行政院國家科學委員會補助專題研究計畫成果報告

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※ 生物材料之物理及受力材料之彈性性質 ※
※ Physics of bio-materials and elasticity of materials under tress ※
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計畫編號：NSC　90－2112－M－032－007－(周子聰)

執行期間：90 年 8 月 1 日至 91 年 7 月 31 日

計畫主持人：　周子聰

共同主持人：

本成果報告包括以下應繳交之附件：

□赴國外出差或研習心得報告一份

□赴大陸地區出差或研習心得報告一份

☑出席國際學術會議心得報告及發表之論文各一份

□國際合作研究計畫國外研究報告書一份

執行單位：淡江大學物理系

中　華　民　國　91 年 10 月 15　日

行政院國家科學委員會專題研究計畫成果報告

NSC Project Reports

計畫編號：NSC 90－2112－M－032－007
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主持人：周子聰　　執行機構及單位名稱: 淡江大學物理系
計畫參與人員：林方庭　執行機構及單位名稱: 淡江大學物理系
計畫參與人員：鐘元振　執行機構及單位名稱: 淡江大學物理系

一、中英文摘要

dsDNA(double-stranded DNA)分子的異乎尋常的彈性性質與生物體的遺傳和演化有密切的關係。一個最近提出的模型(H. Zhou *et. al.*, Phys. Rev. Lett. 82, 4560 (1999), 即 ZZO 模型) 提供了從微觀相互作用力的角度解釋 dsDNA 在所有外力和外力矩範圍內的彈性性質的可能性。我們用解析推導的方法論証了 ZZO 模型在適當的參數選擇下可以約化成為一個新近提出的 dsDNA 的非對稱彈性模型。我們還進一步發現了在這些參數下 ZZO 模型有可能得到與實驗符合得更好的結果。我們推導出了上述非對稱彈性模型所對應的一組形態方程, 並將用該方程組分析 dsDNA 在外力矩作用下的非對稱彈性性質, 以及閉合的 dsDNA 微環的構型及其穩定性。我們還研究了 dsDNA 雙鏈局部分離(local denaturation)與其鹼基對的排列順序的相關性。

彈性系數是材料的最重要的物理量之一. 然而在計算機模擬中如何迅速準確地計算非中心力系統的彈性系數是個長期未能解決的問題. 在中心相互作用力系統我們所發展出的"平衡漲落法"的計算彈性系數的方法已經顯示出收斂快以及可在一次運行中求出所有的系數的優點. 我們進一步推導出適用於非中心力系統的"平衡漲落法"公式並準備用以計算非晶態半導體材料如 Ge_xSe_{1-x} 的彈性系數。我們還求得了兩種交互作用勢在零溫下的彈性系數的嚴格解, 並用於分析相應系統的力學穩定性, 得到了與計算機模擬相符合的結果。

關鍵詞： dsDNA 構型， 穩定性, 彈性性質

Abstract

The novel elasticity of double-stranded DNA(dsDNA) has very important biological significance. A recently proposed model (H. Zhou, Y. Zhang, and Z.-C. Ou-Yang, Phys. Rev. Lett. **82**, 4560 (1999)) seems to be hopeful to provide a microscopic model to account for the fascinating elasticity of dsDNA in all range. We found, by an analytical based derivation, that the ZZO model, can be made agree well with a recent proposed asymmetric elastic ribbon model in the regime around the undistorted *B*-form of dsDNA. Such comparison supports both models, provides some criteria to choose proper parameters in ZZO model, and the possibility to improve the ZZO model to explore the elasticity of dsDNA under high tension and torque. We have derived the shape equations for the above mentioned asymmetric elastic ribbon model and will use these equations to investigate the asymmetric elasticity of dsDNA, as well as the conformations and stability of dsDNA microcircle. We have also studied the relationship between the sequence-specific base pairs and the local denaturation of dsDNA.. We found that, with a proper choice of the landscape, the local denaturation usually occurs at the region with an abrupt increasing of the concentration, to about 70%, of *A*T base pairs.

We derived the general fluctuation expressions for both the isothermal and adiabatic elastic constants of systems with arbitrary inter-particle interactions and under arbitrary loading. The

expressions for these two kinds of coefficients are exactly in the same form though in general their magnitudes should be different. We will use these expressions to calculate the elastic constants of semiconductor glass, Ge_xSe_{1-x} and study its floppy to rigidity transition. We have found some exact results for the elastic constants, for the systems with Lennard-Jones and piecewise linear interparticle interactions at zero temperature and under hydrostatic pressure and applied them to study the mechanical stability of both systems. The results provide a convincing evidence for that, of several different kinds "elastic constants", only the stress-strain coefficients can correctly describe the elasticity and act as the mechanical stability criteria for a stressed material. The results from computer simulation support the above exact results.

