

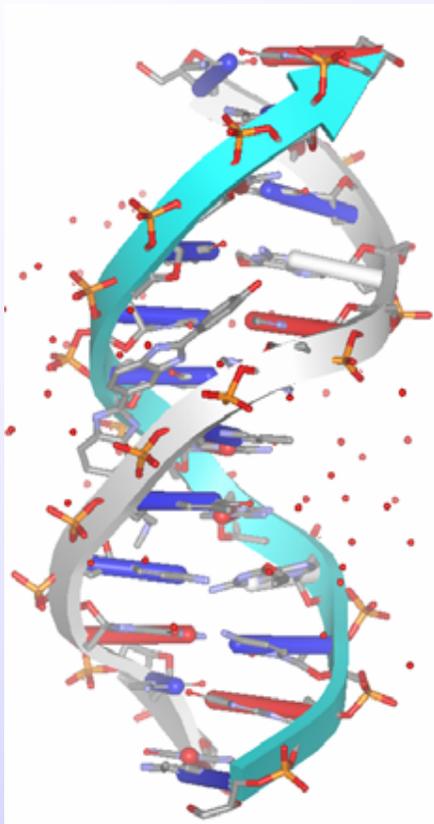
Glyco – MGrid

CyberInfraStructure for *e*-Glycomics



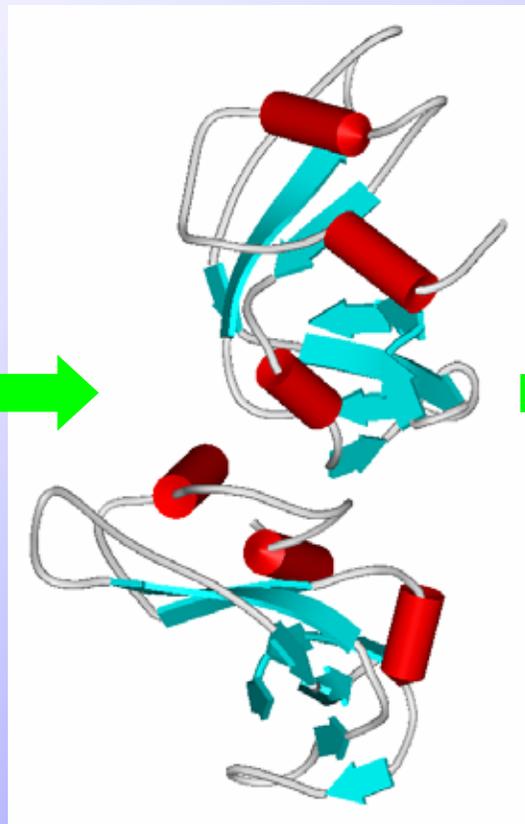
Biomacromolecules & Carbohydrates

- Structural Motif



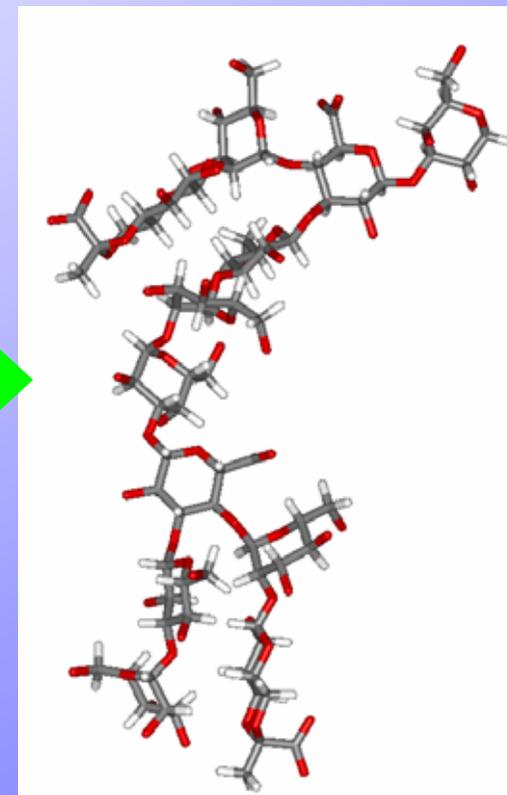
DNA (102D)

CGCAAATTTGCGCGC
AAATTTGCG



Protein (1W4Q)

LYS GLU THR ALA ALA ALA LYS PHE GLU
ARG GLN HIS MET ASP SER SER THR SER
ALA ALA SER SER SER ASN TYR CYS ASN



Carbohydrate (1CAP)

b-D-Manp-(1-6)+
|
a-D-Manp-(1-6)+
| |
b-D-Manp-(1-3)+ b-D-Manp-(1-4)-b-D-GlcpNAc

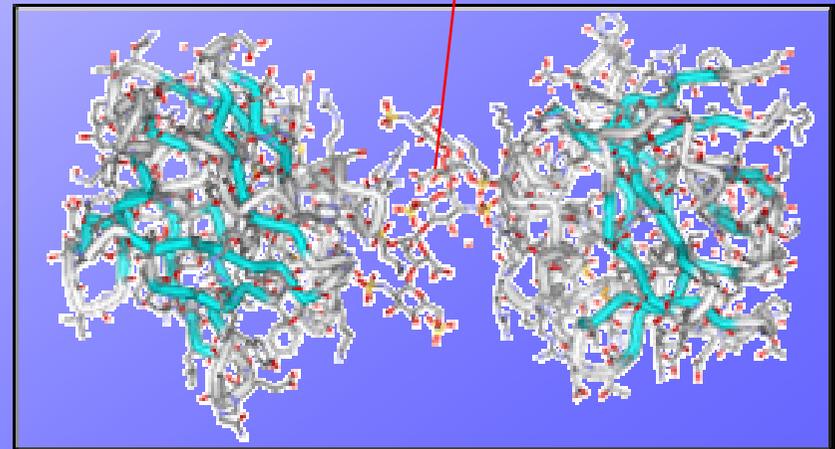
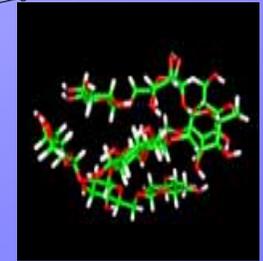
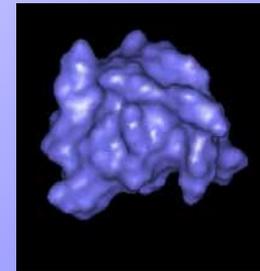
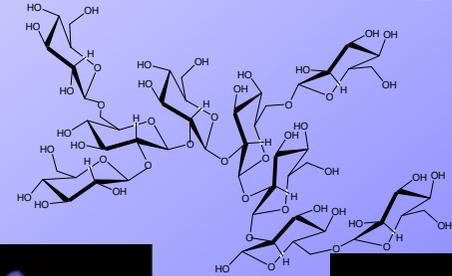
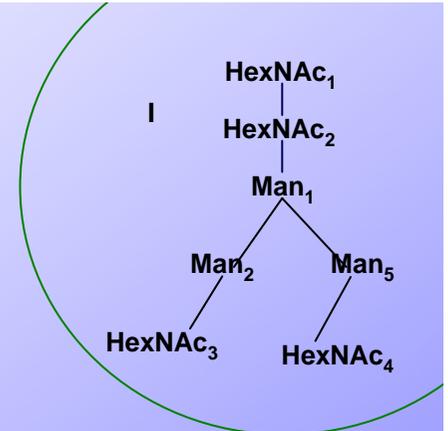
Gene – **Genomics**
Protein – **Proteomics**
Glycoconjugates – **Glycomics**



