The study of Cytochrome C oxidase on EGEE Grid

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Outline

- The Molecular Science community
- The CompChem VO
- Autocorrelation functions and spectra
- The Cytochrome c Oxidase and the ferryl intermediate
- The computational problem
- Results
- Conclusions

The Molecular Science community

- **The understanding of the behavior of molecular systems is of great importance for the progress of**
  - the life sciences
  - several industrial applications
- **The Molecular Science community study the molecular systems performing simulations that are heavy demanding in terms of computational resources.**
- **It is mandatory to put together the competencies of various laboratories to achieve ambitious results:**
  - active collaboration between people with complementary expertise
  - interaction between various computational approaches

The Molecular Science community

- **The EGEE Grid environment represents for this community the high valued infrastructure able to supply**
  - the necessary computational power
  - the proper middleware able to let people collaborate together and access the common resources in a secure way.
- **The CompChem VO has been created to support such computational needs and pivoting the access to the EGEE Grid facilities.**
- **Several EGEE sites are supporting the VO, in particular the Italian EGEE sites, CESGA (Spain), CYFRONET and POZNAN Supercomputing Center (Poland), Hellas Grid and GRNET (Greece), University of Cyprus (Cyprus).**

Compchem VO

- **CompChem VO is running on the EGEE production Grid from the end of 2004 to support Computational Chemistry applications (http://compchem.unipg.it)**
- **The VO contributes to the EGEE production grid with 2 CE:**
  - ce.grid.unipg.it (LCG 3.0) 12 nodes (biproc) PIII
  - cex.grid.unipg.it (Glite 3.0) 8 nodes (biproc) Xeon
  - We made available a powerful UI to CompChem users: ui.grid.unipg.it
- **The CompChem VO is the most active VO of the "Generic Applications" of EGEE (rank 3rd after HEP and Biomed communities)**
- **We are part of the Center of Excellence in Computational Chemistry in EGEE III, that will start in April 2008.**

Compchem users

Country	# of users	Organization
Italy	12	Univ. Perugia, CNR-IMIP, ENEA, Univ. Palermo
Grece	7	FORTH Crete, Universities: Crete, Athens, Tessalonilki
Spain	5	Univ. Basque Country, Univ. Barcelona, CESGA
Austria	4	Univ. Vienna, Univ. Innsbruk
France	3	CNRS
Poland	1	Cyfronet
Sweden	c	PDC, Royal Institute of Technology,Stockholm
UK	1	Imperial College London
Portugal	1	IRICUP
Cyprus	1	Univ. Cyprus
Lithuania	1	Univ Vilnius

Most users are collaborating in the COST CMST D37 Action, GridChem
http://www.cost.esf.org/index.php?id=189&action_number=D37

The TCCC group

- The Theoretical and Computational Chemistry in Crete group is one of the most active groups in CompChem VO
- They are also active in SEE VO on the HellasGrid component of EGEE
- The group is also very active in the COST CMST D37 Action, GridChem
- They start the Grid experience with the ENACTS project in 2002

A joint scientific and technological activity and study on

Grid Enabling Technologies

Sectoral report from the Grid Enabling Technologies study within the ENACTS project

Stavros C. Farantos and **Stamatis Stamatiadis** (FORTH)

