de Rham-Hodge theory modeling and analysis of macromolecules

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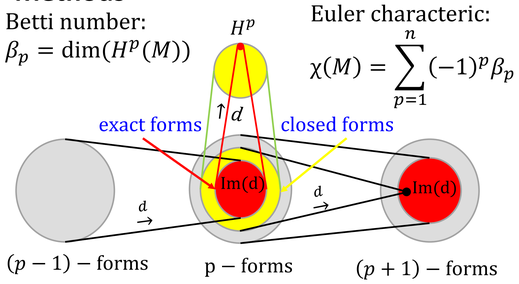
Introduction

The de Rham-Hodge theory is a landmark of 20th Century's mathematics that interconnects differential geometry, algebraic topology, and partial differential equation. It provides a solid mathematical foundation to electromagnetic theory, quantum field theory and many other important physics. However, this important mathematical tool has never been applied to macromolecular modeling and analysis, to the best of our knowledge. This work introduces the de Rham-Hodge theory as a unified paradigm to analyze the geometry, topology, flexibility and natural modes of biological macromolecules.

Methods

Betti number: $\beta_p = \dim(H^p(M))$

Euler characteric: $\chi(M) = \sum_{p=1}^{n} (-1)^p \beta_p$



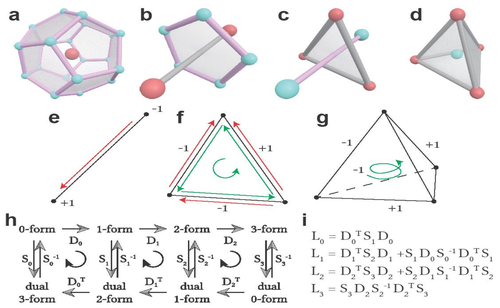


Illustration of *discrete exterior calculus*. **a-d** show the primal and dual elements of the tetrahedral mesh. **e-g** Illustrate orientation. Pre-assigned orientation is colored in red. Induced orientation by δ is colored in green. The vertices are assumed to have positive pre-assigned orientation. **h** describes de Rham's cochain complexes and Hodge duals. **i** depicts the assembly of four types of Laplace-de Rham operators.

Results

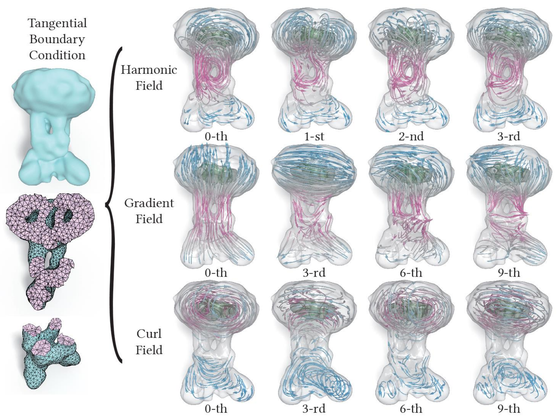


Illustration of tangential spectra of a cryo-EM map EMD 7972. Topologically, EMD 7972 has 6 handles and 2 cavities. The left column is the original shape and its anatomy showing the topological complexity. On the right hand side of the parenthesis, the first row shows tangential harmonic eigen fields, the second row shows tangential gradient eigen fields, and the third row shows tangential curl eigen fields.

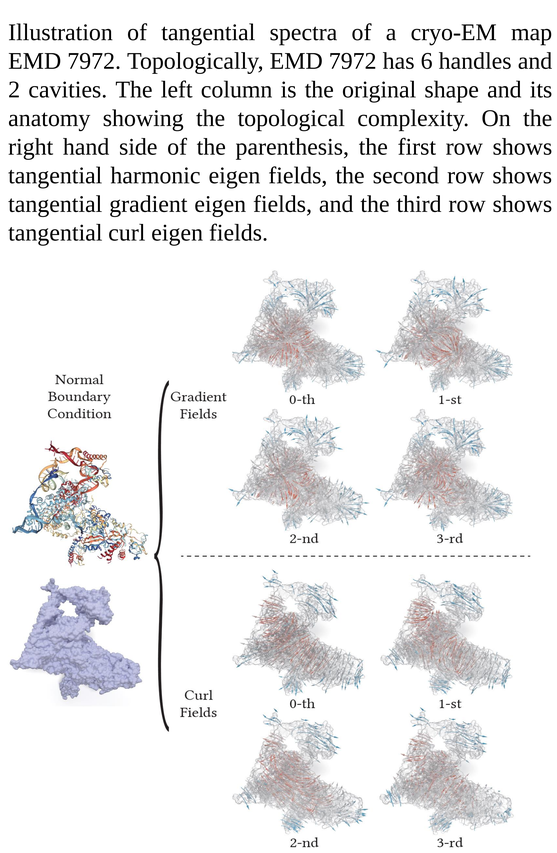
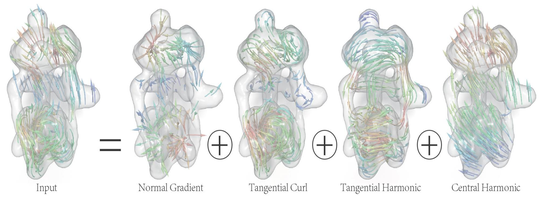