e-Glycomics



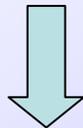
Carbohydrate





Grid computing

Grid protocols link everything else - databases, simulation tools, and underutilized computing power. Computer grids function analogously to the electric grid. **Widely dispersed on-line resources become available to focus on the problem at hand.**



**CharmmGrid,
AmberGrid,
MGRID**

**GaussianGrid
GamessGrid**

**Molecular Simulations,
Informatics, Theory & Analysis**

Glycomics

Glycomics is the effort to **understand and harness sugars that are naturally made** by the human body, in order to improve health by bolstering the immune system or by arresting disease processes. Sounds easy, but there is, as of yet, **no code that determines the structure of the sugars.**



**Structure, DataBase,
Informatics, Simulations**

e-Glycomics & Glyco-MGrid

Web-Portal
Molecular Grid

e-GlycoScience

Novel Knowledge

Data Mining
Prediction

e-GlycoScience

Databases for Carbohydrates and Glyco-compounds in WWW

DataBase	DataBases			Simulations				
	1D Sequence	3D structure	User-Interface	Conformation Computing	Solvent Effect	Carbo-Parameter	Grid System	Sharing System
CarbBank	O	×	O	×	×	×	×	×
SUGABASE	O	×	O	×	×	×	×	×
SWEET	O	O	O	O	×	×	×	×
GlycoMaps Database	×	×	O	O	×	×	×	×
Glydict	×	×	×	O	×	×	×	×
CAZy	O	×	O	×	×	×	×	×
Glycoconjuate DataBank	O	O	O	×	×	×	×	×
GlycoSuite	O	×	O	×	×	×	×	×
Functional Glycomics	O	O	O	×	×	×	×	×
MD-Simulator	×	O	O	O	O	×	×	×
BioSimGrid	×	×	O	O	O	×	O	×
Glyco-MGrid System	O	O	O	O	O	O	O	O

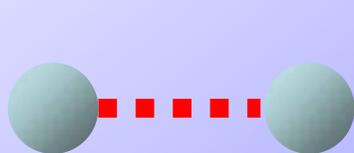
CarbBank <http://bssv01.lancs.ac.uk/gig/pages/gag/carbbank.htm> SugarBase <http://www.boc.chem.uu.nl/sugabase/sugabase.html>
 SWEET <http://www.glycosciences.de/modeling/sweet2/doc/index.php> GlycoMaps <http://www.dkfz.de/spec/glycosciences.de/glycomaps/>
 MD-Simulator <http://www.md-simulations.de/manager/> Glydict <http://www.dkfz.de/spec/glydict/>
 CAZy <http://afmb.cnrs-mrs.fr/CAZY/> Glycoconjugates DB <http://akashia.sci.hokudai.ac.jp/>
 GlycoSuite <https://tmat.proteomesystems.com/glycosuite/> Functional Glycomics <http://www.functionalglycomics.org/static/consortium/>
 BioSimGrid <http://www.biosimgrid.org/>

Molecular Simulations & Energy computation

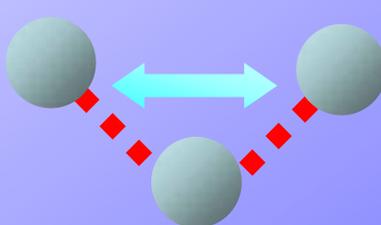
Parameters are derived principally from experimental data, and some calculations. Sources include:

- IR spectra; bond stretching, angle bending, ...
- X-ray crystal structures; geometries and energetics
- solvent simulation to match physical properties (TIP3P)
- ab initio calculations; partial charges
- free energy perturbation with a known experimental result

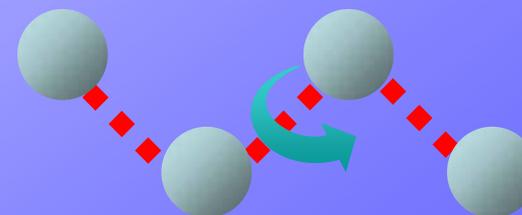
$$E_{total} = \sum_r K_b (r - r_0)^2 + \sum_\theta K_\theta (\theta - \theta_0)^2 + \sum_\phi |K|_\phi - K_\phi \cos n\phi + K_\omega (\omega - \omega_0)^2$$
$$+ \sum \left[\left(\frac{A}{r_{ij}^{12}} \right) - \left(\frac{B}{r_{ij}^6} \right) \right] sw(r_{ij}^2, r_{on}^2, r_{off}^2) + \sum \left(\frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} \right) \left[1 - 2 \left(\frac{r_{ij}}{r_{cut}} \right)^2 + \left(\frac{r_{ij}}{r_{cut}} \right)^4 \right]$$



