

# Study on Biocompatibility of Natural Conformation and Polymer Biomaterials Based on Molecular Engineering

Mohammadi E<sup>1</sup>, Sharma T<sup>2</sup>

<sup>1</sup>Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands

<sup>2</sup>Department of Medical Nanotechnology, Faculty of Medical Nanotechnologies, University of Medical Sciences, Tehran, Iran

**Keywords:** Molecular engineering; natural conformation; polymeric biomaterials; biocompatibility

**Abstract.** Molecular engineering research is the fundamental way and the only way for the development of biomaterials. Based on molecular engineering, the biocompatibility of natural conformation and polymer biomaterials was studied. In this paper, we discuss that natural conformation is the basis of protein biological function, and that the synergistic action of peptide chain and side group is the motive force for protein to construct natural conformation and complete biological function. On the basis of the influence of the adsorption of polymer biomaterials on the natural conformation of proteins, the relationship between biocompatibility of biomaterials and protein conformation is further explained. Studies have shown that bismuth molecular materials can only be applied in the market and have their functionality if they have good biocompatibility. Therefore, the biocompatibility evaluation of new materials has important practical significance.

## Introduction

Since the 1980s, a new high-tech industry based on polymer biomaterials and their products (Catheters, Devices, Prosthetics, and controlled release drugs) is emerging in developed countries [1]. Polymeric Biomaterials is an important marginal field created by the mutual penetration between polymer science and life sciences. These excellent properties of silicone materials make them widely used in aerospace, light industry, chemical, textile, construction, plastics and rubber, medical and health applications [2]. Good biosafety and biocompatibility are the main evaluation criteria for medical materials to be in good contact with the body without causing rejection and producing toxic components [3]. Polymer biomaterials are the inevitable product of the interpenetration and development of macromolecule science and life science. They are also another powerful weapon for human beings to improve their bodies and functions, with unlimited prospects. The so-called macromolecule biomaterials refer to the macromolecule materials used in the physiological environment [4]. Among them, polysiloxane as silicone material is the most widely studied and applied category [5]. Therefore, the evaluation of biosafety and biocompatibility of biomaterials is an indispensable standard for in vivo application of biomaterials [6]. Therefore, this new medical polymer material preparation technology has unique advantages in future biomedical applications.

Since the 1950s, an important feature of the development of polymer science is that, while its subject is further developed in depth, it has begun to penetrate into other related disciplines and formed many new frontier areas. The so-called macromolecule biomaterials refer to the macromolecule materials used in the physiological environment [7]. In the physiological environment, besides inanimate substances, macromolecule materials are exposed to different levels of living organisms, such as organs, tissues, cells, organelles and biological macromolecules [8]. Polysiloxane grafting or block copolymer has become a hot research topic. It not only has the excellent physical and chemical properties of siloxane, but also compensates for some performance defects [9]. Based on this concept, and taking into account the ultimate role of biomedical materials and the role of the object, combined with the bio-design function of the material, to prepare a biomaterial with good compatibility and functionality, this is the side of our work. Focus. Biocompatibility is the crux of the development and application of biomaterials [10]. In science, polymer biomaterials have become an important material pillar for further development of modern medical engineering, pharmaceutical preparations and bioengineering. Silicone rubber is often used

in the seals, flexible conduits and gaskets of spacecraft due to its excellent cold resistance. Therefore, the application significance in the aerospace industry is very important.

