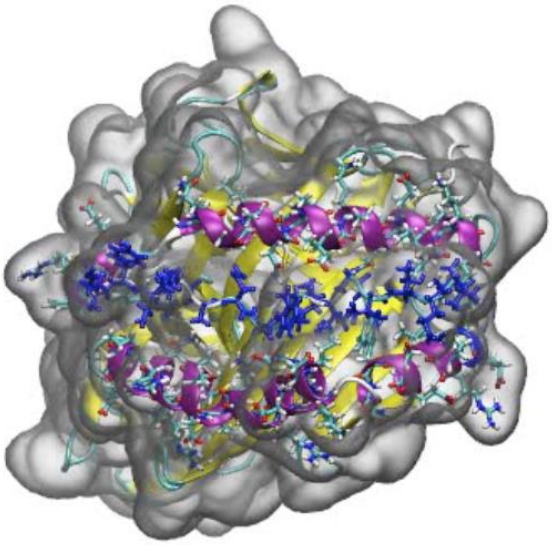
Cadre Research: Molecular Modeling

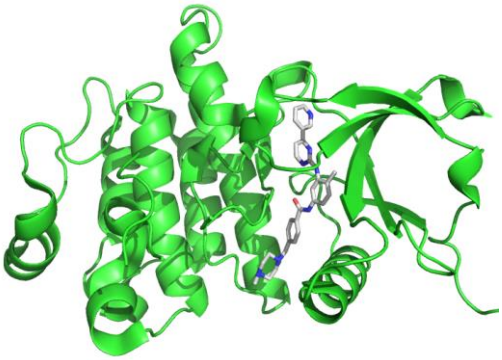
Cadre Research Labs is a Scientific Computing Contract Research Group specializing in Algorithm Development and Technology Transfer for the Biotech and Pharmaceutical industries. Leveraging both internal and university sourced research, Cadre goes beyond off-the-shelf software to develop the next generation of research and discovery tools. Cadre's core of Computer Science and Life Science PhDs provide unparalleled interdisciplinary research expertise. We specialize in utilizing techniques from Computational Biology, Machine Learning, Algorithm Development, and Data Mining to solve custom computational challenges and to analyze 'Big Data'.

Cadre's Modeling services are used to: understand the molecular mechanism of protein:ligand interactions, improve the efficiency of identification of small-molecule lead inhibitors, hypothesize binding modes as a step towards lead optimization, identify patterns and trends in large datasets, optimize protein or peptide sequence towards a measurable outcome.

Molecular Dynamics Simulations: Cadre now offers a contract research service for Molecular Dynamics (MD) simulations. Molecular dynamics simulates a solvated molecular system over time by numerically solving Newton's equations of motion generating a series of conformational molecular snapshots and energies. The individual conformations can be strung into an animation allowing for the identification of conserved structures, motions, and interactions. MD simulations can be extremely useful when attempting to understand the molecular basis of activity. By using the latest Graphical Processing Unit (GPU)-optimized molecular dynamics simulation algorithms we can attain better results than traditional approaches in significantly less time. We've helped collaborators rapidly gain insight into protein:ligand, protein:peptide, and protein:protein interactions. We have studied the interactions between HLA receptors, binding peptides, and small-molecule binders. If a high-resolution protein structure is available for your target we can help you gain critical mechanistic insights. The project deliverables include molecular movies and images illustrating structures and preferred motions. Also provided is a summary of these results with attention to possible interpretations and testable hypotheses.



Molecular Docking / Virtual High Throughput Screening: Our docking service was initially designed for companies that did not have in-house computational screening capabilities but is now open to everyone. Docking saves experimental resources when used as a virtual prescreen prior to wetlab experimental work. It allows you to focus on a small set of promising ligands without having to experimentally screen your entire compound library. Our methods can also guide lead optimization by predicting the binding modes for a set of validated hits or leads. Our models can be part of an iterative cycle where the experimental results of one round guide the computational prioritization of compounds to experimentally screen in subsequent rounds. The project deliverables include a rank list of small molecules as well as structure files, images, and insights into their hypothesized binding modes (locations).



Machine Learning, Statistical Data Analysis, and Data

Mining: Our research team can help you find the proverbial needle-in-the-haystack. Your team is likely generating lots of data. In most cases, this 'big' data contains within it key pieces of actionable intelligence -- knowledge that could provide insight, opportunity, and advantage -- if only you could get at it. Data Science is evolving faster than off-the-shelf commercial offerings can support it. This means that a contract research team, like Cadre, is often the best and most economical solution. Cadre researchers have been working with large interdisciplinary datasets for decades and we have access to large computer resources. The project deliverables vary from project to project, but they typically include a trained (fit) statistical model that can be used by your or our organization to analyze current and future data.

Sequence Optimization: Powerful statistical models can generate sequences optimized for a particular function (*e.g.,* binding affinity, activity, resistance, or reduced aggregation) given a set of previously examined annotated sequences. For example, given the sequences of 100 protein variants each annotated with their binding activity, our models can generate additional sequences predicted to have significant binding activity. We are happy to work with a client through an iterative process of sequence improvement. Project deliverables can include a trained statistical model or more simply a list of optimized sequences.

A Note Regarding Pricing and Variants:

Molecular Modeling services are priced based on the complexity of the molecular system and the questions investigated. System complexity increases with the size and number of molecules present. In almost all cases we start from the experimentally determined high-resolution three-dimensional protein structure (*i.e.,* a crystal structure) of an identical or highly similar protein sequence. If an experimental structure is not available, we can often perform homology modeling. We do offer volume discounts for the analysis of multiple systems and for the examination of multiple variants of the same system.

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