-bond-

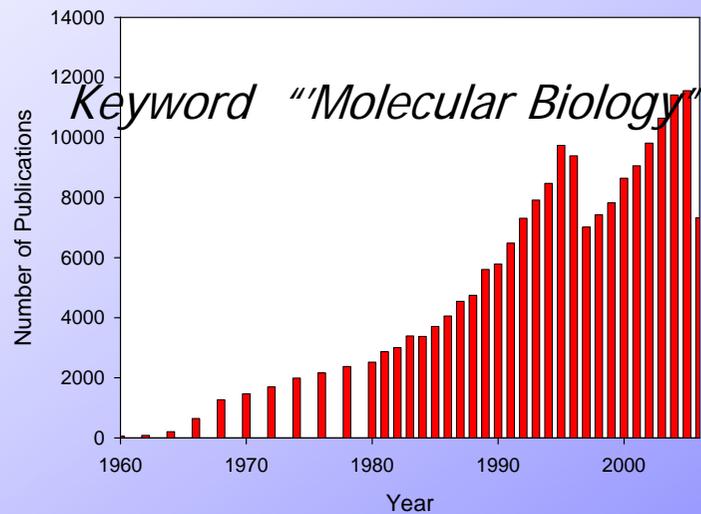
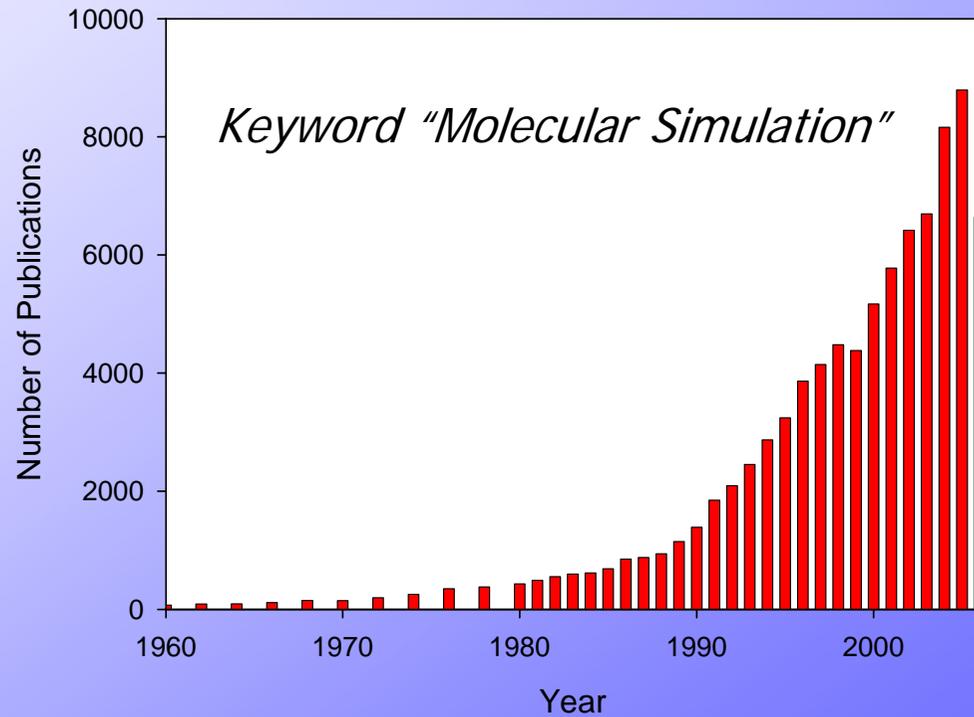
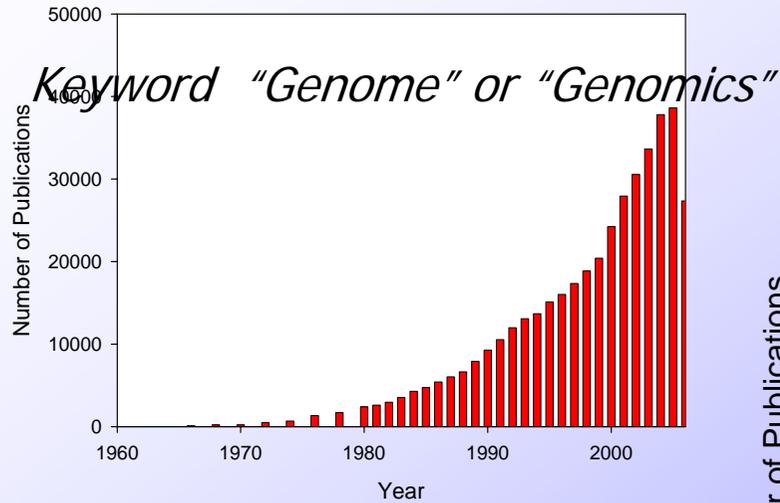


-angle-



-dihedral-

Publication Increase during the last 45 years - *from SciFinder*



"Publish or perish" refers to the pressure to publish work constantly in order to further or sustain one's career in academia. The competition for tenure-track faculty positions in academia puts increasing pressure on scholars to publish new work frequently.

CHARMM

Chemistry at HARvard
Macromolecular Mechanics

Supporting Area

- *Molecular Mechanics*
- *Molecular Dynamics*
- *Monte Carlo*
- *QM/MM*
- *Free Energy Calculation*
- *Coordinate Analysis*

Harvard Department of
Chemistry & Chemical Biology

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Group Pages
Research Areas
Publications
Affiliated Institutes and
Departments

Directory

Martin Karplus

The research of Professor Martin Karplus and his group is directed toward understanding the electronic structure, geometry, and dynamics of molecules of chemical and biological interest. In each study a problem that needs to be solved is isolated and the methods required are developed and applied. In recent years, techniques of *ab initio* and semi-empirical quantum mechanics, theoretical and computational statistical mechanics, classical and quantum dynamics as well as other approaches, including experimental NMR, have been used to obtain the desired solutions.

Solution Dynamics and Thermodynamics. The availability of a deeper understanding of the statistical mechanics of liquids and the development of molecular dynamics and Monte Carlo simulation techniques make it possible to attempt a microscopic (first principles) approach to a variety of problems in the chemistry of solutions. Under study are the conformational equilibria of biopolymers, cage effects in reaction dynamics, and the spectra of molecules in solution.

Protein and Nucleic Acids. These biopolymers play an essential role in living systems. The applications of molecular and harmonic dynamics techniques have delineated the time scales and magnitudes of the fluctuations that occur and have indicated their functional importance. Free energy simulations make it possible to determine the effects of mutations on function and stability. Methods are now being developed to treat active sites and to study enzyme reactions at the same level of detail as is available from the theory of gas phase reactions.

