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C. EUGENE BENNETT
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Using solution NMR spectroscopy to study dynamic protein-drug complexes: Cardiac troponin

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The cardiac troponin complex is the molecular switch that turns heart muscle contraction on and off with every heartbeat in response to calcium transients. We are developing novel compounds that can act as calcium sensitizing troponin activators. The compounds demonstrate activity at the protein, cellular, myofilament, and whole organ levels. We use solution NMR spectroscopy to obtain atomic resolution structures of activated troponin bound to drug, whereas X-ray crystallography yields spurious structures due to crystal packing artefacts. NMR is also able to elucidate dynamic changes in drug binding and protein structure at physiologic temperatures. We are currently developing methods to characterize the structure and dynamics of protein side chains before and after drug binding. Crystal structures often depict these as rigid, but more than half of the side chains on the protein surface are very mobile, so computer docking simulations could potentially be much improved by properly accounting for protein mobility.

Students, meet the speaker after the seminar in a student/postdoc session from 4:45-5:15 pm

Date: Mon, Dec. 2, 2024
Time: 3:30-4:30 pm
Location: Clark Hall 312