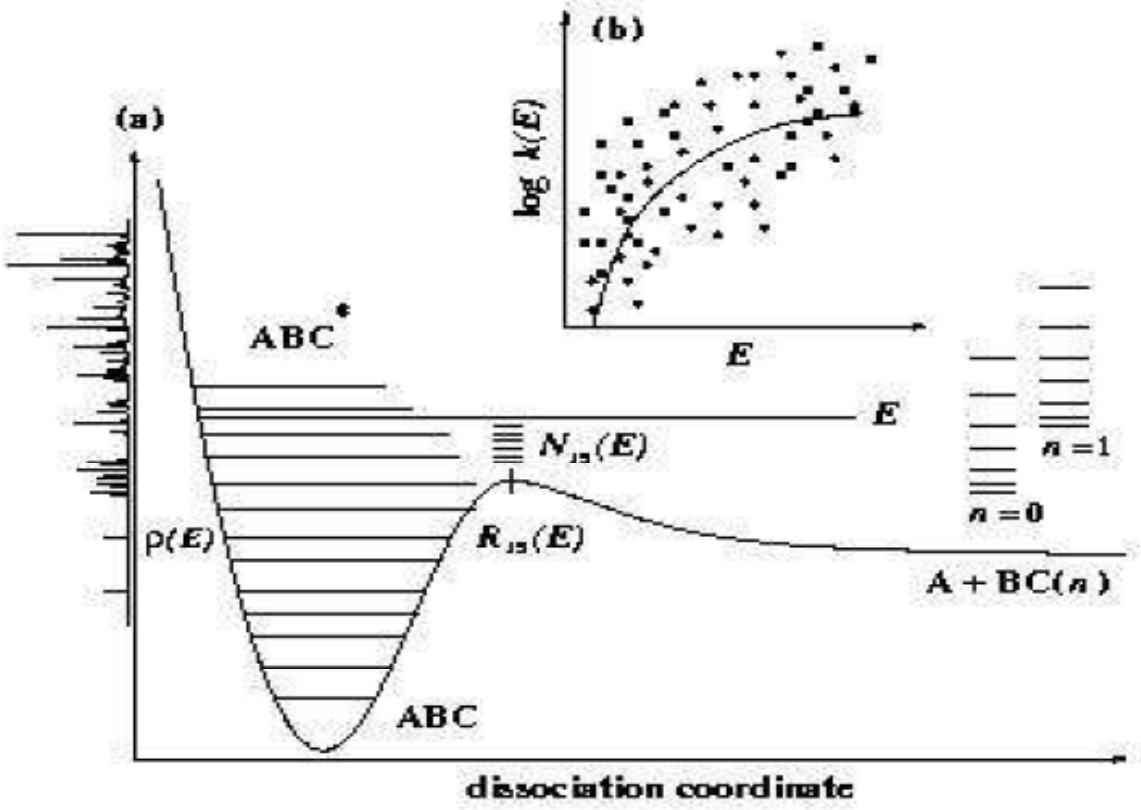
Institute of Electronic Structure and Laser
Foundation for Research and Technology, Hellas

And

Nello Nellari and **Djordje Maric** (ETH-CSCS)

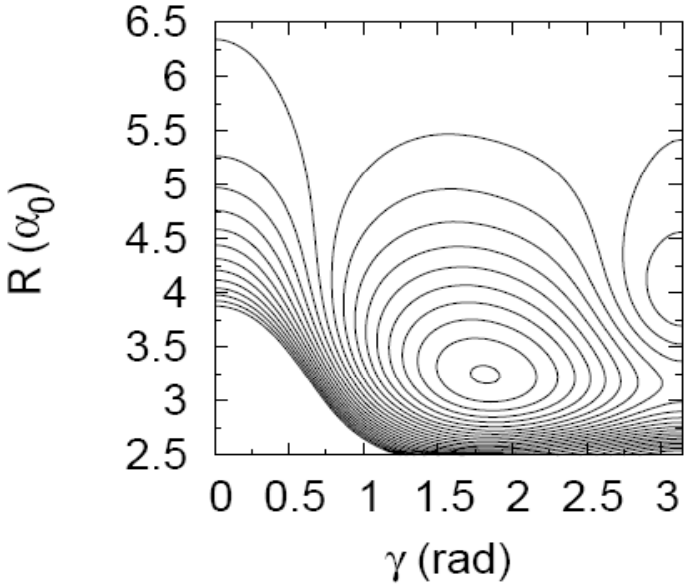
Swiss Center for Scientific Computing

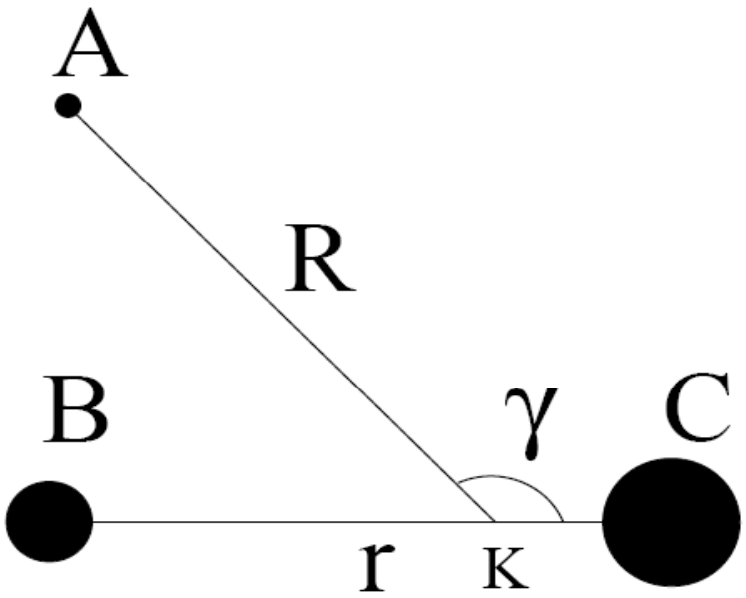
Molecular Potential Energy functions along a reaction coordinate