## Natural conformation of molecular engineering

### Research Status of Molecular Natural Conformation

In the past 40 years, with the clarification of the natural conformation of proteins, the research on the relationship between protein conformation and these biological functions has made great progress. Among them, the annual sales value of medical devices and diagnostic products in foreign countries is 24 billion US dollars; and the various pharmaceutical preparations exceeds 80 billion US dollars. Despite the wide variety of silicone polymers, there are few reactions involving their synthesis. Therefore, exploring the development of new reactions and introduction into the design and preparation of silicone polymer materials can greatly enrich the variety of silicone polymer materials. Thereby expanding the application range and application fields of silicone polymer materials and products. The development of medical biomaterials largely determines the development of modern medical science. Therefore, people are committed to the preparation and research of new medical materials, and strive to solve the pain and bring health to humans. However, in terms of breadth and depth, this research can only be said to be just beginning. Polymer biomaterials have become an international research hotspot. All of these methods use precious metal catalysts. The residual precious metal catalysts seriously affect the application of silicone rubber, which limits its application in biology and medicine. With the emergence of various types of materials such as spring dream after rain, metal biomaterials have emerged as alternatives to artificial marrow joints, and medical consumables made of natural macromolecule cellulose, such as kidney dialysis bags.

The number of articles on macromolecule biomaterials in Chemical Abstracts increases sharply every year (Fig. 1), which shows that the importance of such research is being paid attention by scholars.

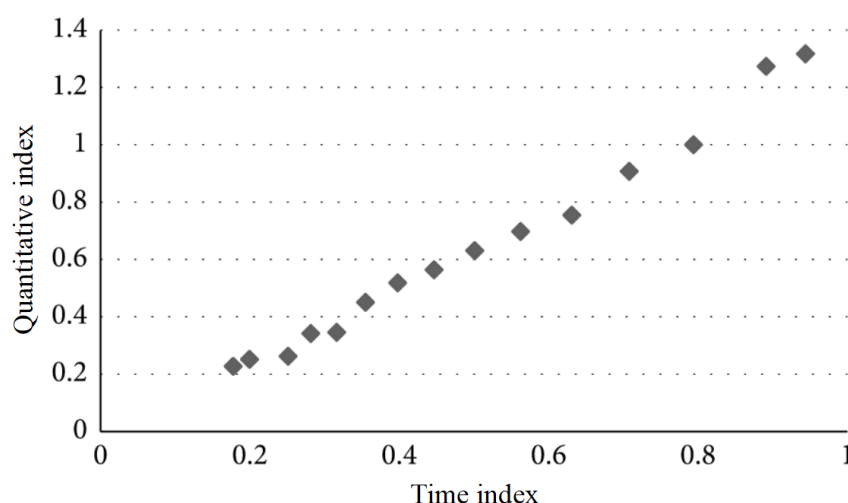


Fig.1. Number of articles on biology of macromolecule materials per year

### Natural conformation is the basis of protein biological function.

The biological functions of proteins are extremely rich and varied. At present, the functions of catalysis, immunity, recognition, transportation, storage, contraction, toxicity, hormone and structure have been recognized. In practice, there are 2700 kinds of medical devices, 2500 kinds of diagnostic products and 39000 kinds of drug preparations related to macromolecule biomaterials. As a result, the degree of freedom of the molecules decreases with the increase of the crosslinking density of silicone rubber, and its flexibility decreases significantly, thus becoming hard. Therefore, it promotes the vigorous development of medical molecule materials, which makes many biomedical polymer materials emerge as the times require. According to the needs of different patients, the personalized biomedical polymer materials suitable for different patients can be quickly and accurately prepared,

and the microstructure of the materials can be precisely controlled at the same time. In order to achieve this functionality better, the field of medical and molecular materials has emerged and developed rapidly. It is precisely because of various demands that the medical seedlings with simple design and stability have become the earliest and most widely used materials in medical materials. At present, the main preparation methods of organosilicon macromolecules are ring-opening polymerization, hydrolysis condensation reaction and addition polymerization. In addition, the clarification of the nature of the interaction between biological materials and living matter and the revealing of the interfacial molecular structure that allows them to be in contact with each other, and to be comfortable and cooperative, is also very important for the development of life sciences.

