



BIOLOGICAL EVALUATION OF BIS(INDOLYL)METHANE (BIM) DERIVATIVES AS BCL-2 INHIBITOR IN HL-60 CELLS



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INTRODUCTION

Indole has shown remarkable anticancer activities which resulted to exploration of compounds containing indole unit. 11 BIMs were synthesized and their antiproliferative activity against HL-60 cell were evaluated. Compounds **4** and **7** (Figure 2) possess best potency of inhibition activity at concentration of 50 μM with IC_{50} values of 21.26 and 41.06 μM , respectively. UV-vis titration with ctDNA indicated the anticancer properties of BIM with the binding constant value (K_b) for **4** and **7** are $6.02 \times 10^4 \text{ M}^{-1}$ and $1.04 \times 10^4 \text{ M}^{-1}$ correspondingly.

RESULTS

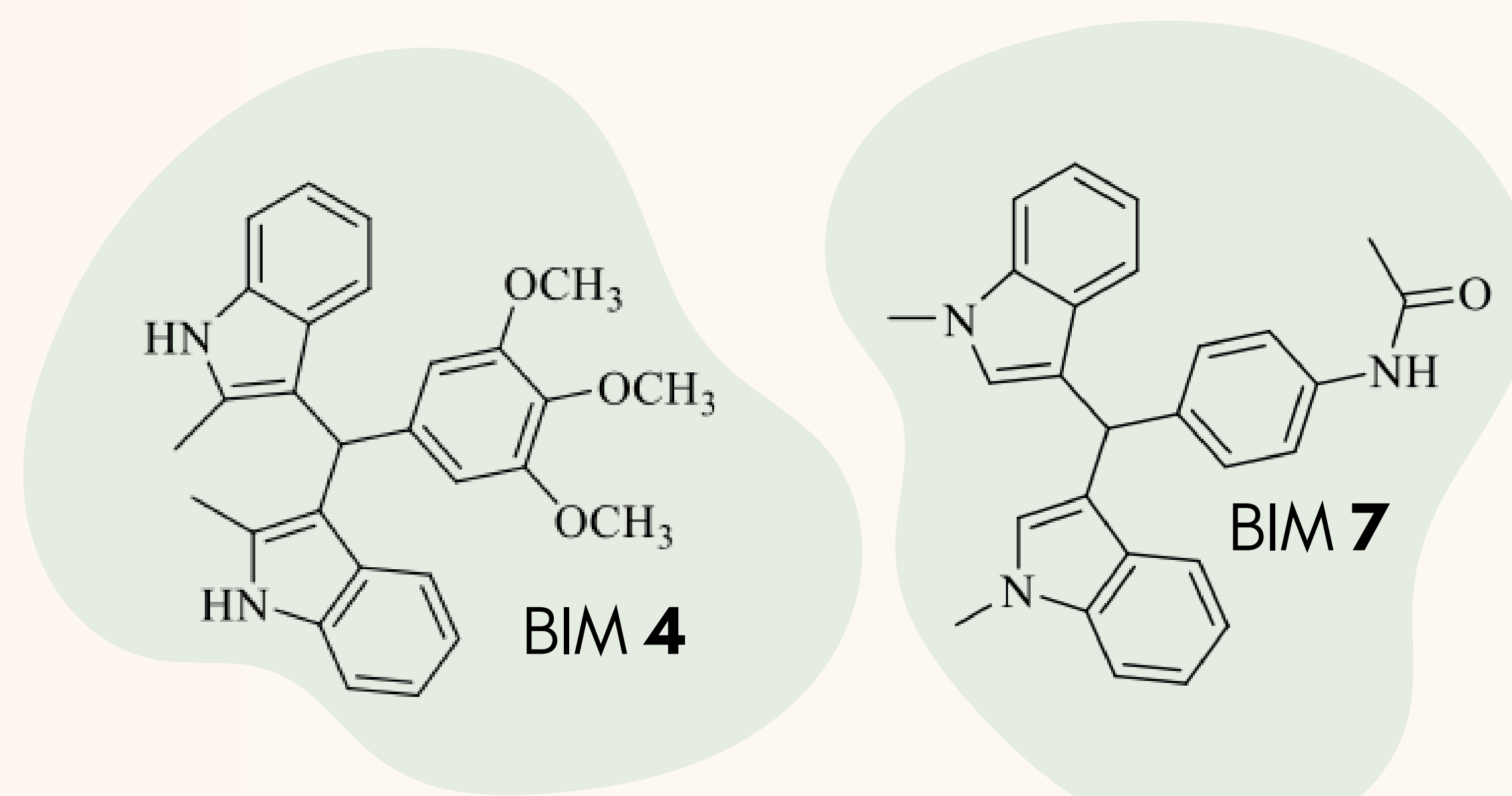


Figure 2. Synthesised BIM **4** and **7**

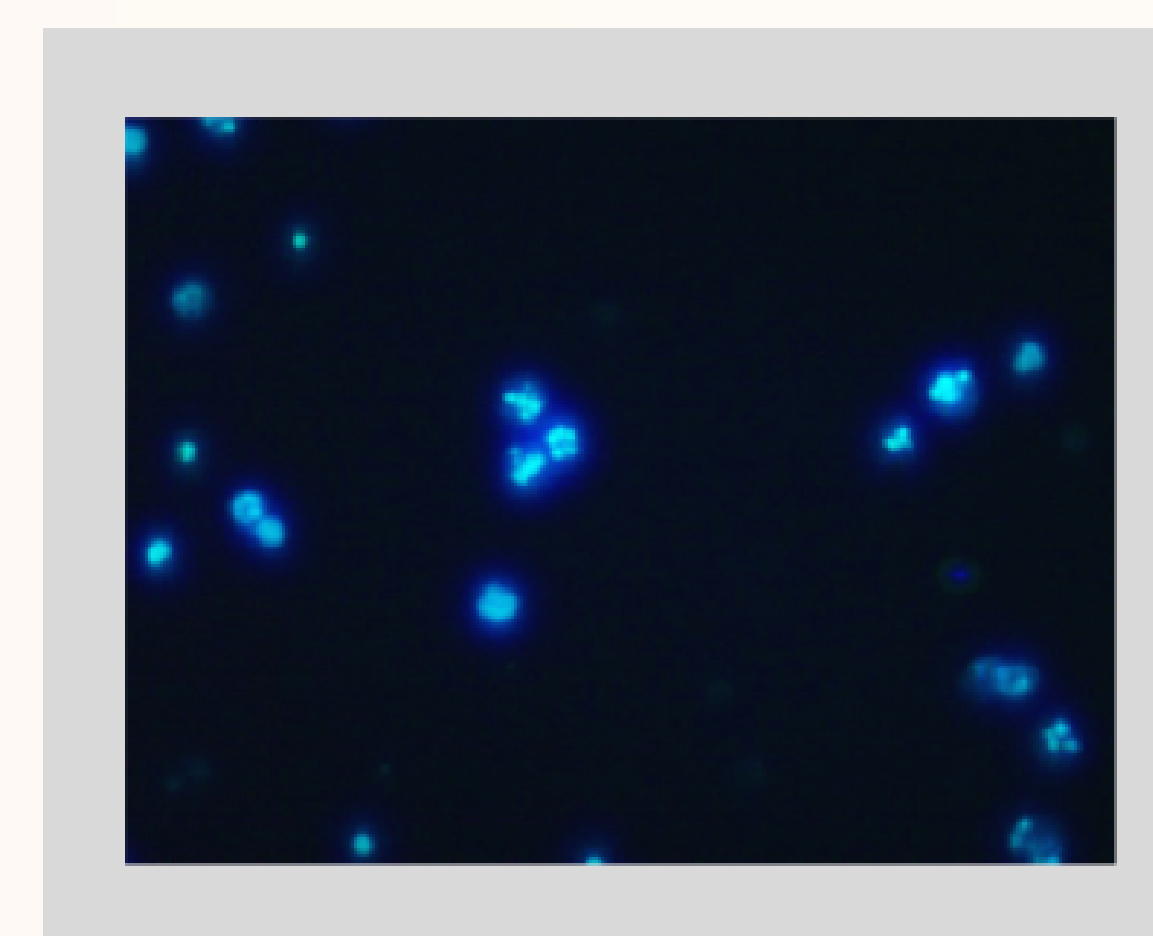


Figure 3. BIM **4** induced cell apoptosis in HL-60 cell

CONCLUSION

ligands **4** and **7** exhibited good cytotoxicity activity. These bis-indolylmethanes possessed antiproliferative potential that can be scrutinized for future developments.

