Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

The inactivation mechanism of chemical disinfection against SARS-CoV-2: From MD and DFT perspectives

Chunjian Tan[a,b,d], Chenshan Gao[c], Quan Zhou[c], Willem Van Driel[a], Huaiyu Ye*[b,d,e], Guoqi Zhang*[a]

[a] Electronic Components, Technology and Materials, Delft University of Technology, 2628 CD Delft, The Netherlands.

[b] School of Microelectronics, Southern University of Science and Technology, Shenzhen 518055, China.

[c] The Key Laboratory of Optoelectronic Technology &Systems, Education Ministry of China, Chongqing University and College of Optoelectronic Engineering, Chongqing University, Chongqing 400044, China.

[d] Shenzhen Institute of Wide-Bandgap Semiconductors, No.1088, Xueyuan Rd., Xili, Nanshan District, Shenzhen, Guangdong, China.

[e] Engineering Research Center of Integrated Circuits for Next-Generation Communications, Ministry of Education, Nanshan District, Shenzhen, Guangdong, China.

Corresponding Author: Huaiyu Ye (yehy@sustech.edu.cn) and G. Q. Zhang (G.Q. Zhang@tudelft.nl).

1. The atomic structures of spike protein and the corresponding system

The spike (S) envelope glycoprotein, as the mediating fusion of viruses and cellular membranes, plays a vital role in the infection of SARS-CoV-2.[1,2] In order to make a thorough understanding of the inactivation mechanism of SARS-CoV-2, the interaction mechanism between S protein and ethanol molecules is investigated by using MD method. The atomic structures of S protein and the S protein-ethanol (75%) system is shown in Fig. S1.

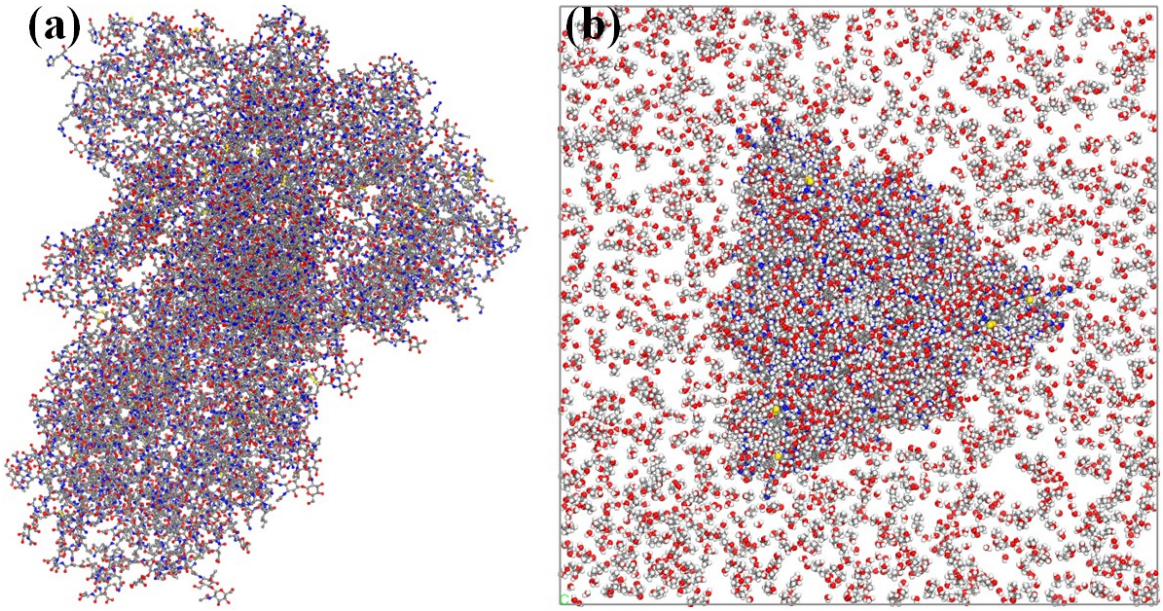

Fig. S1 The atomic structures of (a) S protein and (b) the S protein-ethanol (75%) system

2. Radial distribution function

Through using the steepest descent and conjugate gradient algorithm, the geometric structure of the S protein-ethanol system is fully relaxed. The optimized system clearly that ethanol molecules are mainly concentrated in the vicinity of glutamate acids (GLU) and N-acetylglucosamine (NAG) residues of the S protein. Although ethanol molecules also are observed near other amino acid residues such as aspartic acid (ASP), glutamine acid (GLN), and histidine acid (HIS) residues, the number of adsorbed molecules by them is relatively small compared with that by GLU and NAG residues. The radial distribution function (RDF) of the S protein-ethanol system is analyzed based on the MD simulation trajectories. As illustrated in Fig. S2, the first peak of $g(r)_{O\text{-}O}$ of O(GLU residues)-/O(NAG residues)-O(ethanol) pairs appear around 2.0 Å and 2.5 Å respectively, indicating the bond interactions between ethanol molecules and these two residues. Interestingly, their second peaks are depicted in the vicinity of 3.0 Å and 4.0 Å, respectively. For N(GLU residues)-/N(NAG residues)-O(ethanol) pairs, it can be found that the first peak is located within the range of 9.0-10.0 Å. Therefore, the constraint between GLU/NAG residues and ethanol molecules is contributed by the non-bond interactions, which distinctly indicates that the O atoms of GLU/NAG residues have more

strong interactions with ethanol molecules compared with their N atoms. This conclusion is in agreement with the calculated results of 3CL hydrolase.

