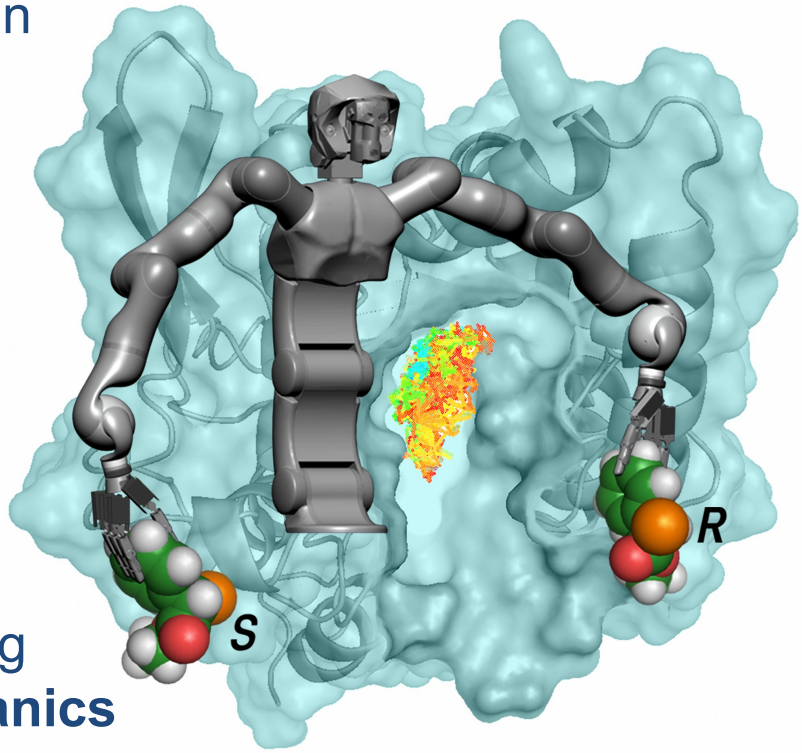
LAAS Days
Research & Technology

Molecular modeling methods for novel health and environmental applications

ALIVE axis

Novel Molecular Modeling Approaches

- **Model-based computational methods** are an essential complement to experimentation for accelerating the **development of new technologies**
- **Multidisciplinary approach**: collaboration between physicists, chemists, biologists and computer scientists
- **Novel methods** based on multi-level modeling and efficient algorithms **inspired from mechanics and robotics**