## **Biocompatible non-biopolymer material**

### **Biocompatible polymer material**

Biocompatible non-biodegradable polymeric materials include polyaryletherketone (PAEK), polyvinyl alcohol, ultra high molecular weight polyethylene, and their composites with nano-hydroxyapatite (HA). Therefore, how to improve anticoagulant has always been the main task and central content of polymer biomaterial research. As a new functional material, silicone elastomer has high temperature resistance, low temperature elasticity, weather resistance, electrical insulation, physical and mechanical properties, chemical resistance, gas permeability and physiological inertness. In order to elevate its inherent regularity from this progress, it began with two different aspects. For lysozyme, its specificity is also attributed to a slit on the surface of its natural conformation that matches the sugar chain of the substrate. A feature of this structure is that the U-structural layer is a scaffold and the outer surface of the scaffold is a side group of amino acid residues. Nevertheless, the authors believe that the anticoagulant properties of biomaterials are determined by the composition and structure of the protein adsorption layer formed on the surface of biomaterials after contact with blood. The composition and structure of the adsorption layer depend on the composition, chemical structure and morphological structure of the material surface. These relationships are not only very complex, but also difficult to achieve unified control. The study shows that the elastic modulus of the polysiloxane elastomer material prepared by the invention is between 30 and 500 kPa. And this gel has good mechanical properties. The relationship between protein adsorption and biocompatibility, and whether the natural conformation of protein molecule changes during the adsorption process on the surface of polymer biomaterials are also known. All these provide favorable conditions for exploring the relationship between molecular structure and biocompatibility on the surface of materials at the molecular level. However, the foundation of molecular engineering research is the establishment of molecular structure model. For anticoagulant materials, the establishment of surface molecular structure model comes from the clarification of the nature of the relationship between surface molecular structure and anticoagulant properties. With the vigorous development of medical materials, many kinds of functional materials emerge in endlessly. While paying attention to their functionality, there are more basic and important evaluation criteria, namely biocompatibility.

Comparing the chromatogram of nursing liquid with that of negative sample without PVP (Fig. 2), it was confirmed that the peak of about 16 minutes was PVP, and the molecular weight distribution of PVP was still wide.

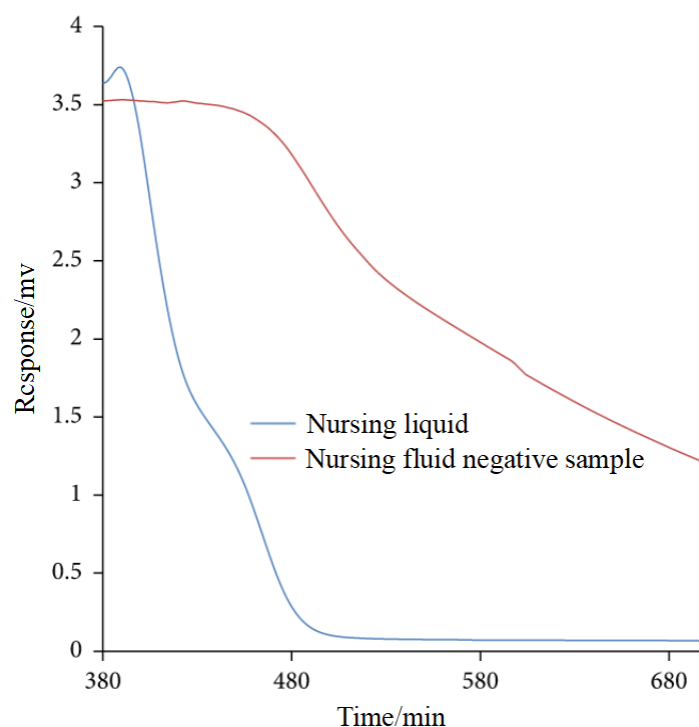


Fig.2. Gel chromatogram of sample of nursing fluid and nursing fluid negative sample in 50mM/L sodium acetate methanol system

