Design and development of digital phantoms to provide guidance for simulations of electrophysiological activity in tissue

Aseem Milind Pradhan, Richard Gray, Abouzar Kaboudian,
Division of Biomedical Physics (DBP),
Office of Science and Engineering Laboratories (OSEL),
Center for Devices and Radiological Health (CDRH).

Abstract

Introduction: Cardiovascular disease remains a leading cause of mortality in the United States. A significant proportion of these deaths stem from hemodynamic collapse caused by disruptions in normal cardiac electrical activity. Numerical simulations of cardiac electrophysiology play an increasingly pivotal role in the context of advancing patient-specific interventions, digital twin technologies, and conducting in-silico clinical trials. Given the computational cost associated with such simulations, the digital models are optimized by employing coarser grids for anatomical tissue representation.

In this study, we aim to establish the minimum spatial resolution necessary for numerical simulations to replicate critical electrophysiological wave dynamics in anatomically realistic tissue models, ensuring both the desired fidelity and computational efficiency.

Methods: We modeled a series of digital phantom structures, including simple rings, and helices of constant and diminishing radii, characterized by a range of thicknesses and spatial resolutions to mimic thinner cardiac tissue components such as pectinate muscles. We conducted simulations of excitation waves within these phantom structures by utilizing the Minimal Atrial/Ventricular, Tusscher-Panfilov, and O'Hara-Virág-Varró-Rudy cellular models. The behavior of the waves in these structures were compared against benchmarks to assess the accuracy of the simulations in replicating key electrophysiological parameters such as wave propagation velocity.

Results: Our findings showed that structures modeled with higher resolution captured the wave propagation velocity more accurately compared to lower resolution structures. Additionally, we obtained more accurate wave propagation results with thicker structures and reduced the error substantially after adding contribution from cross-diagonal terms for thinner structures.

Impact: Digital phantoms provide an effective means to evaluate the accuracy of computational models in thin structures which is essential to ensure efficacy and safety of numerical methods.

Introduction

Cardiac arrhythmias are caused due to disturbances in normal cardiac electrophysiological activity. These health conditions can be life-threatening or reduce quality of life and, therefore, need medical attention. Approximately 5 million Americans are affected by atrial fibrillation (type of arrhythmia).

Thin cardiac structures such as pectinate muscles in the atrium (**Fig. 1**) affect cardiac electrophysiological activity. [Wu et al., 1998, Circulation Research]. Therefore, it is necessary to consider the contribution of these structures while studying cardiac arrhythmias.