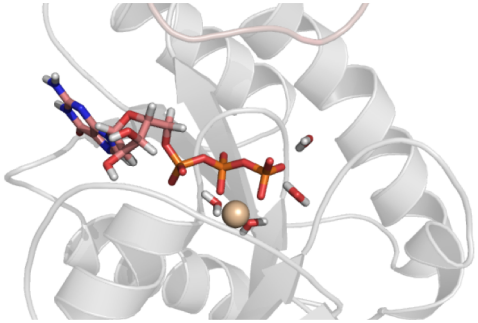
Novel Molecular Modeling Approaches

- Design
- Decision making

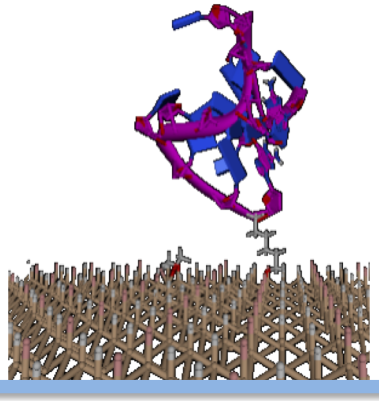
- Guide/control experiments

- Characterization
- Help understanding

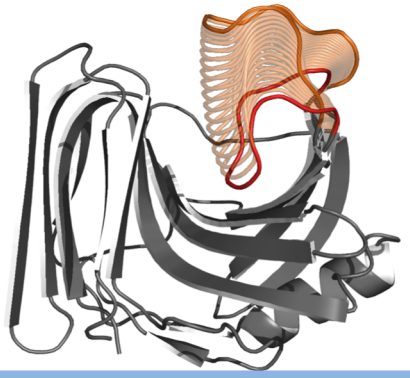
Health



Bio/nano-technologies

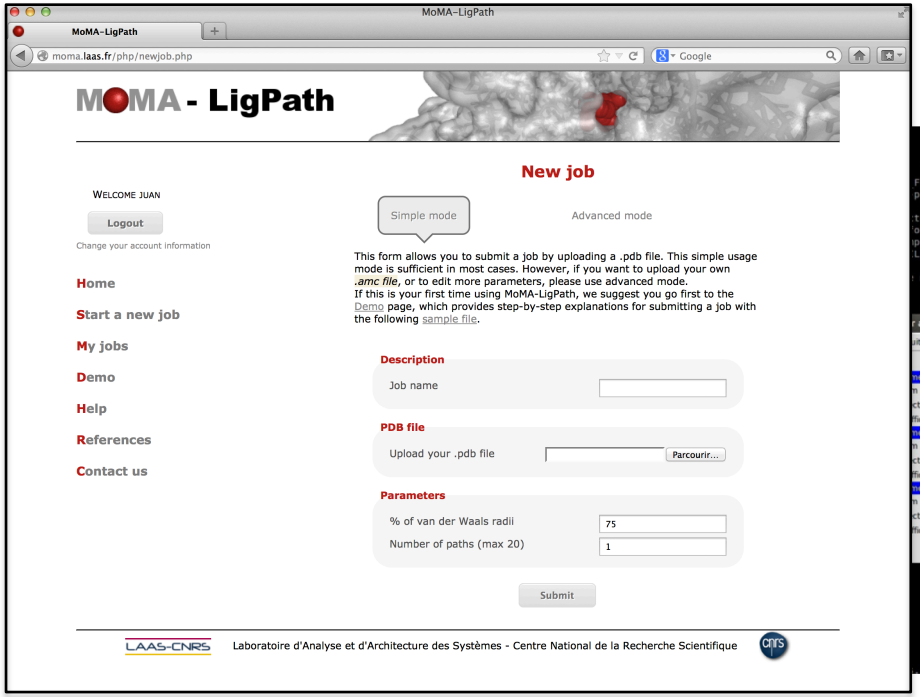


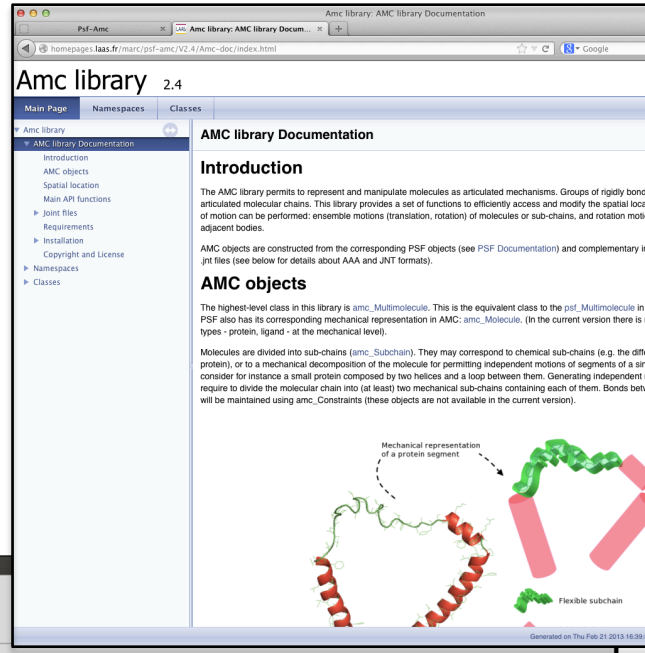
Environment

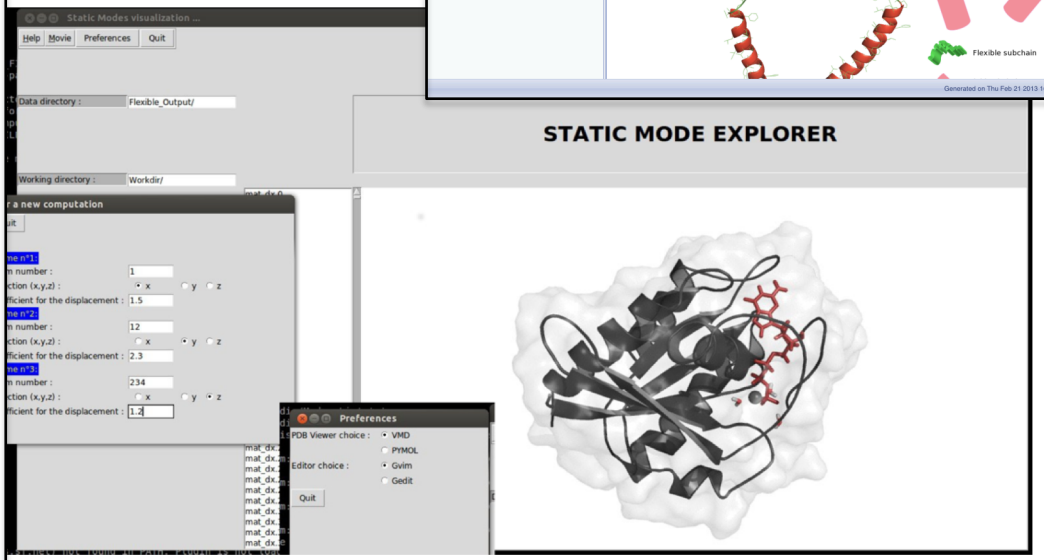


Novel Molecular Modeling Approaches

- **Software Development**:
- Algorithmic modules : http://projects.laas.fr/Psf-Amc
- Web servers : http://moma.laas.fr [Devaurs *et al.*, NAR, 2013]
- Application programs : https://homepages.laas.fr/mbrut/





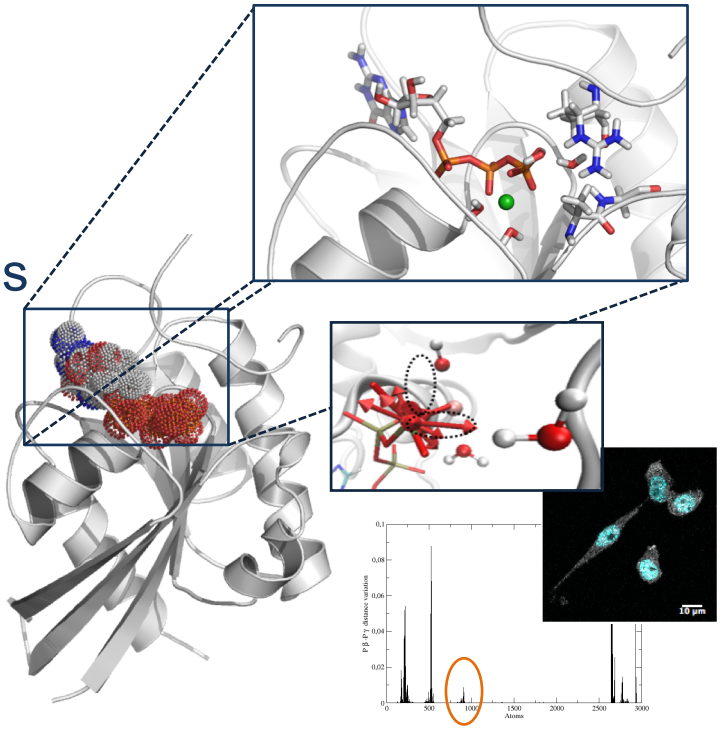


Applications to Health