### Synthetic polymer biomaterial

Compared with natural polymer medical materials, synthetic polymer medical materials have the advantages of easy large-scale preparation and stable structural properties. As for the high activity of the enzyme, it is generally believed that there are many active centers composed of polar groups which are spatially compatible with the conformation of the reaction transition state. Particularly in the VH and VL domains, active residues which are originally distant in the primary structure can be arranged in a specific spatial arrangement on the surface of the structural layer, functioning as a specific binding to the antigen. Therefore, by further optimizing its composition and structure, four different polyurethane biomaterials (PU) were developed. The results show that polysiloxane containing sulfur atoms in the main chain has been endowed with new properties and applications. The refractive index of polysiloxane materials increases linearly with the number of sulfur atoms in the main chain. Hybrid luminescent materials can be obtained by functionalized polysiloxane. Lanthanides exhibit very narrow green or red emission. Although the materials designed by synthesis have good functional design and easy to control physical and chemical properties, chemical properties are stable. They can be sterilized by high temperature, easy to eliminate pathogens, and reduce the risk of material implantation in vivo. That is to say, the immune function of antibodies comes from the conformational changes of their unique natural conformation and characteristics.

### Conclusion

In summary, the effects of biomaterials on proteins and other living organisms in contact with biomaterials are, in the final analysis, the synergistic effects of peptide chains and side groups and the natural conformations constructed therefrom. As mentioned above, the surface molecular structure model of biomaterials based on the "maintaining normal conformation hypothesis" and "chemical amplification" technology is also of guiding significance. According to the ultimate role of the material, we should use the cells in the corresponding tissue to interact with the material. For example, cells extracted from living animals interact with materials, or human cells are purchased and cultured directly with materials to observe cell status for a period of time. In the selection of raw materials, the factors such as biocompatibility, responsiveness, degradation performance and mechanical properties should be taken into account, and it should also be suitable for large-scale

production. Therefore, how to achieve the biological activity of the individual and the overall effect can be improved after the biomacromolecules and their combination cells are immobilized on the surface. It is essential for the biofunctionalization and biointelligence of polymeric biomaterials. Therefore, designing and building surface molecular structures that can eliminate or mitigate the effects of protein peptide-side group synergy and natural conformation on the surface of biomaterials will be an important direction to improve biocompatibility and bio-functionality of biomaterials.

## References

- 1 Y. Deng, Y. S. Ok, D. Mohan, C. U. Pittman Jr, and X. Dou, Carbamazepine removal from water by carbon dot-modified magnetic carbon nanotubes. *Environmental research*. 169, 434-444 (2019)
- 2 A. Omrani, E. Esmailzadeh, M. Jafari, and A. Behzadmehr, Effects of multi walled carbon nanotubes shape and size on thermal conductivity and viscosity of nanofluids. *Diamond and Related Materials*. 93, 96-104 (2019)
- 3 S. Fiorito, *Carbon nanotubes: angels or demons?*, CRC Press, (2019)
- 4 J. Yoon, and C. Ru, Metamaterial-like vibration of doublewalled carbon nanotubes. *Physica E: Low-dimensional Systems and Nanostructures*. 107, 196-202 (2019)
- 5 R. Abbaslou, and A. Dalai, Google Patents, (2019)
- 6 M. Zheng, in *Single-Walled Carbon Nanotubes*, Springer, (2019), pp. 129-164.
- 7 K. B. Knudsen, T. Berthing, P. Jackson, S. S. Poulsen, A. Mortensen, N. R. Jacobsen, V. Skaug, J. Szarek, K. S. Hougaard, and H. Wolff, Physicochemical predictors of Multi-Walled Carbon Nanotube-induced pulmonary histopathology and toxicity one year after pulmonary deposition of 11 different Multi-Walled Carbon Nanotubes in mice. *Basic & clinical pharmacology & toxicology*. 124, 211-227 (2019)
- 8 E. Fleming, F. Du, E. Ou, L. Dai, and L. Shi, Thermal conductivity of carbon nanotubes grown by catalyst-free chemical vapor deposition in nanopores. *Carbon*. 145, 195-200 (2019)
- 9 R. Zhang, and B. D. Ulery, Synthetic vaccine characterization and design. *Journal of Bionanoscience*. 12, 1-11 (2018)
- 10 A. A. Chaudhari, S. Joshi, K. Vig, R. Sahu, S. Dixit, R. Baganizi, V. A. Dennis, S. R. Singh, and S. Pillai, A three-dimensional human skin model to evaluate the inhibition of *Staphylococcus aureus* by antimicrobial peptide-functionalized silver carbon nanotubes. *Journal of biomaterials applications*. 33, 924-934 (2019)
- 11 R. Fang, K. Chen, L. Yin, Z. Sun, F. Li, and H. M. Cheng, The Regulating Role of Carbon Nanotubes and Graphene in Lithium-Ion and Lithium-Sulfur Batteries. *Advanced Materials*. 31, 1800863 (2019)
- 12 R. Zhang, M. M. Billingsley, and M. J. Mitchell, Biomaterials for vaccine-based cancer immunotherapy. *Journal of Controlled Release*. (2018)
- 13 R. Zhang, J. S. Kramer, J. D. Smith, B. N. Allen, C. N. Leeper, X. Li, L. D. Morton, F. Gallazzi, and B. D. Ulery, Vaccine Adjuvant Incorporation Strategy Dictates Peptide Amphiphile Micelle Immunostimulatory Capacity. *The AAPS journal*. 20, 73 (2018)
- 14 K. A. Whitehead, R. Langer, and D. G. Anderson, Knocking down barriers: advances in siRNA delivery. *Nature reviews Drug discovery*. 8, 129 (2009)