Selected Publications

- Aspects of Protein Reaction Dynamics: Deviations from Simple Behavior, *J. Phys. Chem. B* **104**, 11-27 (2000), by M. Karplus.
- Understanding Protein Folding via Free-Energy Surfaces from Theory and Experiment, *PNAS* **97**, 331-339 (2000), by A. R. Dinner, A. Sali, L. J. Smith, C. M. Dobson, and M. Karplus.
- A Dynamic Model for the Allosteric Mechanism of GroEL, *J. Mol. Biol.* **302**, 303-313 (2000), by J. Ma, P. B. Sigler, Z. Xu and M. Karplus.
- Triosephosphate Isomerase: A Theoretical Comparison of Alternative Pathways, *J. Am. Chem. Soc.* **123**, 2204-2290 (2001), by Q. Cui and M. Karplus.

UBB.threads™ Groupeo, Inc.

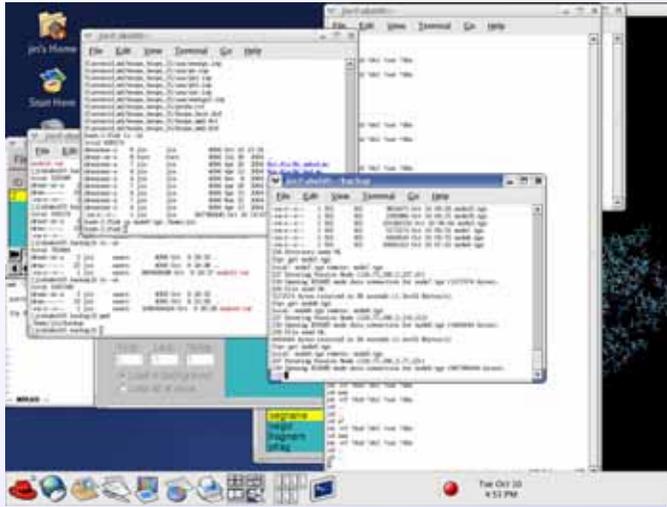
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User Discussion & Questions			
	Threads	Posts	Last post
Setup, I/O, and Basic questions A place for questions regarding the setup of scripts and I/O	783	2999	Re: Box size info during N... (rmv) - 10/10/06 05:39 PM
Energy terms, Constraints, Restraints, and Salvation A place to discuss energy function terms and related topics	300	1098	Re: fix a part of the prot... (rmv) - 10/09/06 05:17 PM
Parameter Set Discussion A place for energy parameters questions and discussions	403	1349	Topology and parameters fr... (Chiraj) - 10/11/06 12:40 AM
Molecular Dynamics A place to discuss MD, trajectory analysis, and related methods	586	2245	Re: crystal build cutoff (lennart) - 10/10/06 02:23 PM
Minimization, Normal modes, Monte Carlo,... A place to discuss non-MD based energy methods	140	496	Re: Minimization - Residue... (vink) - 09/29/06 06:12 PM
QM/MM Discussion and Questions A place for QM/MM questions: semi-empirical and <i>ab initio</i>	96	293	Change changes after Games... (Renee) - 10/04/06 12:36 PM
Installation and Performance A place to discuss compilation, execution, and performance issues	253	1090	Re: Help with installation... (lennart) - 10/10/06 11:02 AM
Other User Discussion and Questions A place for miscellaneous CHARMM questions	103	299	Re: Segmentation fault with... (lennart) - 10/02/06 02:00 PM
General Chemistry Discussions Forum to discuss general computational chemistry questions	15	57	- 09/08/06 02:15 AM
CHARMM Interfaces			
	Threads	Posts	Last post
MMTSB MMTSB CHARMM interface forum	49	155	Re: MMTSB Toolset Website... (meskel) - 10/10/06 08:51 AM
Insight & Quanta Discussion related to using CHARMM with Insight or Quanta	41	103	Re: parameter file creatio... (saravanaprakash) - 08/18/06 04:55 AM
GAMNESS-UK discussion A place to discuss QM/MM calculations using GAMNESS-UK	7	18	Re: Total and QM Energies... (tong) - 04/09/06 02:36 PM
CHARMM Community			
	Threads	Posts	Last post
CHARMM News A place to inform the community about news and publications	15	41	Re: Hardware status update (tim) - 07/11/06 06:45 PM
Bug Reports & Fixes A place to submit or review bug reports and bug fixes	90	236	Re: MaxFn in RMSDyn (Shany) - 09/07/06 10:15 AM
Script Archive A place to post and download CHARMM scripts	64	319	Re: hbonds.mg (rmv) - 10/04/06 10:59 AM
Suggestions and Requests A place to suggest new features for CHARMM or this website	14	38	License demanding (bluesky) - 03/23/06 12:41 AM
CHARMM Course Place to discuss the CHARMM Course	21	36	modified an hoc replica ex... (rmv) - 09/28/06 10:56 PM