Keywords: dsDNA conformations, elasticity, stability.

二、緣由與目的

Double-stranded DNA(dsDNA) is a double-helical biopolymer in which two chains of complementary nucleotides wind around a common axis to form a double-helical structure. As the genetic material, dsDNA molecule is of fundamental important in living organisms, and therefore a thorough understanding of dsDNA molecule is a great challenge of our time. Despite definite progress made recently, our knowledge of DNA is still far from complete, especially in theoretical aspect concerning its conformations, deformation, replication, combination and denaturation.

The special structure of dsDNA leads to mainly three kinds of deformations in dsDNA: stretching and bending of the molecule, twisting of one nucleotide chain relative to its counterpart. The recent experiments have revealed that dsDNA has novel elastic property. The relation between force and extension of a dsDNA molecule has clearly four elastic regimes. At first, it requires only a small force (<10 picoNetwon (pN)) to remove thermal bending from the random coil and to extend to its native B-form conformation. It follows a rather rigid and nearly linear regime up to force about of 65 pN. If the external force is increased further, a force plateau appears and the dsDNA chain becomes highly extensible again up to a new conformation, the so called S-form DNA. The contour length of S-DNA is about 1.7 times of the B-form. Beyond about 75 pN, a large increasing force is needed for further extension. Besides external force, it is also possible to apply torsional constraint to dsDNA by external torque and adds more complexions to the elasticity of dsDNA. Experiments showed that if the external force is increased to be larger than a threshold of about 0.3 pN, negatively and positively supercoiled dsDNA molecules behave quite differently. Moreover, Analysis of the images showed that the dsDNA microcircles are markedly puckered with a small excess of negatively writhed molecules. All these deformations have vital biological significance and therefore to understand DNA elastic property theoretically has attracted a lot of attentions recently. Although a uniform elastic rod model, which regards DNA as an inextensible wormlike chain characterized by an effective bending persistence length of about 53 nanometer, is adequate to describe macroscopic mechanical properties of long DNA chains up to moderate external stretching forces, a proper model to account for all aspects of elasticity of dsDNA is still unavailable. We have shown that a model, proposed by Zhou, Zhang, and Ou-Yang (ZZO, Phys. Rev. Lett. **82**, 4560 (1999)), can be reduced into the well accepted wormlike rod chain(WLRC) model in the regime around the undistorted *B*-form. Recently we found further that with proper choice of parameters, the ZZO model can be made agree well with a recent proposed asymmetric elastic ribbon model which can account well the asymmetric elasticity of dsDNA. A deeper view on these two models is therefore a significant subject.

Furthermore, the sequence-specific property of dsDNA affects to a considerable extent many important biological processes involving interactions between DNA and proteins, especially the recognition of specific nucleotide sequences by various regulatory proteins, (for instance, DNA/RNA

polymerases, *lac* repressor, TATA box-bonding protein, p53 protein, etc.) and the subsequent binding of such proteins on these recognized sequences. Especially, during DNA transcription and replication, hydrogen bonds between the complementary DNA bases should be broken and the two nucleotide chains should be separated upon heating or external force—a process known as denaturation. Denaturation will be energetically favored when the energy of deformation relieved by the partial relaxation exceeds the cost of the conformational transition. The localization of denaturation at specific site results from the sequence dependence of the denaturation energy. It has been well known that the binding between *GC* base pairs is in general stronger than that between *AT* base pairs. Consequently, sites of local denaturation tend to be concentrated at *A*T-rich regions within a negatively superhelical domain. Could it possible to find a simple and general criterion based on the concentration of *A*T pair to predict the sites of local denaturation is therefore an intrigue topic.