Illustration of the normal spectra for protein-DNA complex 6D6V.



Hodge decomposition of a synthetic vector field in EMD 1590.

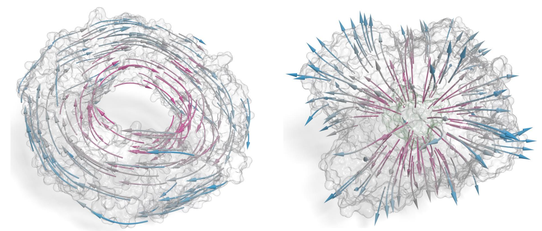
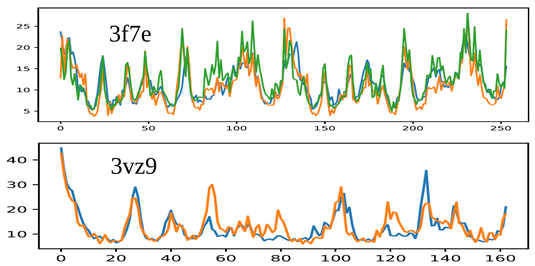


Illustration of de Rham-Hodge topological analysis. **Left:** Eigen field of the null space of the tangential Laplace-de Rham operator for a handle. **Right:** Eigen field of the null space of the normal Laplace-de Rham operator for protein pocket.

Hodge Laplacian B factor:

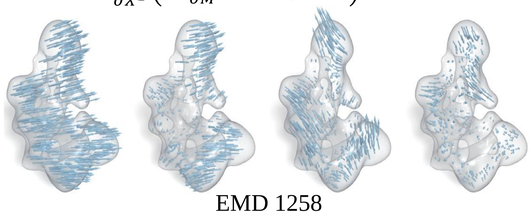
$$B_{k,i}^{dRH} = a \sum_j \frac{1}{\lambda_j^k} \left[\omega_j^k(\boldsymbol{r}) \left(\omega_j^k(\boldsymbol{r}') \right)^T \right]_{\boldsymbol{r}=\boldsymbol{r}_i, \boldsymbol{r}'=\boldsymbol{r}_i}$$



Laplace-de Rham-Helfrich operator:

$$E_\mu = d_0 \star_0^{-1} d_0^T \star_1 + \star_1^{-1} d_1^T \star_2 d_1 + G^T Q G$$

where $Q = \frac{\partial^2}{\partial x^2}\left(\mu \int_{\partial M} (H - H_0)^2 dA\right)$



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Conclusions

Biomolecules have intricate structures that underpin their biological functions. Understanding their structure-function relationships remains a challenge due to their structural complexity and functional variability. Although de Rham-Hodge theory has had great success in mathematics and physics, it has not been applied for macromolecular systems. In this work, we introduce de Rham-Hodge theory as a unified paradigm for analyzing the geometry, topology, flexibility, and natural mode of macromolecules. Geometric characteristics and topological invariants are obtained either from the Helmholtz-Hodge decomposition of the scalar, vector and/or tensor fields of macromolecules or from the spectral analysis of various Laplace-de Rham operators. We propose a Laplace-de Rham spectral based model for predicting macromolecular flexibility. We construct a Laplace-de Rham-Helfrich operator for revealing cryo-EM natural modes of macromolecule. Extensive experiments are carried out to demonstrate that the proposed de Rham-Hodge theory paradigm is one of the most versatile tools for the multiscale modeling and analysis of biological macromolecules. Accurate, reliable and topological structure-preserving algorithms for discrete exterior calculus (DEC) have been developed to facilitate the aforementioned modeling and analysis of macromolecules.

Acknowledgements

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Reference

1. Rundong Zhao, Menglun Wang, Yiying Tong and Guo-Wei Wei, A unified paradigm for analyzing geometry, topology, flexibility and natural mode of macromolecules. 2019.

2. M. Desbrun, E. Kanso, Y. Tong, Discrete differential forms for computational modeling, Discrete differential geometry, 287-324, 2008.

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