Quantum and (semi)classical autocorrelation functions and spectra

Potential Energy Hypersurface on a triatomic molecule

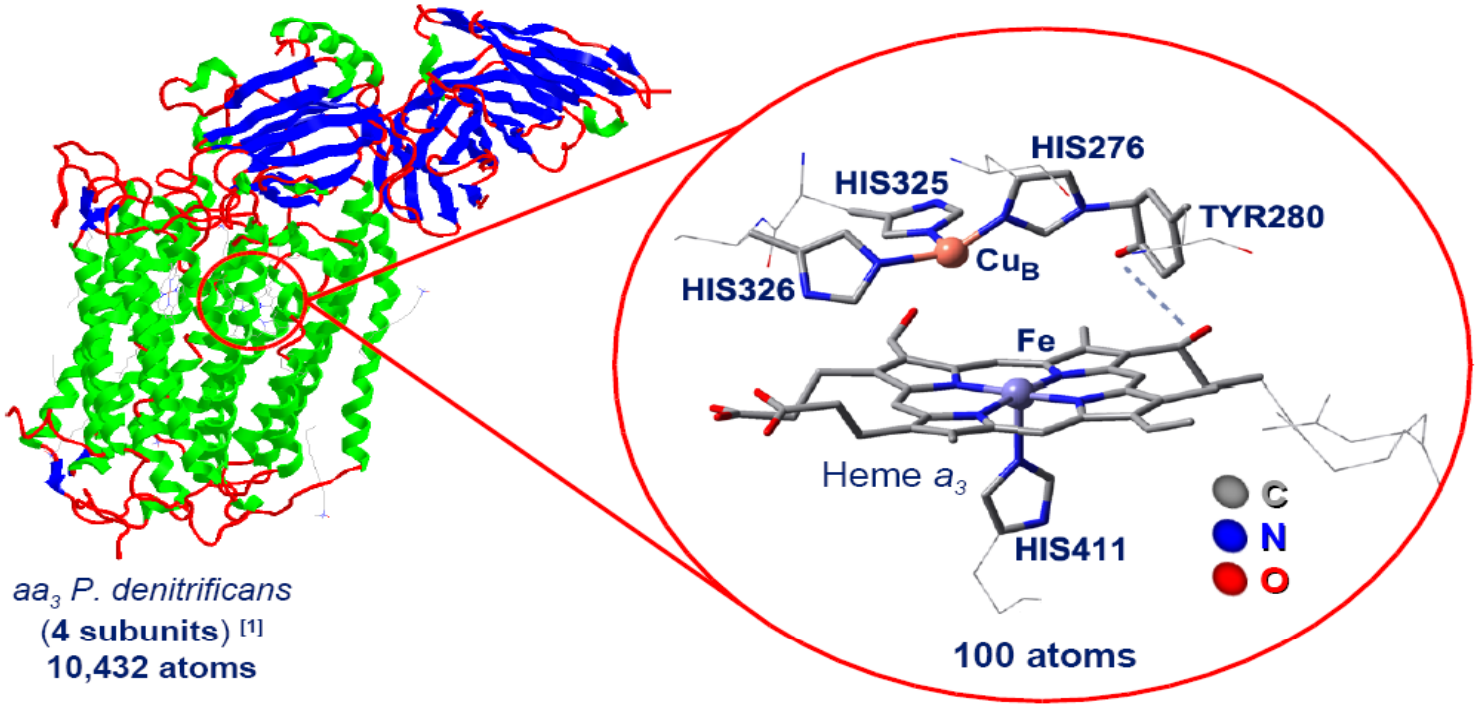




Quantum and (semi)classical autocorrelation functions and spectra