- 15 D. R. Wilson, R. Sen, J. C. Sunshine, D. M. Pardoll, J. J. Green, and Y. J. Kim, Biodegradable STING agonist nanoparticles for enhanced cancer immunotherapy. *Nanomedicine: Nanotechnology, Biology and Medicine*. 14, 237-246 (2018)
- 16 Q. Wu, M. Chen, M. Buchwald, and R. A. Phillips, A simple, rapid method for isolation of high quality genomic DNA from animal tissues. *Nucleic acids research*. 23, 5087 (1995)
- 17 R. Xavier, and D. Podolsky, Unravelling the pathogenesis of inflammatory bowel disease. *Nature*. 448, 427 (2007)
- 18 Z. Yaari, D. Da Silva, A. Zinger, E. Goldman, A. Kajal, R. Tshuva, E. Barak, N. Dahan, D. Hershkowitz, and M. Goldfeder, Theranostic barcoded nanoparticles for personalized cancer medicine. *Nature communications*. 7, 13325 (2016)
- 19 A. J. Mukalel, R. S. Riley, R. Zhang, and M. J. Mitchell, Nanoparticles for Nucleic Acid Delivery: Applications in Cancer Immunotherapy. *Cancer letters*. (2019)
- 20 J. D. Smith, L. N. Cardwell, D. Porciani, J. A. Nguyen, R. Zhang, F. Gallazzi, R. R. Tata, D. H. Burke, M. A. Daniels, and B. D. Ulery, Aptamer-displaying peptide amphiphile micelles as a cell-targeted delivery vehicle of peptide cargoes. *Physical biology*. 15, 065006 (2018)
- 21 T. Ouyang, Y. Q. Ye, C. Y. Wu, K. Xiao, and Z. Q. Liu, Heterostructures Composed of N-Doped Carbon Nanotubes Encapsulating Cobalt and  $\beta$ -Mo<sub>2</sub>C Nanoparticles as Bifunctional Electrodes for Water Splitting. *Angewandte Chemie International Edition*. 58, 4923-4928 (2019)
- 22 Z. Noorimotlagh, S. A. Mirzaee, S. S. Martinez, S. Alavi, M. Ahmadi, and N. Jaafarzadeh, Adsorption of textile dye in activated carbons prepared from DVD and CD wastes modified with multi-wall carbon nanotubes: Equilibrium isotherms, kinetics and thermodynamic study. *Chemical Engineering Research and Design*. 141, 290-301 (2019)
- 23 X. Jia, and F. Wei, in *Single-Walled Carbon Nanotubes*, Springer, (2019), pp. 299-333.
- 24 R. Zhang, J. D. Smith, B. N. Allen, J. S. Kramer, M. Schauflinger, and B. D. Ulery, Peptide Amphiphile Micelle Vaccine Size and Charge Influence the Host Antibody Response. *ACS Biomaterials Science & Engineering*. 4, 2463-2472 (2018)
- 25 R. Akbarzadeh, M. Ghaedi, S. N. Kokhdan, and D. Vashaei, Remarkably improved electrochemical hydrogen storage by multi-walled carbon nanotubes decorated with nanoporous bimetallic Fe–Ag/TiO<sub>2</sub> nanoparticles. *Dalton Transactions*. 48, 898-907 (2019)
- 26 M. L. Yola, and N. Atar, Simultaneous determination of  $\beta$ -agonists on hexagonal boron nitride nanosheets/multi-walled carbon nanotubes nanocomposite modified glassy carbon electrode. *Materials Science and Engineering: C*. 96, 669-676 (2019)
- 27 R. Zhang, C. N. Leeper, X. Wang, T. A. White, and B. D. Ulery, Immunomodulatory vasoactive intestinal peptide amphiphile micelles. *Biomaterials science*. 6, 1717-1722 (2018)
- 28 X. Shen, and D. R. Corey, Chemistry, mechanism and clinical status of antisense oligonucleotides and duplex RNAs. *Nucleic acids research*. 46, 1584-1600 (2017)
- 29 J. Viger-Gravel, A. Schantz, A. C. Pinon, A. J. Rossini, S. Schantz, and L. Emsley, Structure of Lipid Nanoparticles Containing siRNA or mRNA by Dynamic Nuclear Polarization-Enhanced NMR Spectroscopy. *The Journal of Physical Chemistry B*. 122, 2073-2081 (2018)
- 30 L. Warren, P. D. Manos, T. Ahfeldt, Y.-H. Loh, H. Li, F. Lau, W. Ebina, P. K. Mandal, Z. D. Smith, and A. Meissner, Highly efficient reprogramming to pluripotency and directed differentiation of human cells with synthetic modified mRNA. *Cell stem cell*. 7, 618-630 (2010)
- 31 R. Zhang, L. D. Morton, J. D. Smith, F. Gallazzi, T. A. White, and B. D. Ulery, Instructive Design of Triblock Peptide Amphiphiles for Structurally Complex Micelle Fabrication. *ACS Biomaterials Science & Engineering*. (2018)

