对称性是生命科学中一个非常基本的自然现象，对称性破缺被认为是新的生命产生和生命进化的驱动力。近年来的研究表明，DNA中CpG的含量及分布都具有非常明显的特异性。我们在前期的研究工作中也发现，CpG密度与其甲基化水平在总体上有着非常明显的互补特性，而在一些功能性区域（例如启动子区域），这些互补特性又会发生缺失。目前这些与CpG及甲基化状态相关的对称性与对称性破缺现象的发生机理尚不清楚。在本项目中，我们拟采用分子动力学方法，从原子尺度上研究这些对称性与对称性破缺现象发生的机理。我们将在Bs-seq测序大数据分析的基础上获取到的大量CpG及其甲基化状态数据，建立描述其对称性及对称性破缺状态的数学模型。基于该数学模型，产生能描述各种对称性及对称性破缺状态的特征DNA序列。随后，我们将使用分子动力学模拟的方法获取这些特征DNA序列的能量图谱并从能量变化的角度解释对称性与对称性破缺发生的分子机理。

Symmetry is a nature phenomenon of life science and symmetry breaking is thought to be the driven force of new life form generation and life evolution. Recent studies revealed that CpG density and distribution has very obvious specificity. In our previous work, we also found that CpG density and the corresponding methylation level are complementary. In some functional regions such as promoter regions, this kind of complementary disappears. The mechanism of how these kind of symmetry and symmetry breaking happens is still unknown. In this study, we will utilize molecular dynamics method to study the mechanism on atomic level. First, we will analyze Bs-seq sequencing data using bioinformatics method and build mathematical model to describe asymmetry levels. Base on this model, representative DNA sequences will be generated. Then structural models of these DNA sequences will be build and molecular dynamics simulations will be performed. The energy profiles will be used to study the symmetry breaking mechanism.

[DNA中CpG分布及其甲基化对称性与对称性破缺的分子动力学研究](https://isisn.nsfc.gov.cn/egrantweb/main?datetimestamp=1457571375897###)

对称性破缺是生命进化的重要驱动力。随着物种的进化，CpG的含量和分布都有明显的向不均匀性方向变化的趋势，其甲基化水平也出现关联性变化。目前这些变化的原因尚不清楚。我们的前期工作发现，这些变化可能由微观上DNA分子结构的对称性破缺所引起。分子动力学是DNA分子结构研究的重要手段，申请人在这方面有非常丰富的经验（Appl. Surf. Sci.，2014; J. Appl. Phys.，2014）。 在本项目中，我们拟采用分子动力学方法，从原子尺度上研究进化中CpG及其甲基化状态变化的对称性破缺机理。首先，我们将在Bs-seq测序大数据分析的基础上，建立描述对称性状态的数学模型。 基于该数学模型产生不同对称性状态下的特征DNA序列及分子结构模型。随后，我们将使用分子动力学获取对称性状态与能量变化的关系，深入分析对称性破缺发生的机理。这些机理对理解由甲基化异常所引起的各种疾病有重要的理论意义。

Symmetry breaking is an important driving force of life evolution. CpG content and distribution have obvious evolutional tendency towards inhomogeneous direction. The methylation level also changes accordingly. The reasons why these changes happen are still unclear. Our preliminary work shows that these changes may be caused by the symmetry breaking of DNA molecular structure in microcosm. Molecular dynamics is an important method in DNA structure study and the applicant has a lot of research experience in this field (Appl. Surf. Sci.，2014; J. Appl. Phys.，2014). In this project we will use molecular dynamics method to study the symmetry breaking mechanism of the evolution of CpG contents and its methylation state at the atomic scale. First, we will build the mathematical model to describe the asymmetry states of CpGs and its methylation based on bioinformatics analyze of Bs-seq sequencing data. This model will be used to generate representative DNA sequences and the corresponding molecular structures. Then, we will use molecular dynamics method to obtain the relationship between the asymmetry levels and the energy states, from which the mechanism of symmetry breaking will be revealed. The success of this project will help us to understand the inducements of various diseases caused by methylation aberrance theoretically.