METHODOLOGY

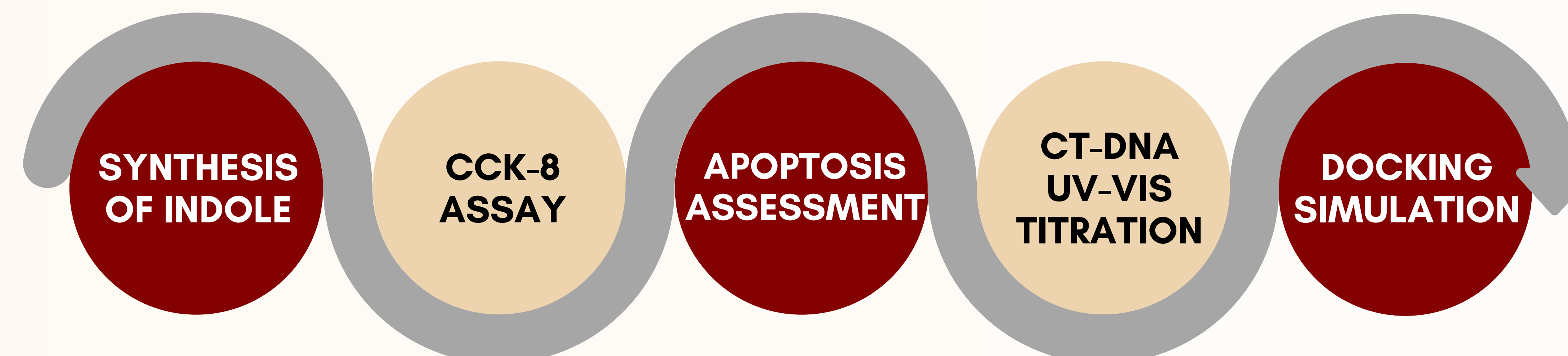


Figure 1. Methods involve in evaluation of BIM as Bcl-2 inhibitor

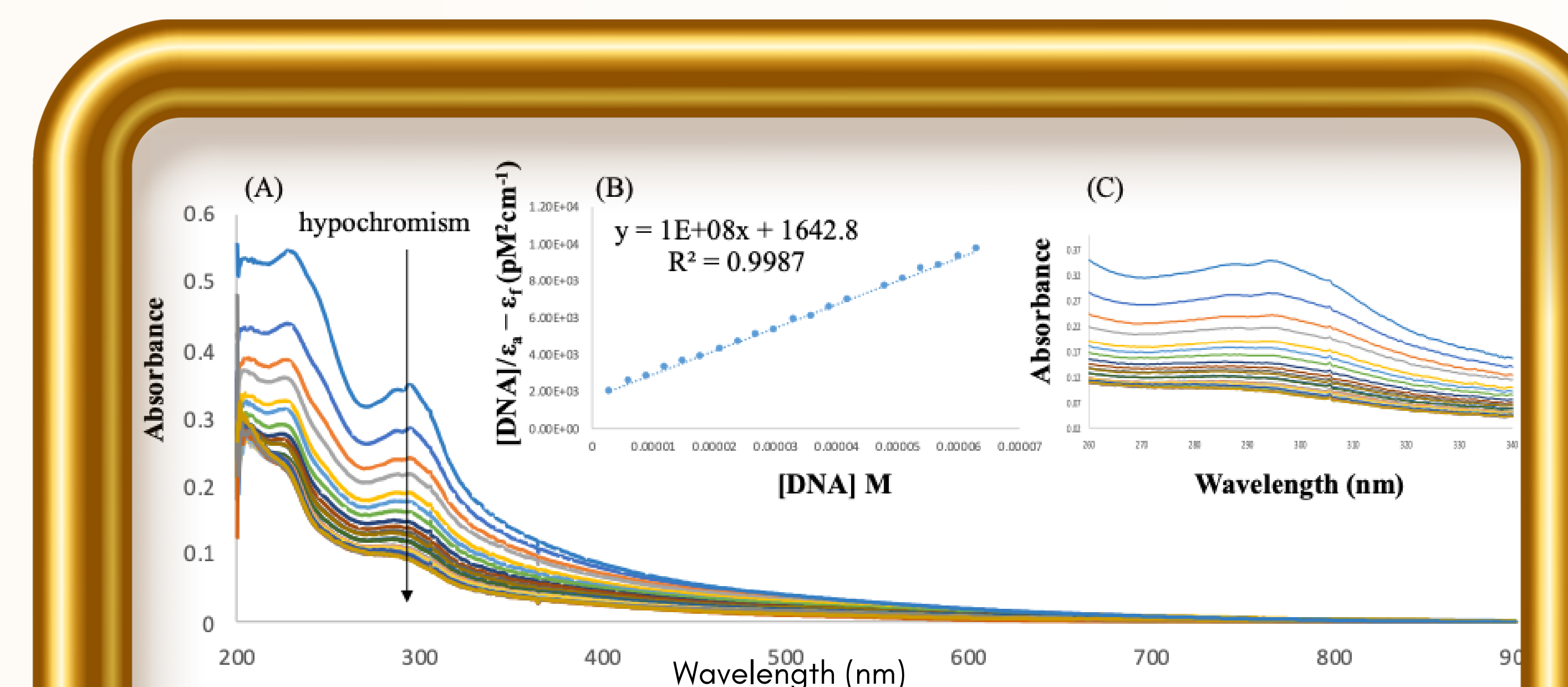


Figure 4. (A) Absorption spectral changes of bis-indolylmethane **4** (30 μM) with incremental concentration of ctDNA added. Arrow ($\downarrow$) denotes to hypochromic effect. (B) Plot of $[\text{DNA}]/\epsilon a - \epsilon f$ ($\text{pM}^2\text{cm}^{-1}$) as function of DNA concentration calculated from absorption spectral results (C) Zoom version of (A) that focus the wavelength between 260 to 340 nm