- Molecular modeling for the understanding of **mechanisms of drug action and resistance**

- **Goal**: modulate protein function
- **Challenge**: multi-level/methods requirements
- **Mechanobiology + quantum chemistry** algorithms to access both protein structure and activity

- Applications: ***cancer-type targeted therapies, drug resistance, drug receptors…***



[Brut et al., J Phys Chem B, 2011]

[Tichauer et al., Biophys J, 2018, *in revision*]

- **Collaborators:**

CRCT Centre de Recherches en Cancérologie de Toulouse – Oncopole
CPTP Centre de Physiopathologie Toulouse Purpan
IPBS Institut de Pharmacologie et de Biologie Structurale
Université Paris Descartes
Université de Reims Champagne-Ardenne

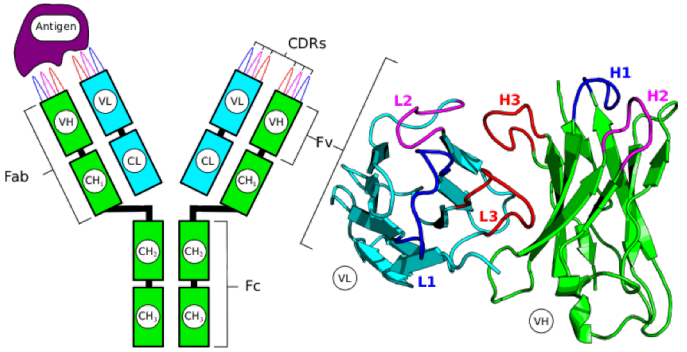
Funding:

cnrs
Inserm
Institut Claudius Regaud
La Région Occitanie Pyrénées - Méditerranée

Applications to Health

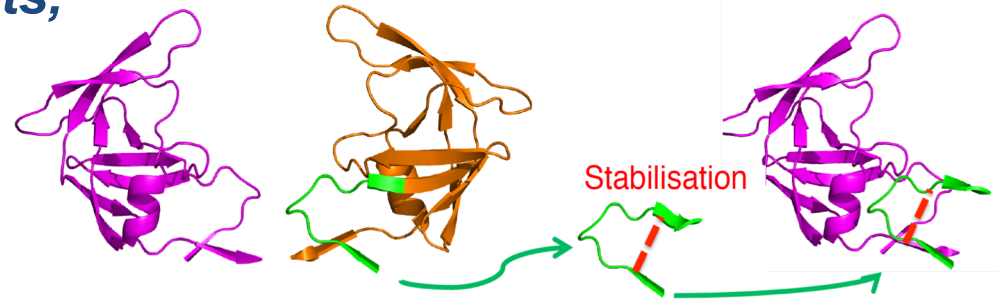
- Modeling/design of **antibodies for immunotherapy** and **cyclic peptides for inhibition of protein interactions**

- **Goal**: enhance affinity/specificity/stability
- **Challenge**: highly-flexible molecules
- **Coupling efficient robotics-inspired exploration algorithms and molecular modeling tools**



- Applications: ***vaccines, diagnostic tests, caspase inhbition (apoptosis), ...***

[Barozet et al., Immunol. Lett., 2018]
[Jusot et al., JCIM, *submitted*]



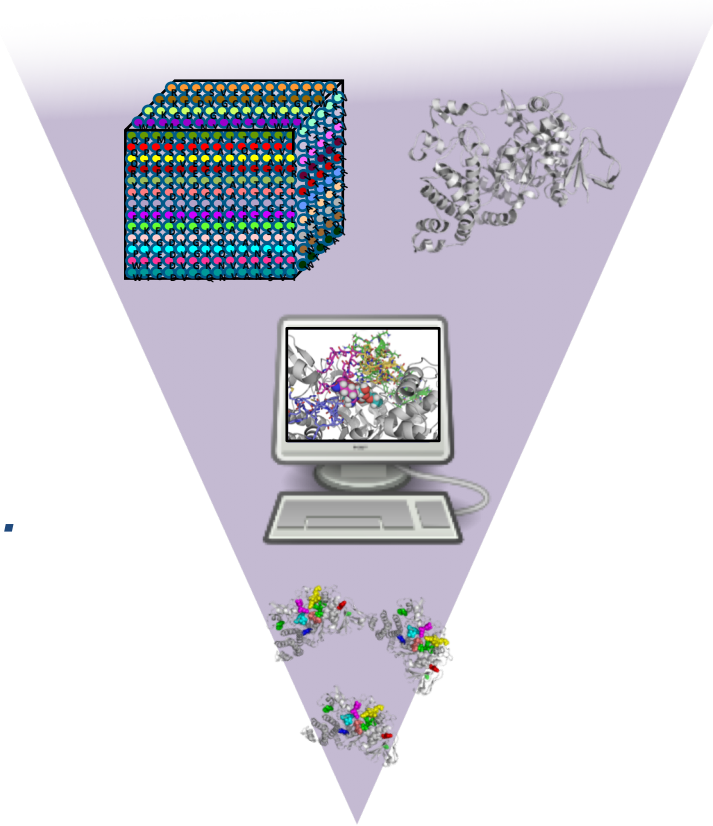
- **Collaborators:** SANOFI, UPMC SORBONNE UNIVERSITÉS

Funding: ANR ASSOCIATION NATIONALE RECHERCHE TECHNOLOGIE

Applications to Biotechnology

- **Enzyme design** for diverse applications in biotechnologies

- **Goal**: produce new enzymes with new functions or improved properties with respect to natural proteins
- **Challenge**: huge number of possible sequences
- **Computation Protein Design (CPD)** algorithms reduce the time and cost of developments
- Applications: ***eco-friendly bioprocesses, valorization of renewable carbon resources, …***
- Software prototype : ***CUSTOZYME***



[Lafaquière et al., ChemBioChem, 2009]
[Molloy et al., IJRR, 2018]

- **Collaborators:** LISBP, MIA TOULOUSE

Funding: Agence Nationale de la Recherche ANR, Région Midi-Pyrénées, Agri Sud-Ouest Innovation, twb