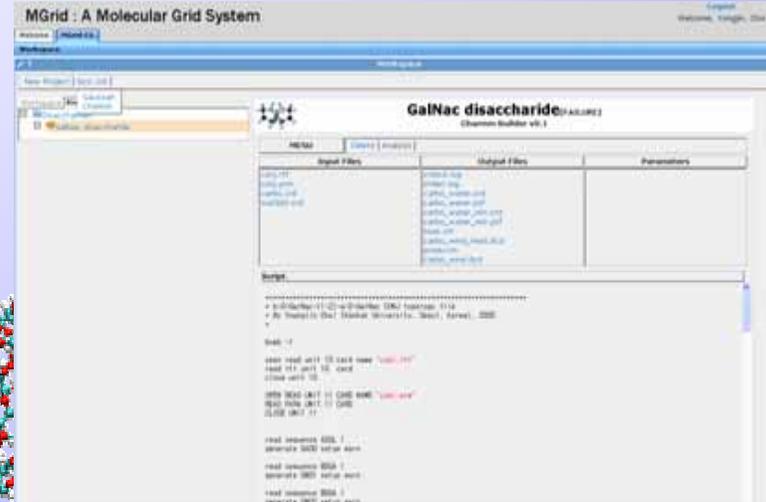
<http://www.charmm.org>

Shell Terminal

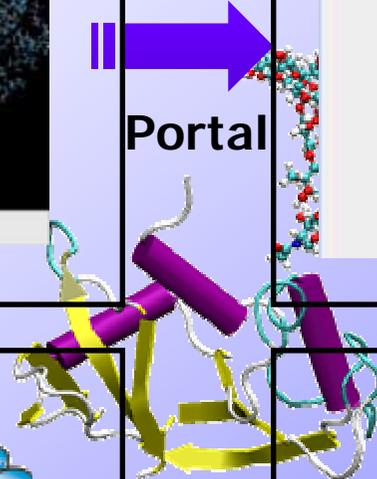


Molecular Simulations & e-Science

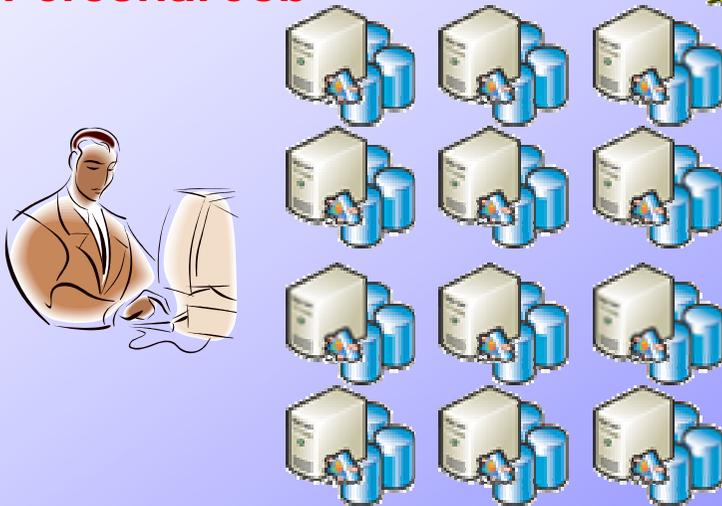
Web-Interface



Portal

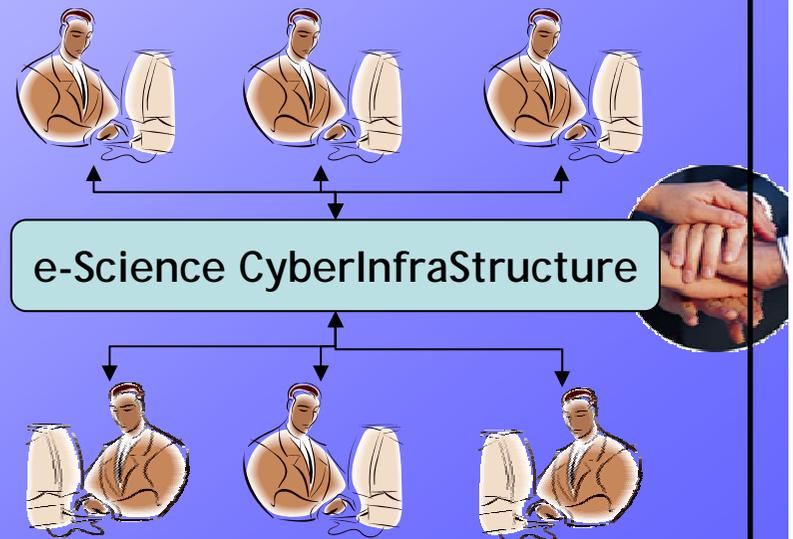


Personal Job

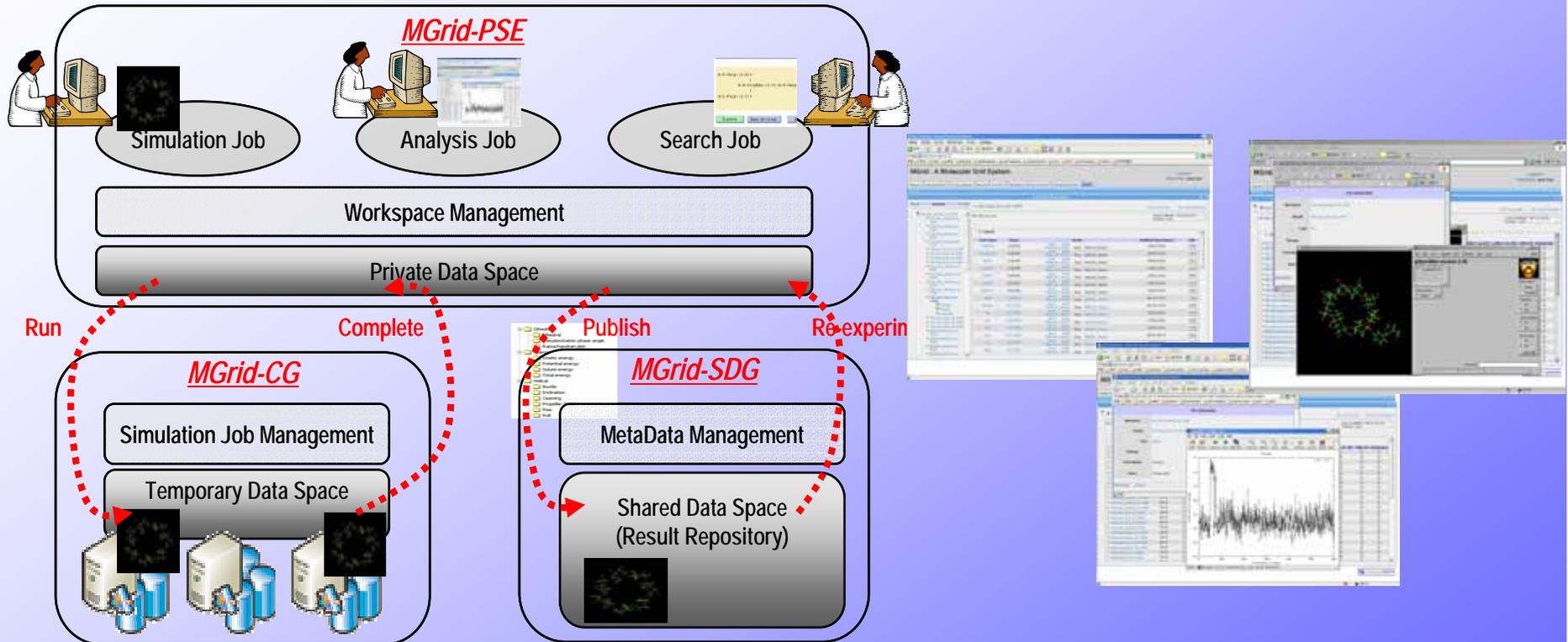


Collaboration

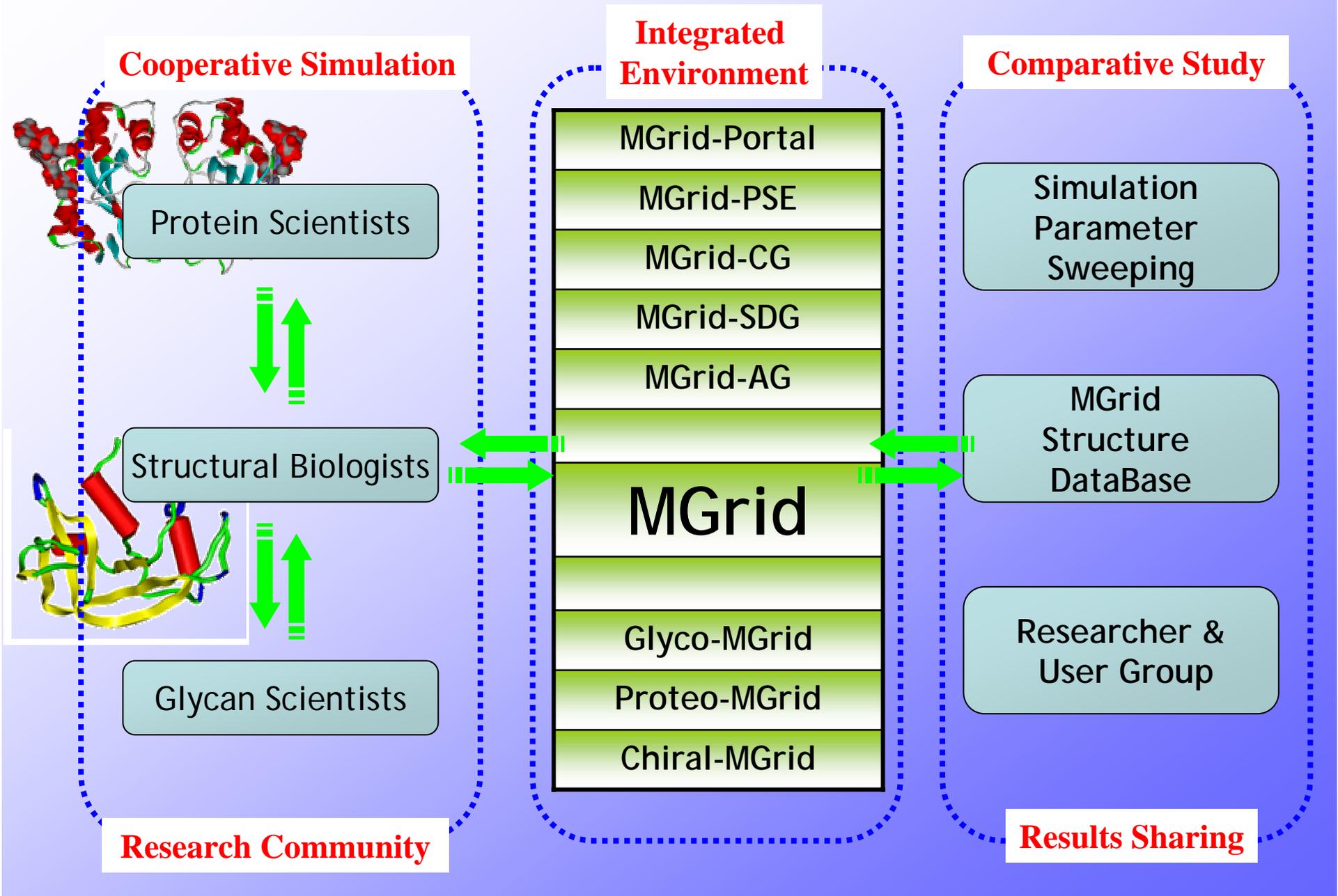
Multidisciplinary Work