On the other hand, elastic constants yield valuable dynamical and mechanical information about materials. For example, they yield information concerning the stability and strength of materials. Furthermore, the comparison of experimentally measured and theoretically calculated elastic constants has been widely used as an important means of probing the interatomic forces. Elastic constants were also related to the mechanical stability criteria. For comparison of experimental results with theory, it is necessary not only to have accurate experimental data, but also to have a reliable method of calculation. However, how to calculate elastic constants rapidly and accurately in computer simulation is not yet a well solved problem. In specially, we do not even know the exact results for many well known interparticle potentials at zero temperature and it prevents us from having a complete knowledge on structures of these systems. We have developed a so called "equilibrium fluctuation formulae" to calculate elastic constants for a central force system under arbitrary stress and at any temperature. This method has applied successful into many systems in computer simulation approach and showed the obvious advantages that it converges rapidly for a solid material and can calculate all elastic constants in a single run without performing any deformation. The method can also find exact solutions of elastic constants at zero temperature for a perfect lattice. However, the interatomic force in a real material is in general non-central and so that the corresponding expression for the non-central force should be more useful but such an expression is not yet available. To derive such expressions is therefore a very intrigue topic. The new set of "equilibrium fluctuation formulae" also provides the possibility to derive some exact results using the new formulae for elastic constants for some empirical interparticle potentials at zero temperature but arbitrary loading. These exact results must be very useful since it can provide a standard for some theoretical works and in many materials the elastic constants at the temperature of interest are very close to its zero temperature values. Using these exact results, it will become possible to obtain a throughout understanding of the possible structural transformations for these systems at zero temperature.

三、結果與討論:

1. We derived the general fluctuation expressions for both the isothermal and adiabatic elastic constants of systems with arbitrary inter-particle interactions and under arbitrary loading. The expressions for these two kinds of coefficients are exactly in the same form though in general their magnitudes should be different. We find some exact results for the elastic constants, for the systems with Lennard-Jones and piecewise linear interparticle interactions at zero temperature and under hydrostatic pressure, and applied them to study the mechanical stability of both systems. These results provide a convincing evidence for that, of several different kinds "elastic

constants", only the stress-strain coefficients can correctly describe the elasticity and act as the mechanical stability criteria for a stressed material. The results from computer simulation support the above exact results.

2. We found, by an analytical based derivation, that a new model, proposed by Zhou, Zhang, and Ou-Yang (ZZO, Phys. Rev. Lett. **82**, 4560 (1999)), about the elasticity of dsDNA can be made agree well with a recent proposed asymmetric elastic ribbon model in the regime around the undistorted *B*-form of dsDNA. Such comparison supports both models, provides some criteria to choose proper parameters in ZZO model, and the possibility to improve the ZZO model to account for the elasticity of dsDNA under high tension and torque. We have derived the shape equations for the above mentioned asymmetric elastic ribbon model and will soon use these equations to investigate the asymmetric elasticity of dsDNA, as well as the conformations and stability of dsDNA microcircle. We have also studied the relationship between the sequence-specific base pairs and the local denaturation of dsDNA. We found that, with a proper choice of the landscape, the local denaturation usually occurs at the region with an abrupt increasing of the concentration, to about 70%, of *A*T base pairs.
3. We investigated the abrupt extension of the contour length in the transition from the *B*-form to *S*-form of a dsDNA under a stretching force in the framework of ZZO model. Using a classical mechanical approach, equations governing the structure of the dsDNA under external forces and torques are derived. The transition from the *B*-form to *S*-form can be understood in terms of an effective potential with a barrier separating these two states and resulting in a first-order transition. Detail structural configurations, such as loci of the two strands, relative extension, amount of self-untwisting and the threshold stretching force are calculated. Our results agree reasonably well with the observed experimental data.
4. Biomolecules, such as DNA, are often modeled by the Worm-Like Chain (WLC) model when pulled by an external force. We examine the classical mechanical solution of a WLC arbitrarily grafted at one end while stretching with an external force acting on the other end. Shape equations governing the configurations of the WLC are derived and chain configurations are solved numerically for arbitrary contour lengths and grafting conditions. Analytic results for the case of low force limit as well as near the fully stretched limit and long chain limit are also derived.
5. We study the rigidity of a two dimensional site-diluted central force triangular networks under tension and at zero temperature. We calculate the shear modulus μ and find that the critical behavior of elasticity is sensitive to the stress.

四、計畫成果自評

原計畫在兩年左右的時間在國際期刊發表 6-7 篇論文, 並在第一年內得到 3-4 篇論文。從本報告的第三部份以及第五部份我們可以看到論文數量基本相符並且有超出。

原計畫要用兩年左右的時間研究: 1. 蛋白質摺疊的非格點模型; 2. dsDNA 彈性性質和 dsDNA 微環構型及其穩定性以及 dsDNA 雙鏈分離的序列相關性; 3. 推導出適用於非有心力系統的"平衡漲落法"公式並把其應用以研究一些具體材料在高壓下的機械性質和相變行為以及推導出零溫下一些常見的相互作用勢的彈性系數的嚴格解。