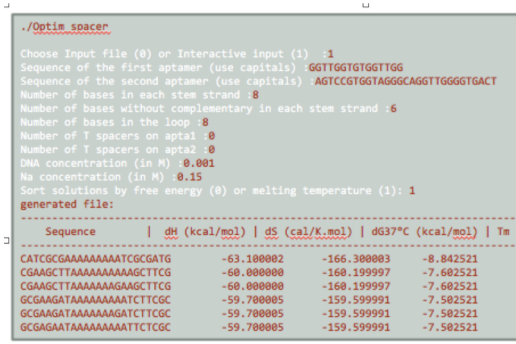
Applications to Nanotechnology

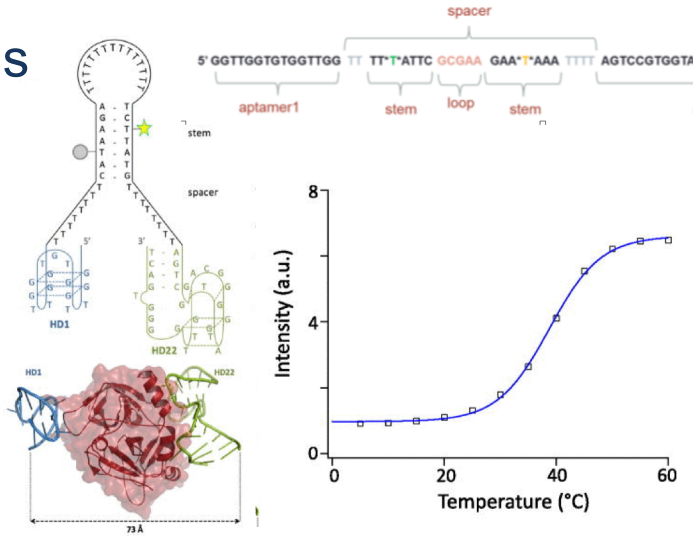
- **Design and functionalization of DNA** for biological sensing and imaging applications

- **Goal**: integrate active functions into nanodevices
- **Challenge**: bio / non-bio interface
- **Sequence design + molecular dynamics** algorithms to predict sensor structure and properties

- Applications: ***DNA-based sensors, quantum dots for medical imaging***

[Trapaidze et al., APL, 2015]
[Brut et al., APL, 2012]





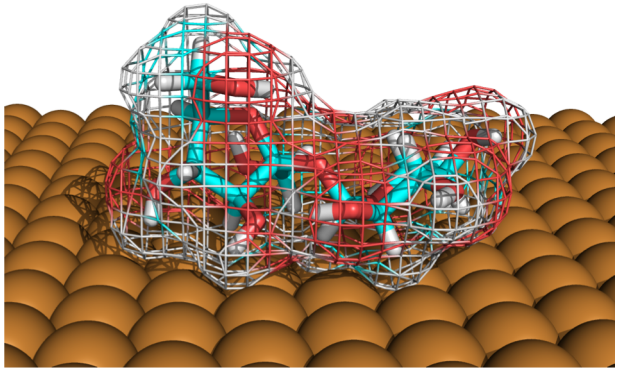
- **Collaborators:**

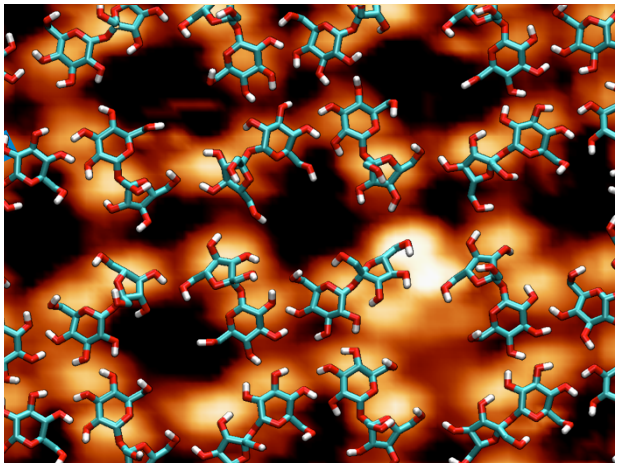
Funding:

Applications to Nanotechnology

- Modeling **biomolecules on surfaces**

- **Goal**: Predict structural and kinetic properties of complex molecular systems
- **Challenge**: bio/non-bio interface, weak interactions
- **Synergistic coupling of experimental techniques and multi-model computational methods**
- Applications: ***implants (biocompatibility), physical scaffolding, pharmaceutical applications, imaging, …***





[Abb et al., *in preparation*]

[A. Hémeryck et al. APS, 2017]

- **Collaborators:**

IRCP Institut de Recherche de Chimie Paris

MAX-PLANCK-GESELLSCHAFT

CEMES

CIRIMAT Toulouse

Funding:

cnrs

Université de Toulouse

Conclusions and Future Directions

- Efficient tools to accelerate the development of new technologies
- Reinforce collaborations with experimentalists and technologists at LAAS
- Open to new external collaborations in different application domains