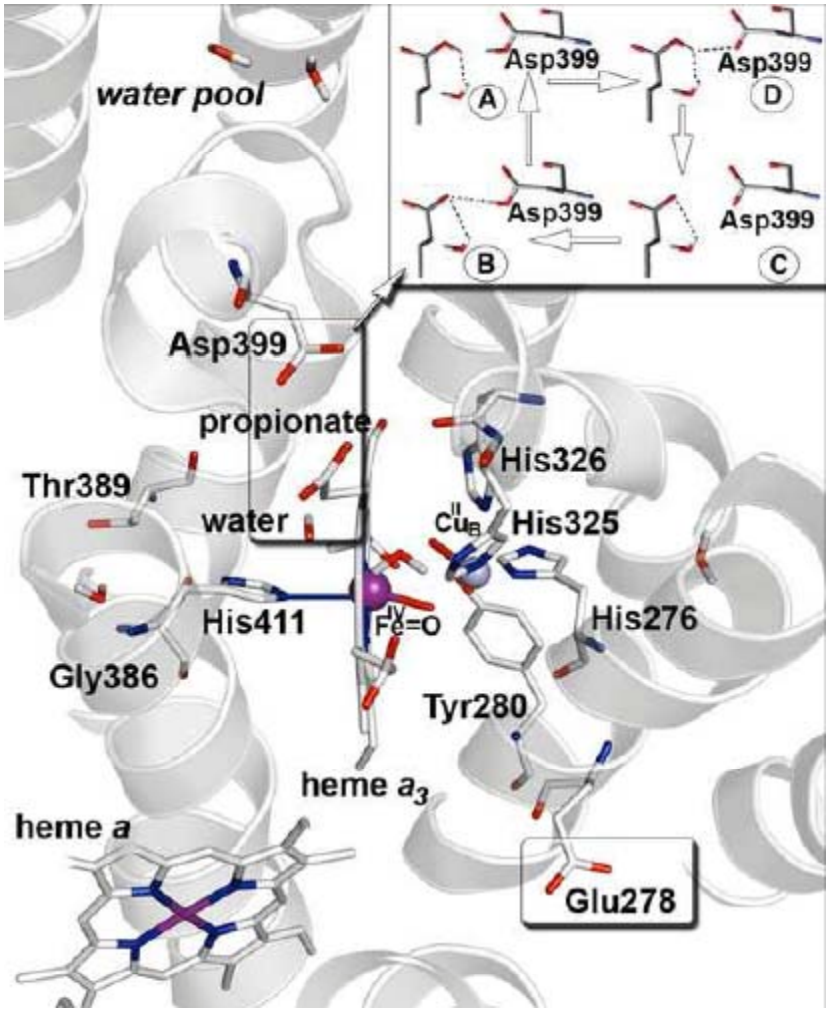
The computational problem

- **Cytochrome c Oxydase (CcO) consists of approximatively 10.000 atoms and the dynamics calculations are unfeasible on ordinary clusters (2.4 years are required for a simulation of 5.2 ns).**