上述第三項內容已經完成並已再 Phys. Rev. B 上發表了一篇論文, 還有一篇相關的論文正在撰寫中並將投往國際期刊。

上述第二項內容已經部分完成。未完成的原因之一是原計畫本身需要兩年時間。另外本人教學任務比預期繁重(每週 10-12 個鐘點加上一年級導師), 且沒有外加的人力支援, 而兩位碩士

班研究生的質量遠不如預期。但更主要原因在於在上一個計畫里(“Physics of soft matter and related topics in elasticity”, NSC89－2112－M－032－032), 有關 dsDNA 分子異乎尋常的彈性性質還有相當多可進一步深化研究的課題, 因此本人把大部分時間和精力都投到這些課題, 並有相當的進展。從已完成的工作量而言,這一部分實際上是比預期的多, 其質量亦不比預期的差。

上述第一項內容還在準備階段。進展有限的主要原因在於缺乏足夠的精於計算機模擬的人力。

總而言之, 本計畫的研究成果的數量和質量符合預期並略有超過。但由於難於預期的原因, 研究方向與原計畫略有偏差。另外, 如果能得到足夠的人力支援, 例如有 1-2 位博士後研究人員, 本計畫的後續工作將可望得到相當豐富的產出。

五、參考文獻: 90 年 8 月 1 日至 91 年 7 月 31 日期間著述:

I. 已發表的期刊論文:

1. **Zicong Zhou(周子聰)** and Béla Joós
   “Fluctuation formulae for the elastic constants of an arbitrary system”, Phys. Rev. B. **66**, 054101-1--054101-7(2002).
2. Pik-Yin Lai and **Zi-cong Zhou**
   “Worm-Like Chain under an External Force: A Classical Mechanical Approach”, Chinese Journal of Physics **39**, 641(2001)

II. 國際研討會論文:

1. **Z. Zhou(周子聰)** and B. Joós
   “Elastic constants and mechanical stability for the systems under loading”**,** International Conference on Theoretical Physics, Paris, UNESCO, 22-27 July 2002
2. **Z. Zhou(周子聰)** and Pik-Yin Lai
   “On the consistency of elastic models for double-stranded DNA”, StatPhys-Taiwan-2002, 26 May -1 June, 2002, Institute of Physics, Academia Sinica, Taipei
3. Pik-Yin Lai and **Z. Zhou(周子聰)**
   “B-form to *S*-form Transition in a Double-stranded DNA under a stretching force”
   The 4th International Conference on Biological Physics (ICBP2001), July 30- August 3, 2001, Kyoto, Japan
4. **Z. Zhou(周子聰)**
   “Elastic Constants and Mechanical Stability”, The 3rd International Symposium on Electronic and Atomic Structures, Dec. 13-14, 2001, Tamkang University, Tamsui, Taiwan(*invited talk*).

III. 國內研討會論文:

1. **Zicong Zhou(周子聰)**
   “Fluctuation formulae for the elastic constants of an arbitrary system”, 2002 中華民國物理學會年匯暨研究成果發表會, 2002 年二月四日至六日, 台中市東海大學物理學系
2. **Zicong Zhou(周子聰)** and Fang-ting Lin (林方庭)
   “Elasticity and Stability of the System with a Piecewise Linear Interparticle Interaction”, 2002 中華民國物理學會年匯暨研究成果發表會, 2002 年二月四日至六日,台中市東海大學物理學系
3. Pik-Yin Lai(黎璧賢) and **Zicong Zhou(周子聰)**
   “B-form to S-form Transition in a Double-stranded DNA”, 2002 中華民國物理學會年匯暨研究成果發表會, 2002 年二月四日至六日,台中市東海大學物理學系(*invited talk*)
4. **Zicong Zhou(周子聰)**, Béla Joós and Pik-Yin Lai
   "Elasticity of a stressed diluted network", 2001 軟凝態物理研討會, 2001 年 11 月 17 日至 18 日,宜蘭明池山莊

IV. 已投期刊的論文:

1. Pik-Yin Lai and **Z. Zhou**
   "B-form to *S*-form Transition in a Double-stranded DNA", *submitted to* Europhys. B.

V. 正在撰寫中的論文:

1**..** **Zicong Zhou**(**周子聰**), Béla Joós and Pik-Yin Lai
   "Elasticity of a stressed diluted network", *will be submitted to* Phys. Rev. Lett.
2. **Zicong Zhou**(**周子聰**) and Fang-ting Lin (林方庭)
   "Elasticity and stability of two two-dimensional systems"