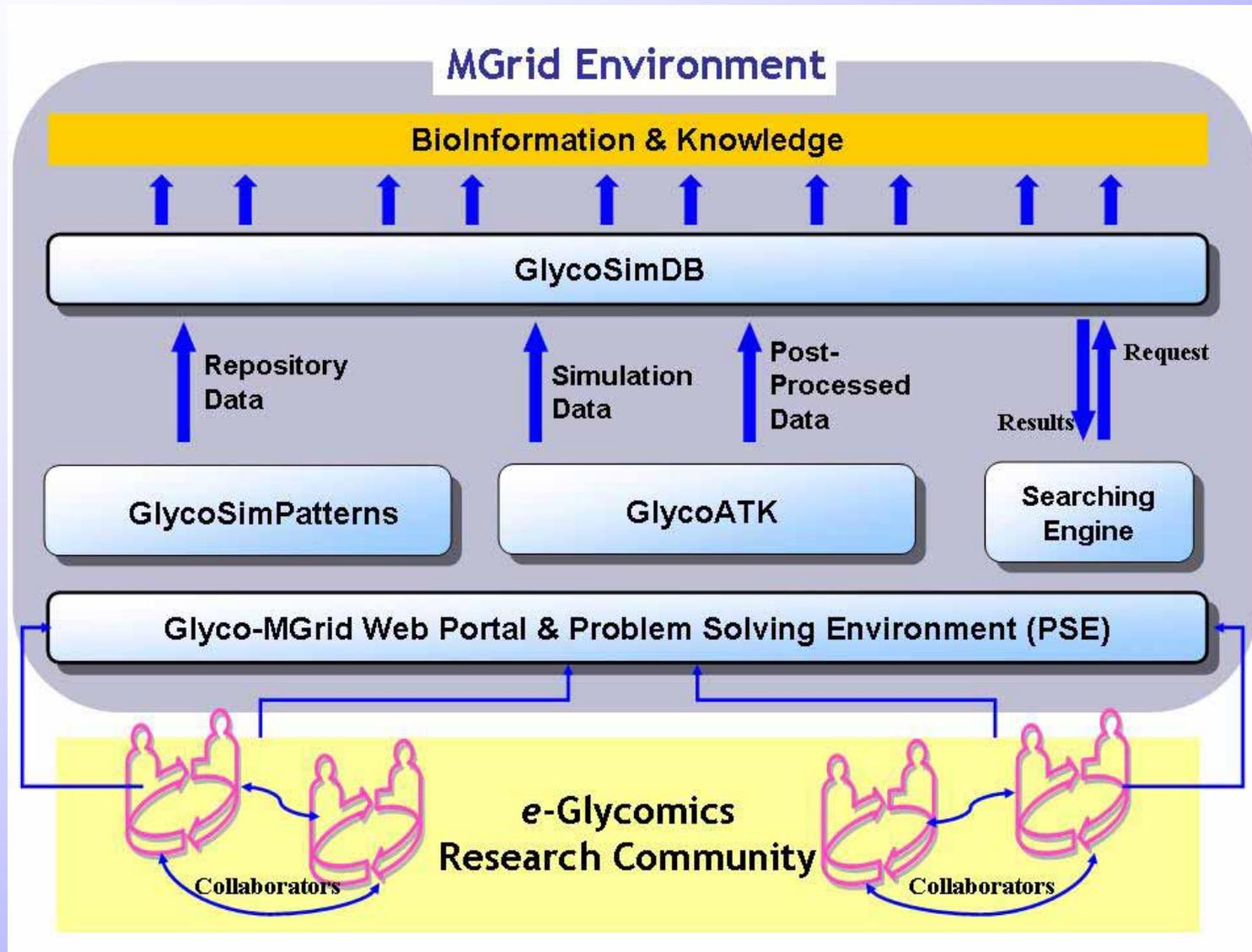
Architecture of MGrid



Vision of MGrid



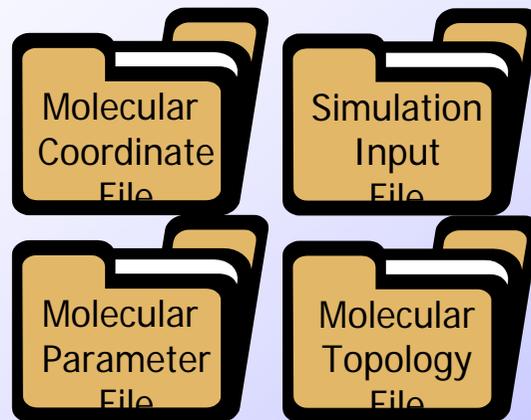
Architecture of Glyco-MGrid



Components of Glyco-MGrid

Computation Facility

Simulation Program



Computing Resources

DataBase Facility

Simulation Input



Job Title
Job Description
Molecular Name
Force Field
Program
Target System



Temperature
Pressure
Frame Number
Temp. Bath