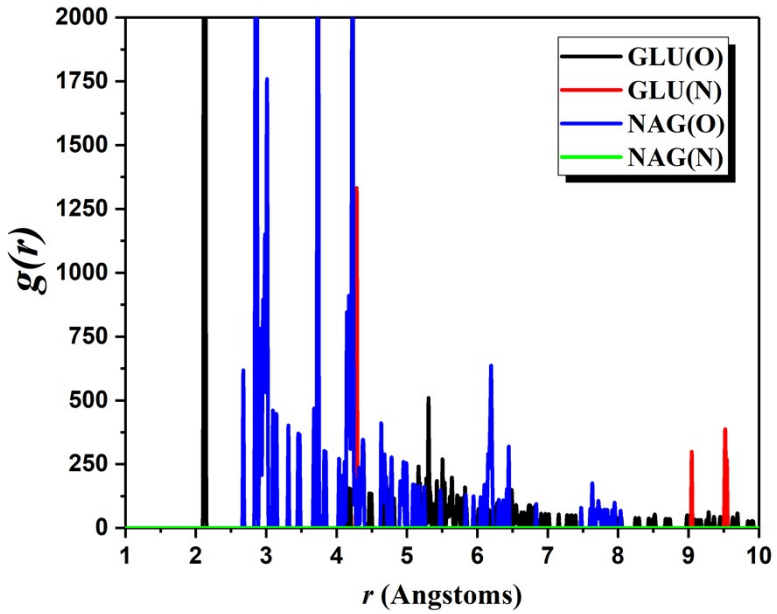

Fig. S2 Pair correlation function g(r) of S protein with ethanol molecules

3. Comparison of inactivation mechanism

For ethanol disinfection, the primary mechanism of pathogen inactivation can be attributed to the denaturation and coagulation of proteins.[3] The proteins of pathogens are bonded with hydroxide radical (-OH) of ethanol molecule via hydrogen bonding, which damages the structural and functional integrity of viral proteins.[4] On the basic of the calculated results, it is found that the interactions between the -OH of ethanol molecules and the O atoms of amino acid residues of 3CL hydrolase and spike proteins belongs to the category of hydrogen bonds and chemical bonds. This is in accordance with the conclusion of Yoo.[4] For sodium hypochlorite disinfection, pathogen inactivation depends on high pH ($^{-}$OH action) and ClO^{-} oxidation, which can lead to the destruction of membrane and denaturation of proteins.[5] Due to the presence of the hydrophobic layer, ionized ClO^{-} is difficult to penetrate the envelope membrane of pathogens. However, the amino acid residues of S glycoprotein, envelope protein, and membrane protein possess highly nucleophilic sites that can react with ClO^{-} or HClO molecules.[6,7] In the case of the 3CL hydrolase-hypochlorite system, the calculated results show that the O atoms of hypochlorite bind to the O atoms of GLU and ASP residues with a strong interaction. For silver ion disinfection, interference with electron transport, interaction with the cell membrane, and binding to the DNA are three possible mechanisms for pathogen inhibition.[8] It is similar to the most of heavy metals, silver also can bind to electron donor groups containing S, O, and N atoms.[9] Additionally, metals may complex with bases or molecules in the order: sulfur-rich bases, nitrogen/oxygen bases, oxygen bases, and coordination to water molecules.[10] In our works, the amino acid residues containing S atoms are not exposed to the surface of 3CL hydrolase and S protein,

thus it is difficult to interact with silver ions. By contrast, the amino acid residues with the unsaturated O atoms, such as GLU and ASP residues, have a strong constraint force with silver ions. This is in agreement with the results of previous studies.[9,10]

4. References

1. C. Peng, Z. D. Zhu, Y. L. Shi, X. Y. Wang, K. J. Mu, Y. Q. Yang, X. B. Zhang, Z. J. Xu and W. L. Zhu, chemrxiv, 2020, DOI: 10.26434/chemrxiv.11877492.v1.
2. J. A. Jaomes, N. M. Andre, J. K. Millet and G. R. Whittaker, biorxiv, 2020, DOI: 10.1101/2020.02.10.942185.
3. G. MacDonnel, 2nded. Washington DC: ASM Press, 2017, 255-69.
4. J. H. Yoo, Infect. Chemother., 2018, 50, 101-109.
5. C. Estrela, C. R. A. Estrela, E. L. Barbin, J. C. Spano, M. A. Marchesan, and J. D. Pecora, Braz. Dent. J., 2002, 13, 113-117.
6. J. M. Albrich, C. A. McCarthy, and J. Hurst, Proc. Natl. Acad. Sci., 1981, 78, 210-214.
7. S. Fukuzaki, Biocontrol Sci., 2006, 11, 147-157.
8. R. C. Tilton, and B. Rosenberg, Appl. Environ. Microbiol., 1978, 35, 1116.
9. N. Grier, Block, S. S., Ed., Lea & Febiger, Philadelphia, 1983, 375.
10. J. M. Wood, Metal ions in biological systems, 1984, 18, 334.