The ferryl-oxo intermediate

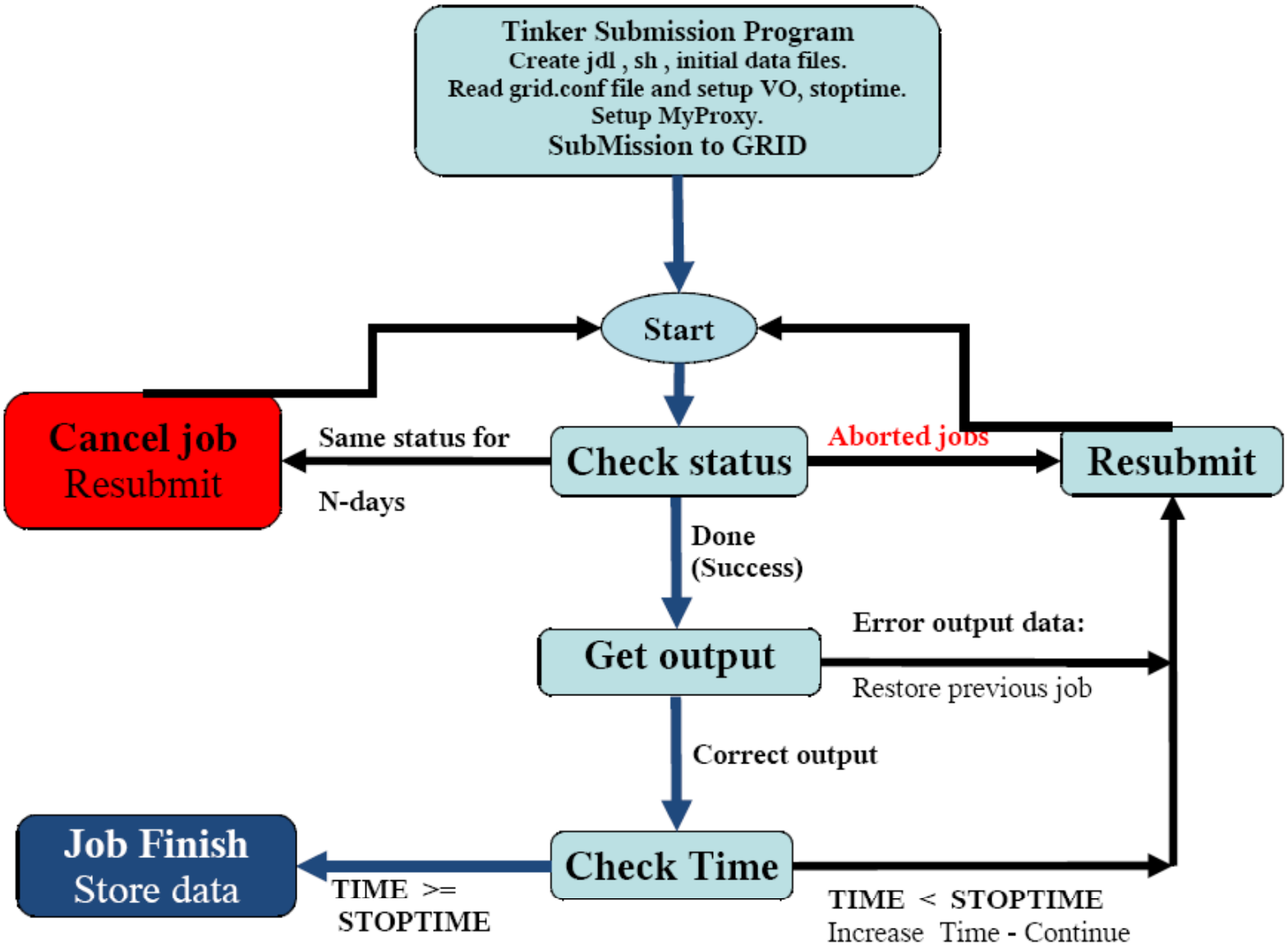
- CcO couples the four electron reduction of the Oxygen molecule to water with the pump of four protons across the inner mitochondrial membrane attributing to the electrochemical gradient that is used to synthesize ATP
- Electrons from CcO pass through a heme *a* group and are transferred to the binuclear heme a_3/Cu_B active site where the dioxygen is reduced
- We study the dynamics of the protein matrix near the active site at the ferryl-oxo oxidation level concentrating on the v(Fe-O) and the role of Glu278



Computational method

- Simulations were performed at T=300K using for the integration of equations of motion a time step = 0.15fs
- The MD package Tinker was used with the Amber99 force field
- All amino acids were free to move during the simulations.
- For non-bonded interactions a cutoff distance of 12A with a smooting window between 9.6-12A was applied
- Structures were minimized and equilibrated at constant temperature before each simulation.