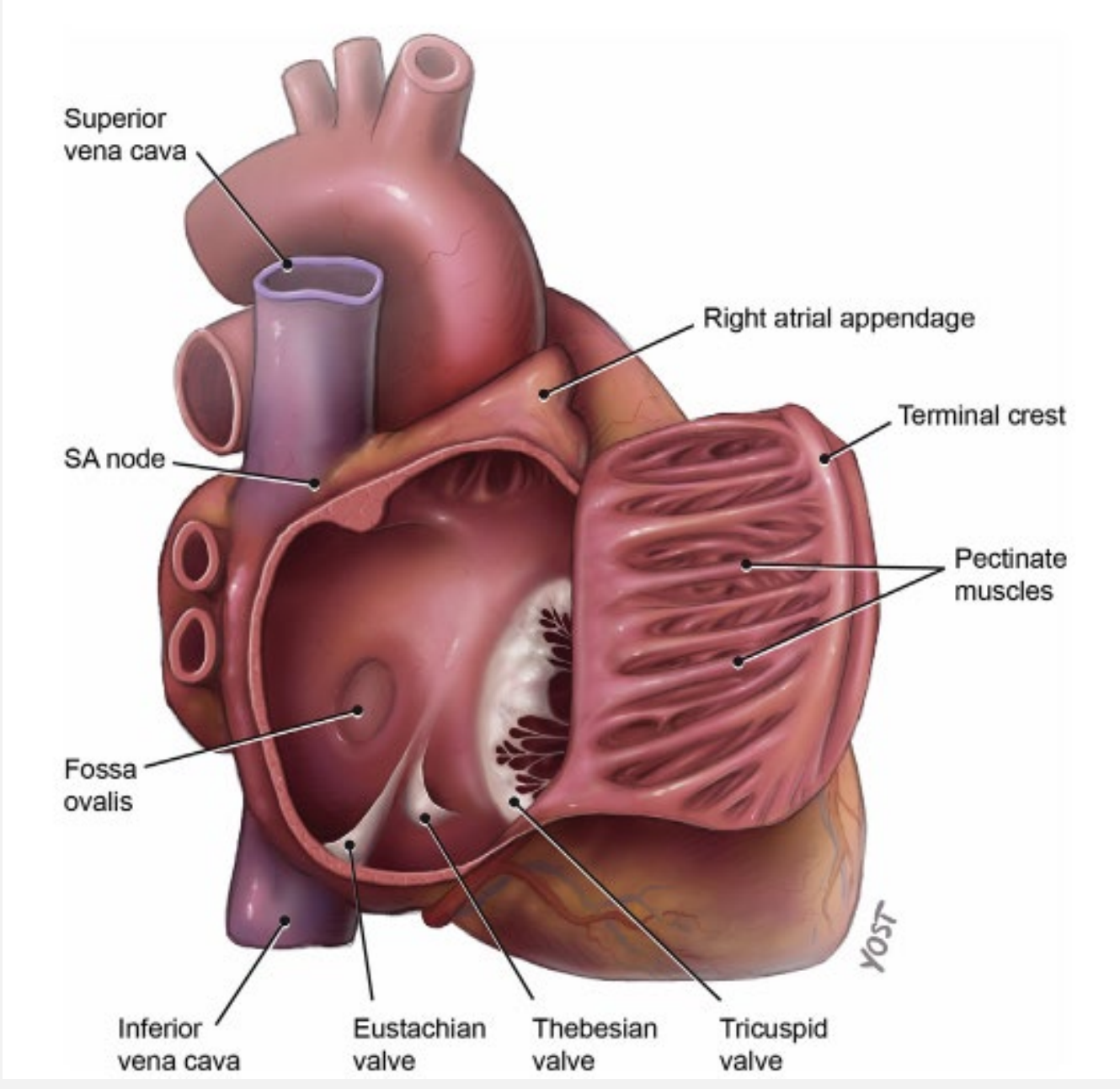


Figure 1. Cardiac structure with the pectinate muscles (thin structures) highlighted.