Pressure Bath



Solvation
PBC
Crystal Type
Ensemble
Dielectrics
NonBond Option



Simulation Time
Time Step
Total Step
Update Number
Save Frequency
Restart Saving

Simulation Output



Trajectory File
Structure File
Coordinate File
Restart File
Velocity File
Output Log File

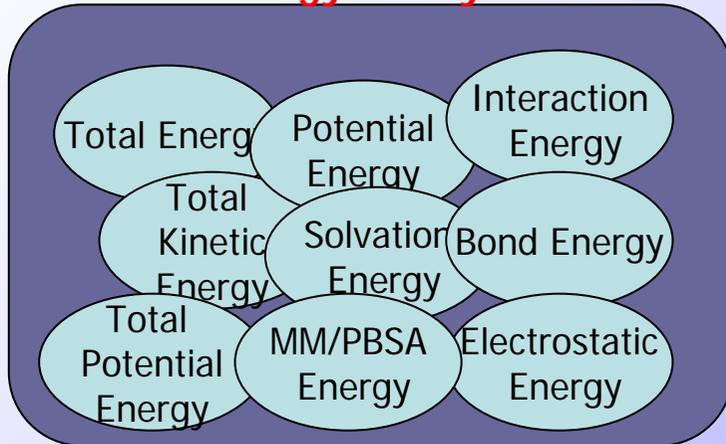


Float Number
Number List
Molecular Figure
Data Plotting
2-D Scatter Plot
Probability Plot

