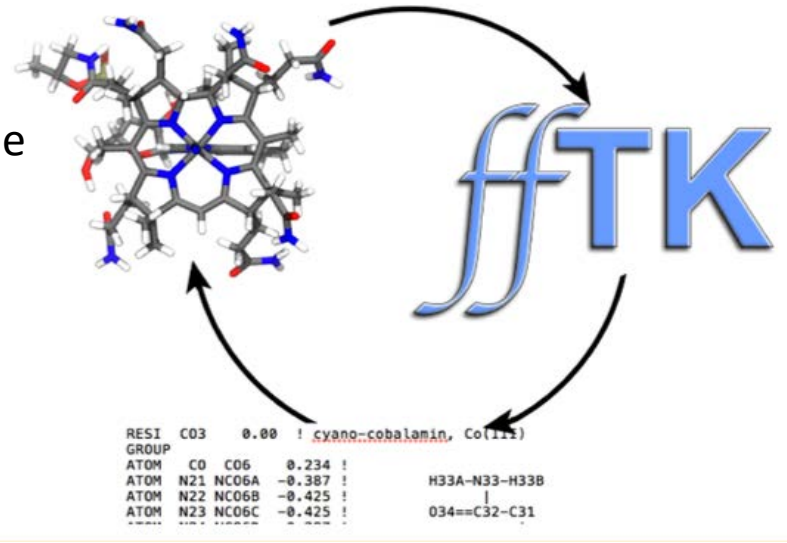
# Methylmercury Speciation and Dimethylmercury Production in Sulfidic Solutions

## Challenge

- Many environmentally important enzymes require cobalamin-like (i.e. corrinoid) cofactors. Performing biomolecular simulations of these complex systems requires an accurate description of cofactor-protein and cofactor-solvent interactions.

## Approach and Results

- We developed CHARMM-compatible force field parameters for several corrinoid cofactors in three oxidation states: $Co^{3+}$, $Co^{2+}$, and $Co^{1+}$, and with various axial ligands.
- Simulations accurately reproduce quantum chemical calculations and X-ray structural data.
- Readily modifiable to enable simulation of newly discovered corrinoid systems.




## Significance and Impact

- These parameters enable accurate simulations of biomolecular systems such as HgcA, reductive dehalogenases, and corrinoid proteins involved in carbon metabolism.

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**Reference:** Pavlova A, Parks JM and Gumbart JC. **Development of CHARMM-Compatible Force-Field Parameters for Cobalamin and Related Cofactors from Quantum Mechanical Calculations**, *J. Chem. Theory Comput.*, **2018**, 14, 794-798. **DOI**: 10.1021/acs.jctc.7b01236

ABSTRACT: Corrinoid cofactors such as cobalamin are used by many enzymes and are essential for most living organisms. Therefore, there is broad interest in investigating cobalamin−protein interactions with molecular dynamics simulations. Previously developed parameters for cobalamins are based mainly on crystal structure data. Here, we report CHARMM-compatible force field parameters for several corrinoids developed from quantum mechanical calculations. We provide parameters for corrinoids in three oxidation states, $Co^{3+}$, $Co^{2+}$, and $Co^{+}$, and with various axial ligands. Lennard-Jones parameters for the cobalt center in the Co(II) and Co(I) states were optimized using a helium atom probe, and partial atomic charges were obtained with a combination of natural population analysis (NPA) and restrained electrostatic potential (RESP) fitting approaches. The Force Field Toolkit was used to optimize all bonded terms. The resulting parameters, determined solely from calculations of cobalamin alone or in water, were then validated by assessing their agreement with density functional theory geometries and by analyzing molecular dynamics simulation trajectories of several corrinoid proteins for which X-ray crystal structures are available. In each case, we obtained excellent agreement with the reference data. In comparison to previous CHARMM-compatible parameters for cobalamin, we observe a better agreement for the fold angle and lower RMSD in the cobalamin binding site. The approach described here is readily adaptable for developing CHARMM-compatible force-field parameters of other corrinoids or large biomolecules.