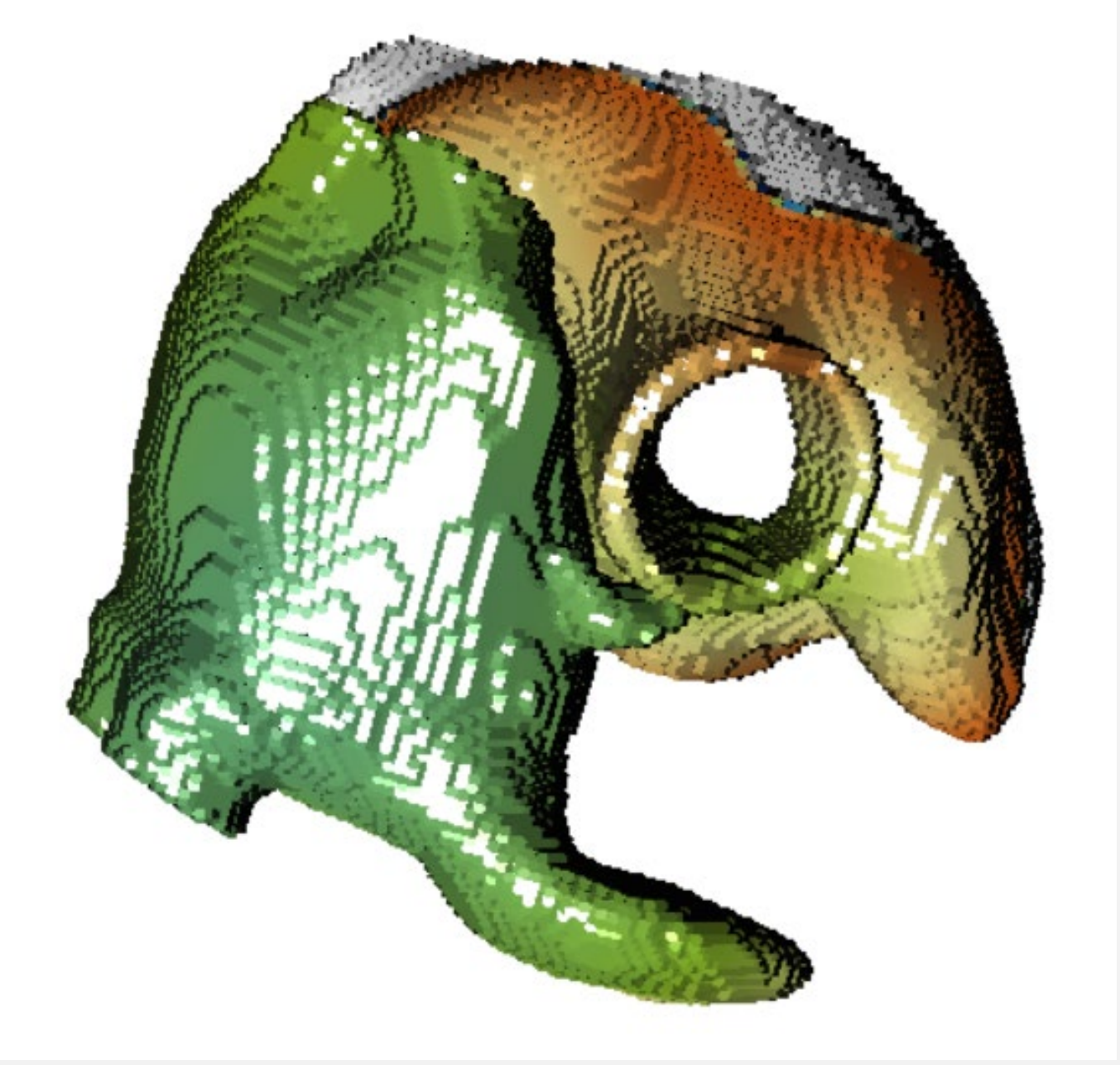


Figure 2. Voltage distribution obtained using a computational simulation of the atrial chambers.

Computational simulations of cardiac electrophysiology are increasingly being used for understanding the relation between cardiac structure and the resultant electrophysiology. However, these simulations are computationally expensive. Therefore, coarser meshes and larger timesteps are employed which could compromise accuracy.

Research Question: What is the minimum spatial resolution that is necessary for capturing the electrophysiology accurately?

Materials and methods

A] Computational Setup:

- **Primary Equation to solve:**
  Cable Equation (Passive electric current through tissue)

$$\frac{\partial V}{\partial t} = \vec{\nabla} \cdot \left(D\overrightarrow{\nabla V}\right) + \frac{I_{sum}}{C_m}$$

$V = membrane\ potential$
$D = diffusion\ tensor$
$I_{sum} = sum\ of\ ionic\ currents$
$C_m = membrane\ conductivity$

- Other equations to solve:
  Time- and Voltage-Dependent Gating Variables.

