMID: 17353659]
[5] Roterman I & Konieczny L. *Entropy (Basel)*. 2023 **25**:850. [PMID: 37372194]
[6] Kullback S & Leibler R.A. *Ann. Math. Statist*. 1951 **22**:79. [DOI: 10.1214/aoms/1177729694]
[7] Roterman I *et al. Comput Struct Biotechnol J*. 2024 **23**:3827. [PMID: 39525086]
[8] Schiffmann Y. *Biochem Soc Trans*. 1997 **25**:S690. [PMID: 9450117]
[9] Palacios ER *et al. J Theor Biol*. 2020 **486**:110089. [PMID: 31756340]
[10] Wills PR. *Entropy (Basel)*. 2023 **25**:1281. [PMID: 37761580]
[11] Nédélec F *et al. Curr Opin Cell Biol*. 2003 **15**:118. [PMID: 12517713]
[12] Zhao X *et al. Chem Soc Rev*. 2010 **39**:3480. [PMID: 20498896]
[13] https://pubmed.ncbi.nlm.nih.gov/38285809/
[14] Gallina I & Duxin JP. *Nature*. 2020 **579**:499. [PMID: 32210381]
[15] Medkour Y *et al. Int Rev Cell Mol Biol*. 2016 **321**:259. [PMID: 26811290]
[16] Tsutsumi S *et al. Exp Biol Med (Maywood)*. 2003 **228**:1089. [PMID: 14530521]
[17] Perkins DI *et al. Pharmacol Ther*. 2010 **127**:53. [PMID: 20399807]
[18] Wang Y *et al. Mol Biol Rep*. 2025 **52**:361. [PMID: 40183835]
[19] Baraona E & Lieber CS. *Recent Dev Alcohol*. 1998 **14**:97. [PMID: 9751944]
[20] Puddey IB *et al. Novartis Found Symp*. 1998 **216**:51. [PMID: 9949787]
[21] Petersen OH. *Function (Oxf)*. 2021 **2**:zqab008. [PMID: 35330811]
[22] Nordback I *et al. Am J Pathol*. 2026 **196**:68. [PMID: 40254129]
[23] Roterman I & Konieczny L. *Bio-Algorithms and Med-Systems*. 2020 **16**:1. [DOI: 10.1515/bams-2020-0029]
[24] Roterman I *et al. Coronaviruses*. 2022 **3**:45. [DOI: 10.2174/2666796703666220602155421]
[25] Zhang F & Zhang W. *Ageing Res Rev*. 2024 **98:**102341. [PMID: 38759893]
[26] Rostagno AA. *Int J Mol Sci*. 2022 **24:**107. [PMID: 36613544]
[27] Rudman MD *et al. Cell* 2026 **189:**4193**.** [PMID: 42425064]
[28] He H *et al. Ageing Res Rev*. 2026 **117:**103055. [PMID: 41654144]
[29] Wear D *et al. Alzheimers Dement*. 2026 **22**:e71099. [PMID: 41618481]
[30] Deng HX *et al Front Immunol*. 2026 **17:**1879874. [PMID: 42534756]
[31] Lemus L *et al. EMBO J*. 2026 **45:**564. [PMID: 41350939]
[32] Xiao F *et al. Autophagy*. 2026 **22:**779. [PMID: 41518198]
[33] Young C *et al. Thyroid*. 2026 **36:**441. [PMID: 41801750]
[34] Lisowski B *et al. Sci Rep*. 2026 **16**:4904. [PMID: 41513988]