Management of jobs

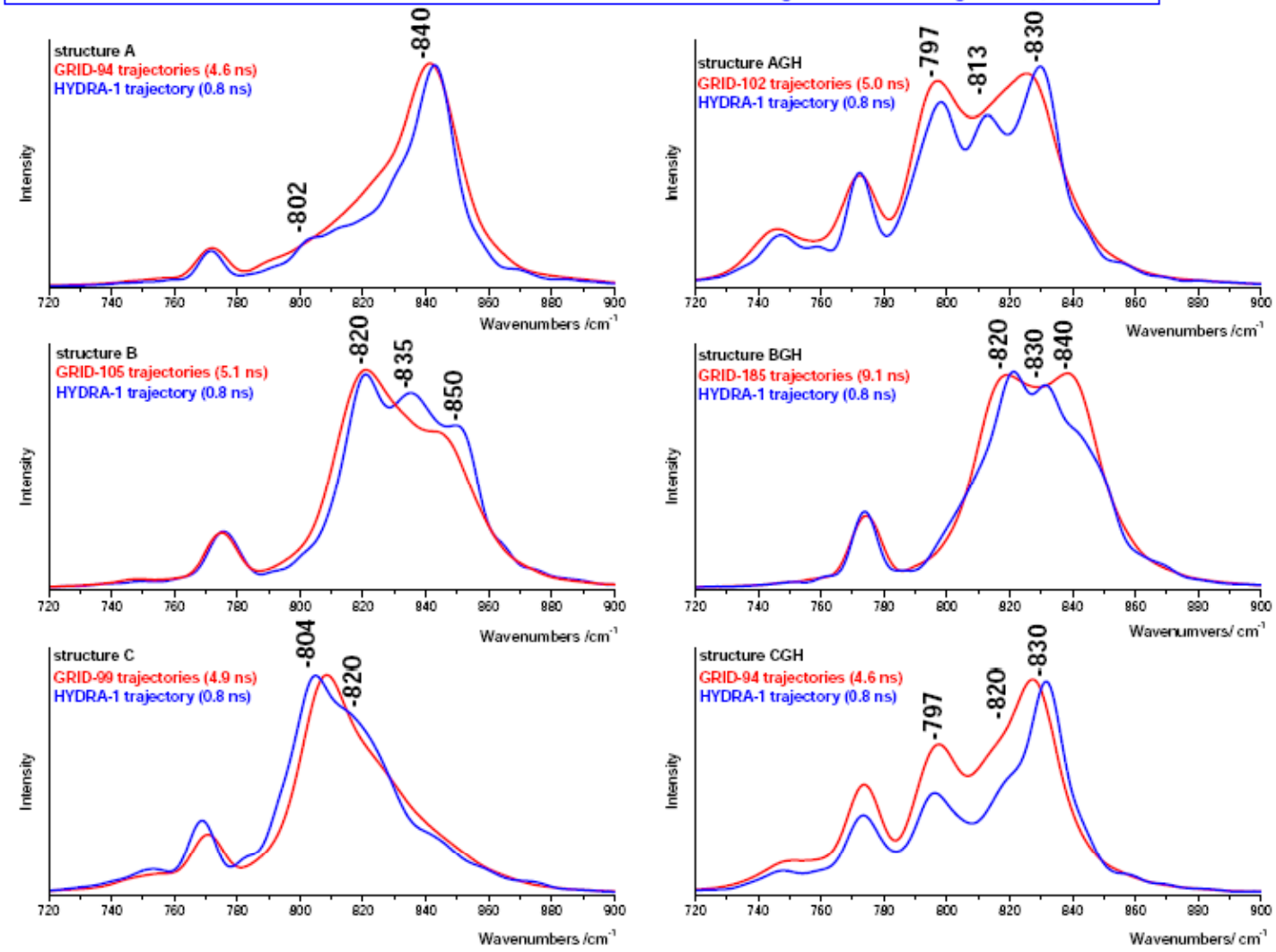


Comparison of 1- to N- trajectories

Structures A, B & C with Glu278 protonated/ deprotonated

FFT with Mathematica 6.0 (signal processing)

Smoothing with Microcal Origin 7.5E (FFT)



Statistics on jobs

CompChem VO

Structure	1ar1A_B18	1arA_BGH18	1ar1A_DGH18
Execution time (days)	29	31	30
# of submitted jobs	1854	1902	1864
# of aborted jobs	180	273	228
# of canceled jobs	35	17	18
# of succeeded jobs	1639	1612	1618
Efficiency	**88.4%**	**84.8%**	**86.8%**

# of succeded jobs	**4869**
# of aborted jobs	**681**
# of canceled jobs	**70**
Efficiency	**86.4%**
Size (MB) /job	**14**
IO (GB)	**80**
CPU time (days)	**3043**

Conclusions

- The EGEE production Grid environment has been used to perform the study of the protein dynamics and the spectroscopy of the ferryl-oxo intermediate of Cytochrome c Oxydase
- The large number of CPU available on the Grid has made it possible to carry out a study unfeasible on conventional clusters
- The efficiency of the runs is satisfactory, considering that some jobs are automatically aborted if they do not terminate in a predefined time
- The project has been made possible thanks to the collaboration among different research groups made possible by the COST D37 Action GridChem