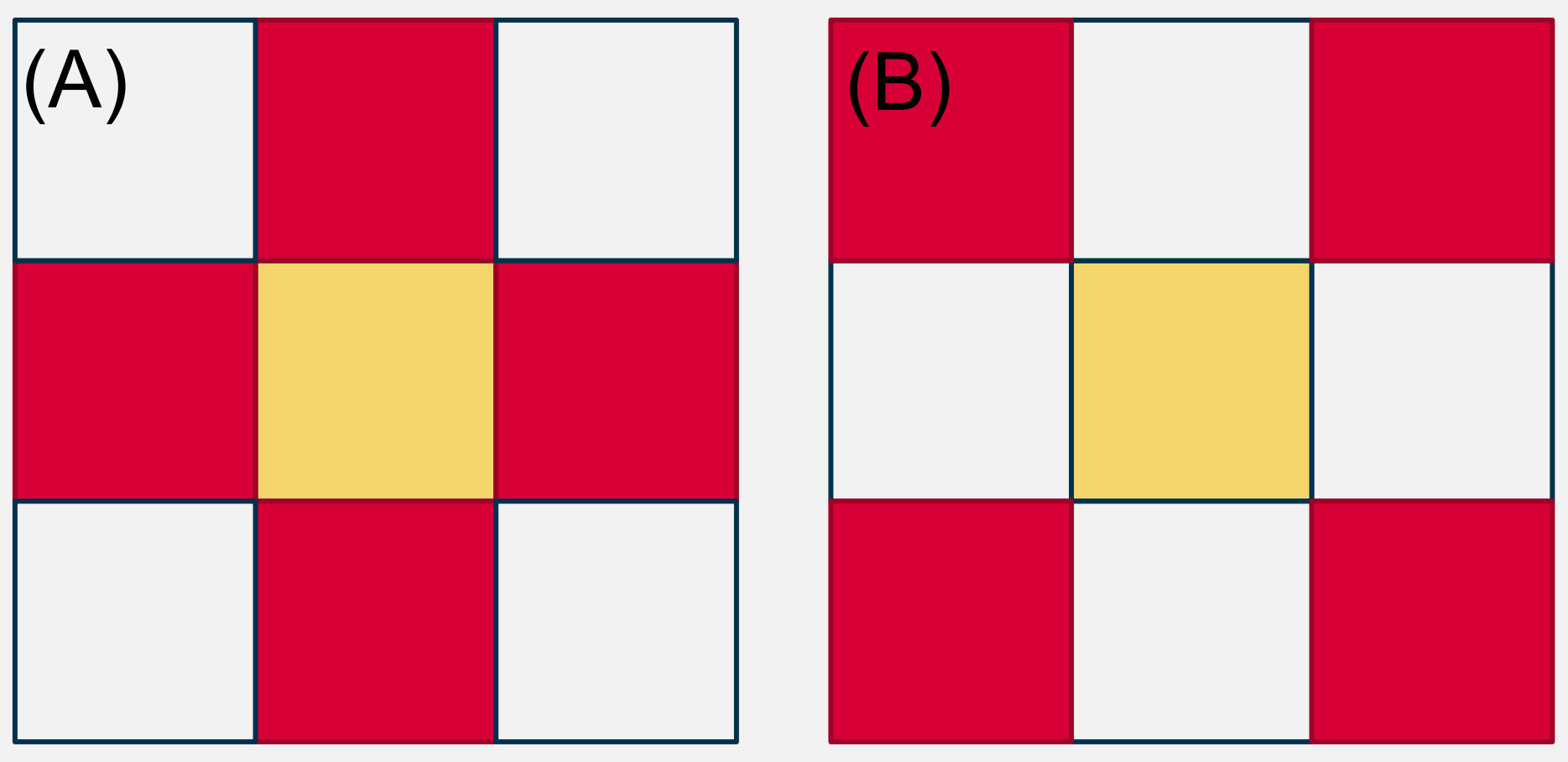


Figure 3. Finite Difference Scheme details: Central element (light yellow) and the neighbors considered (in dark red) for the (A) without and (B) with cross-diagonal terms.