- 32 C. J. Barnett, C. Evans, J. E. McCormack, C. E. Gowenlock, P. Dunstan, W. Adams, A. Orbaek-White, and A. R. Barron, Experimental measurement of angular and overlap dependence of conduction between carbon nanotubes of identical chirality and diameter. *Nano Letters*. (2019)
- 33 I. Jeon, Y. Matsuo, and S. Maruyama, in *Single-Walled Carbon Nanotubes*, Springer, (2019), pp. 271-298.
- 34 P. Mu, Z. Zhang, W. Bai, J. He, H. Sun, Z. Zhu, W. Liang, and A. Li, Superwetting Monolithic Hollow-Carbon-Nanotubes Aerogels with Hierarchically Nanoporous Structure for Efficient Solar Steam Generation. *Advanced Energy Materials*. 9, 1802158 (2019)
- 35 P. G. Guimaraes, R. Zhang, R. Spektor, M. Tan, A. Chung, M. M. Billingsley, R. El-Mayta, R. S. Riley, L. Wang, J. M. Wilson, and M. J. Mitchell. Ionizable lipid nanoparticles encapsulating barcoded mRNA for accelerated in vivo delivery screening” *Journal of Controlled Release* (2019). 2019 Dec 28;316:404-417
- 36 M. Billingsley, N. Singh, P. Ravikumar, R. Zhang, C. H. June, M. J. Mitchell. “Ionizable lipid nanoparticle mediated mRNA delivery for human CAR T cell engineering” *Nano Letters* (2020). Mar 11;20(3):1578-1589