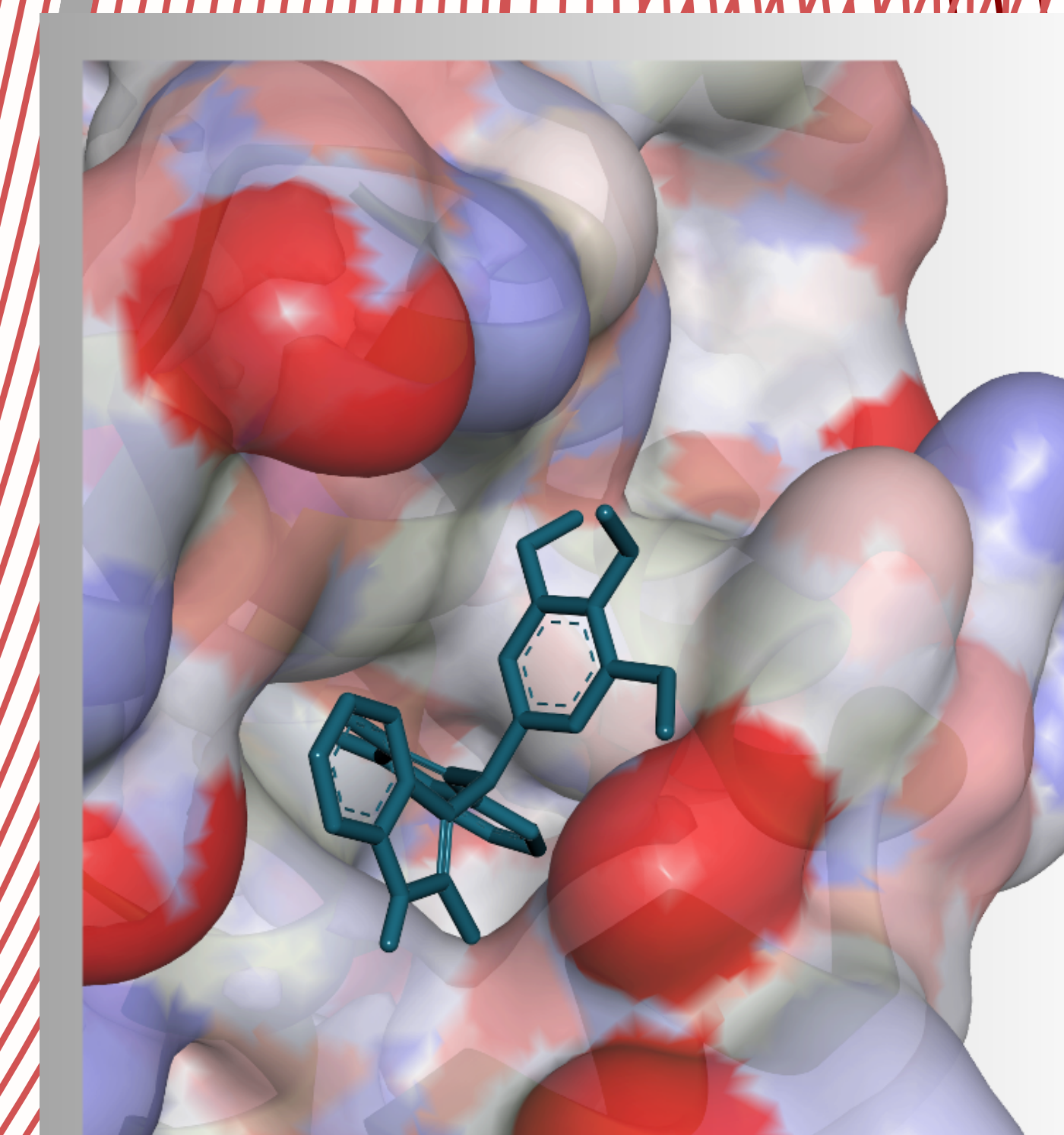
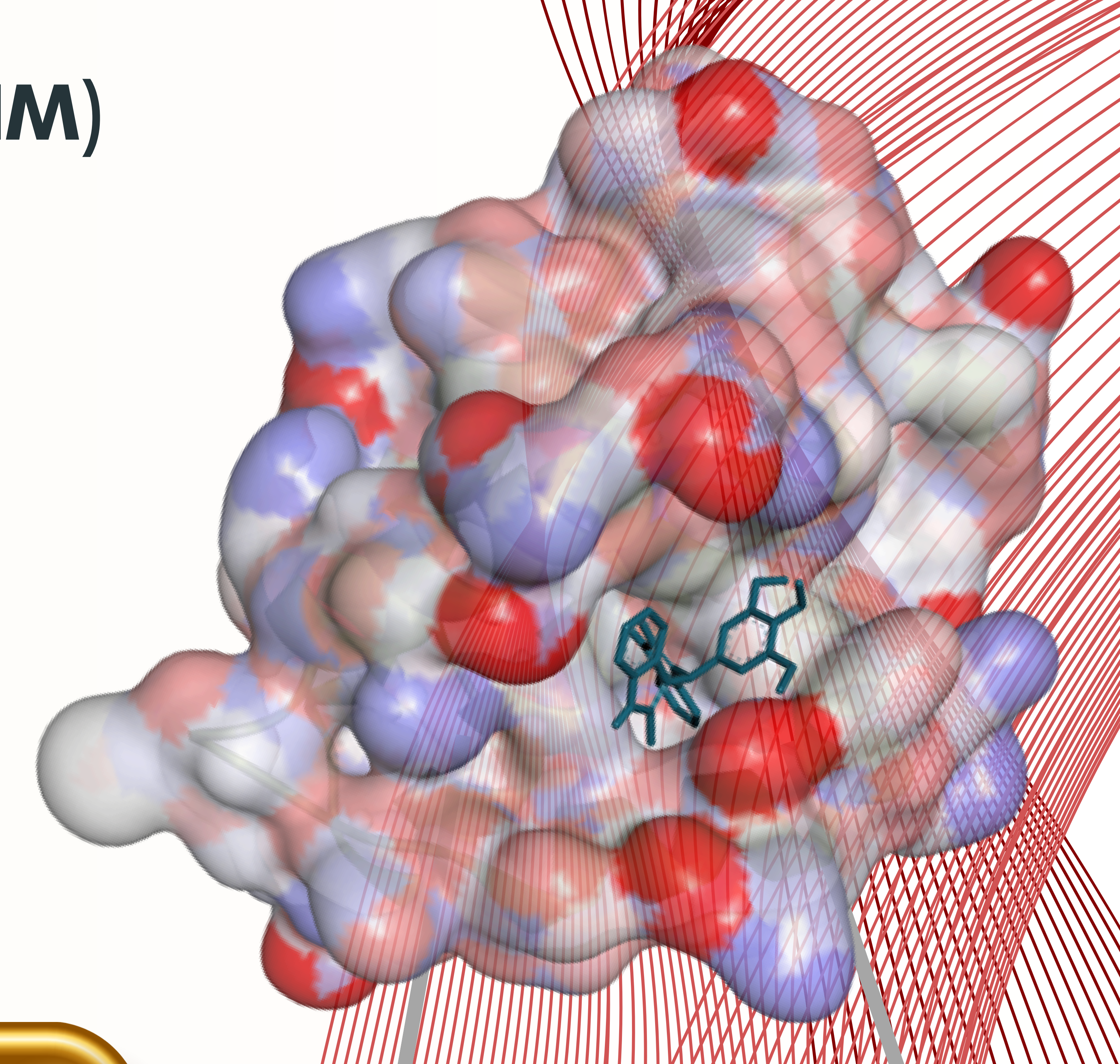


Figure 5. 3D Bcl-2 molecular surface map displaying the docked pose of BIM **4** into P2 and P4 binding hot spots