Materials and methods

B] Digital Phantoms:

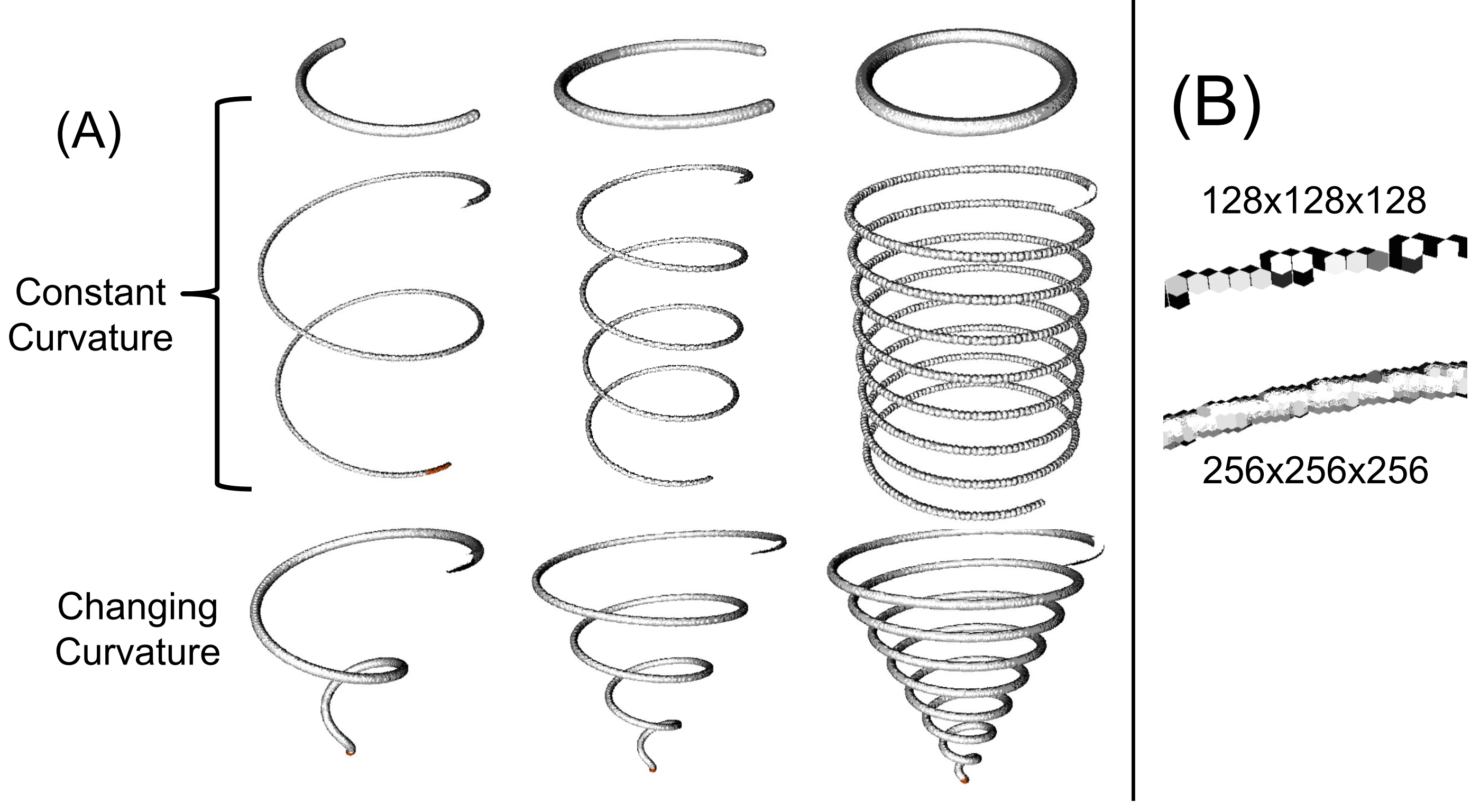
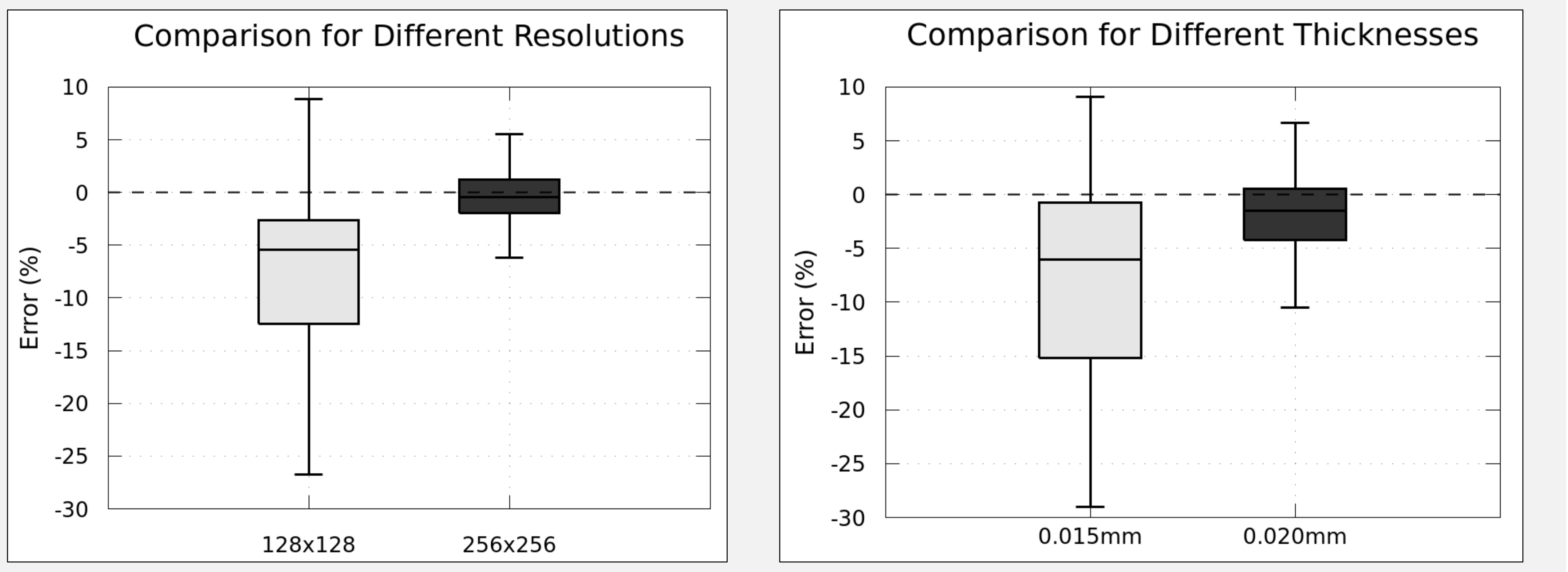
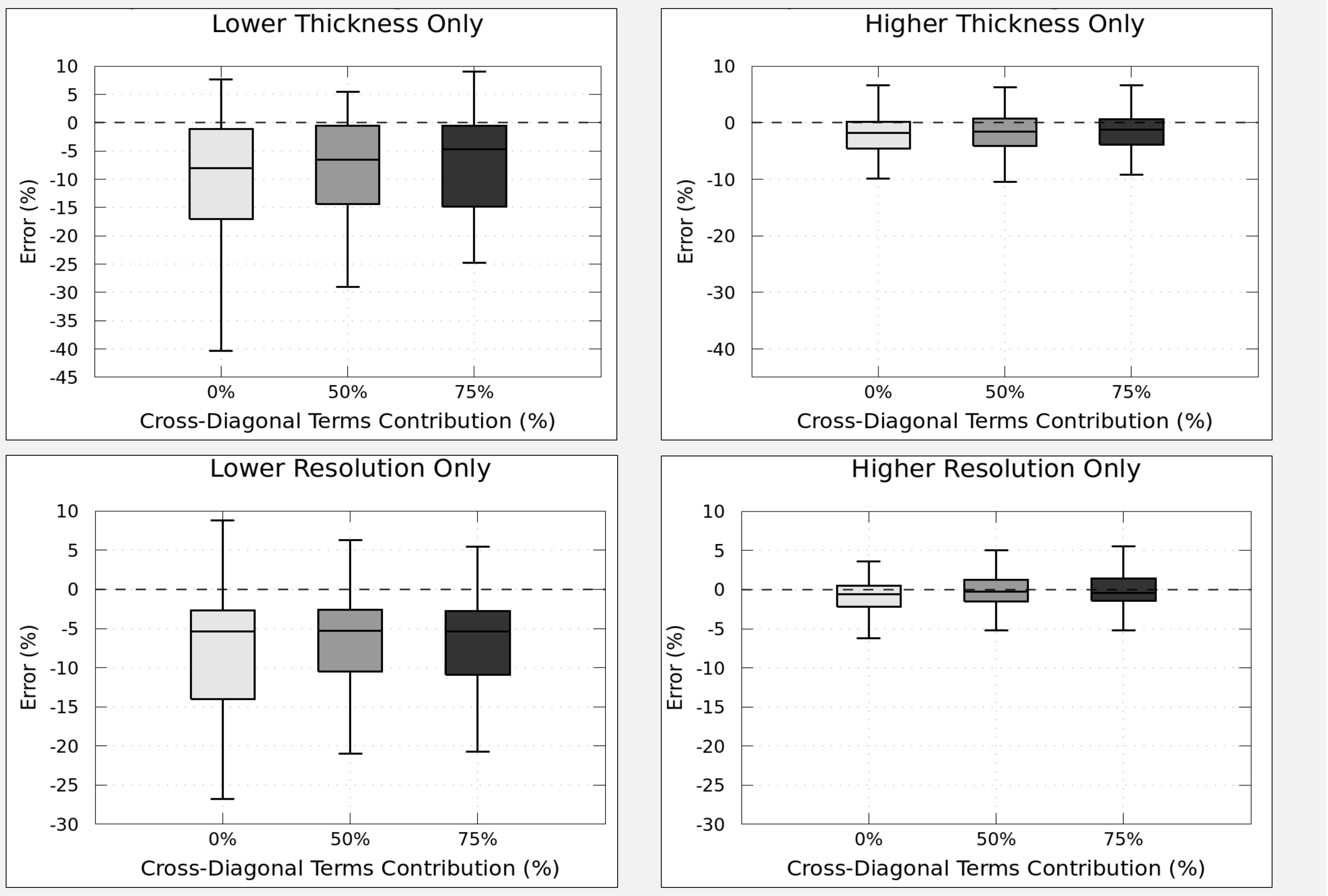


Figure 4. (A) Examples of Digital Phantoms – simple rings, helices with constant and varying radii. (B) Zoomed view of a thin structure for different resolutions.

Results and discussion



Using the Minimal Model, the wave speeds were captured more accurately for structures modeled using higher resolution and for structures with higher thickness.



The wave speed errors reduced substantially after adding the contribution of the Cross-Diagonal terms for lower thickness and lower resolution.

Conclusions

- Accurate wave speed propagation in thin tissue structures was obtained by using higher resolution grids or by adding the contribution of the cross-diagonal terms.
- The cross-diagonal terms are most effective in increasing accuracy of wave propagation dynamics when dealing with thin structures in lower resolution grids. In thicker structures, the most effective way of increasing accuracy is through increasing the resolution of the grid.
- Initial analysis of the effect of curvature indicated the accuracy of the finite difference schemes reduces the more tightly the structures are coiled.

Disclaimer

Acknowledgements

This project was supported in part by an appointment to the Research Participation Program at the Center for Devices and Radiological Health, U.S. Food and Drug Administration, administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the U.S. Department of Energy and FDA.