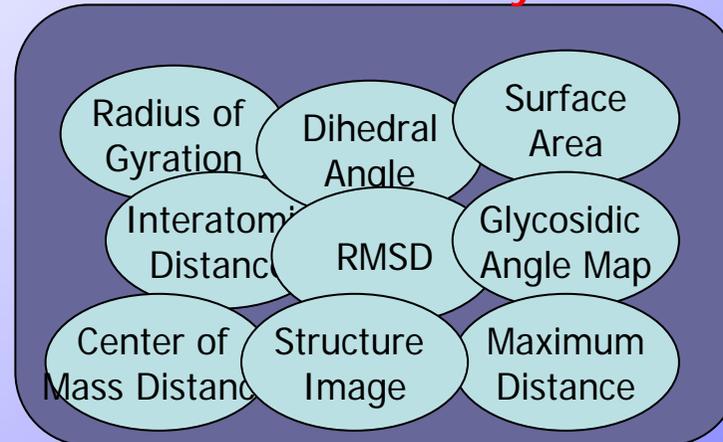
Components of Glyco-MGrid

AnalysisToolKit Facility

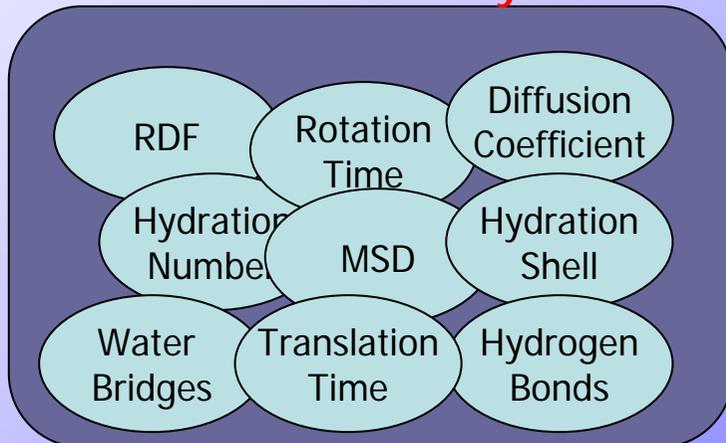
Energy Analysis



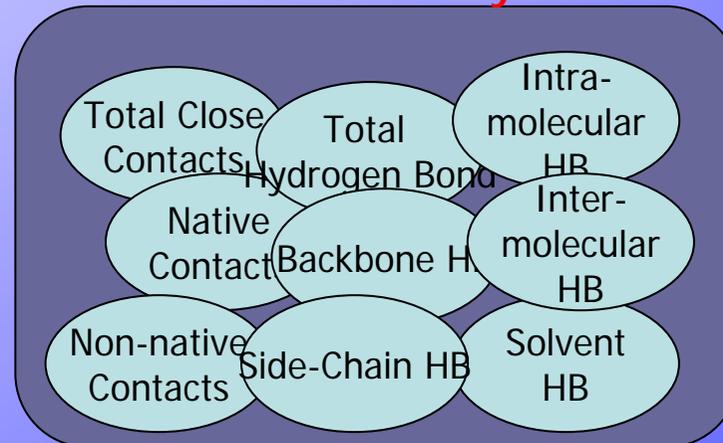
Structure Analysis



Solvation Analysis



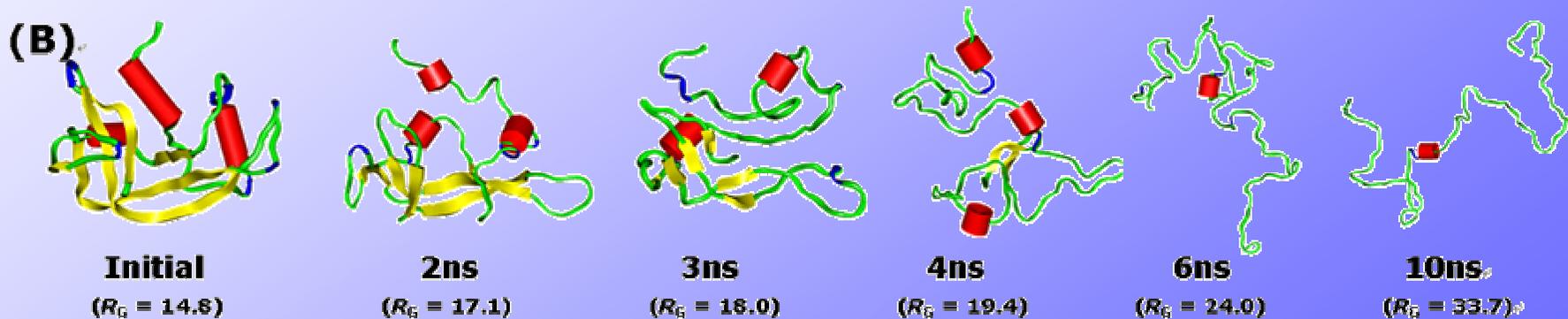
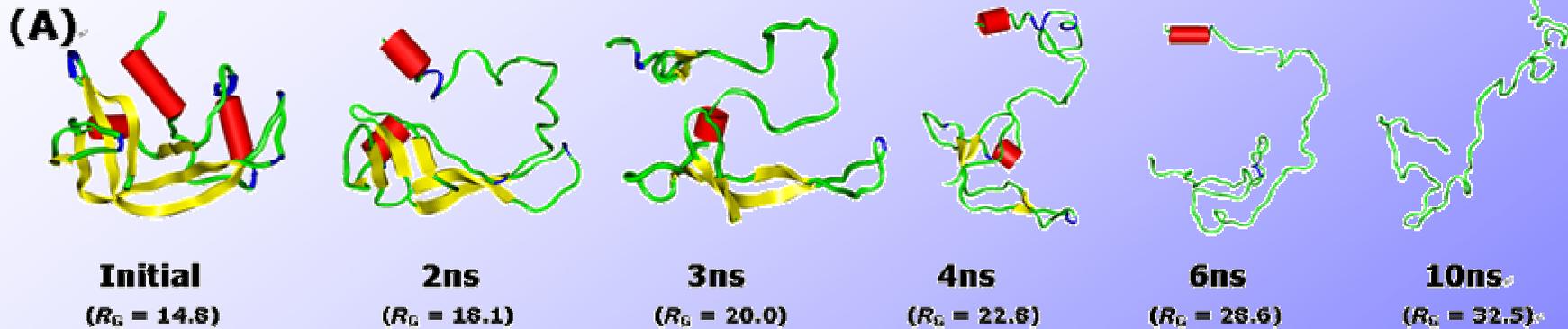
Number Analysis



Research Example

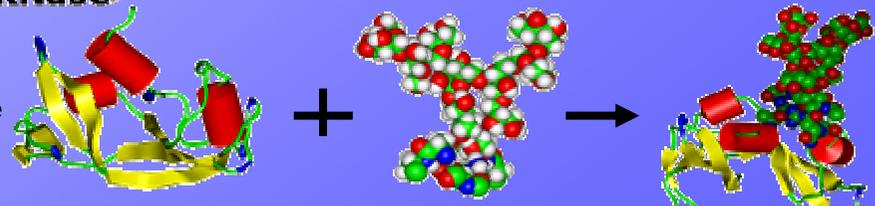
Thermal Stability of Unglycosylated RNaseA and *N*-acetylglycosylated Glc_RNase

RNaseA



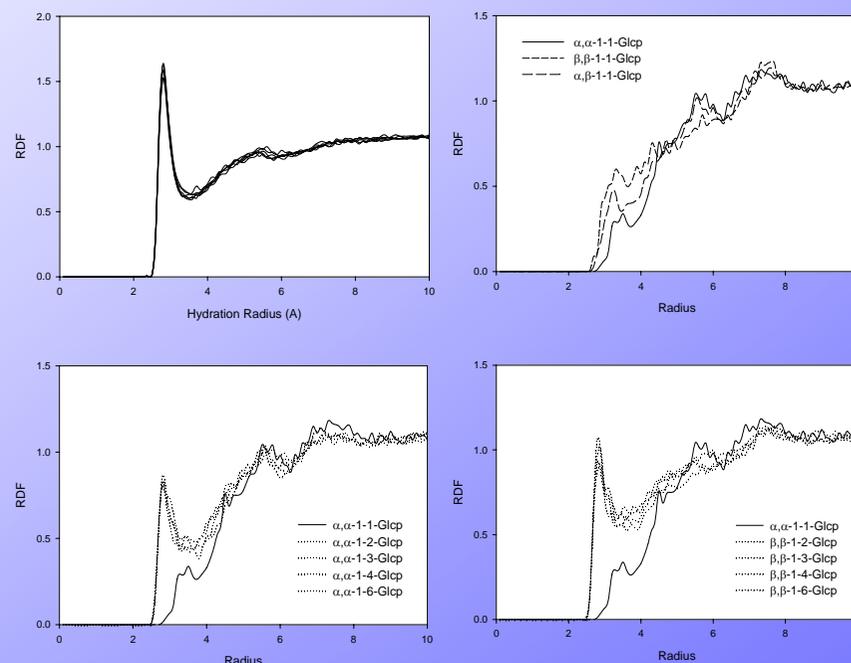
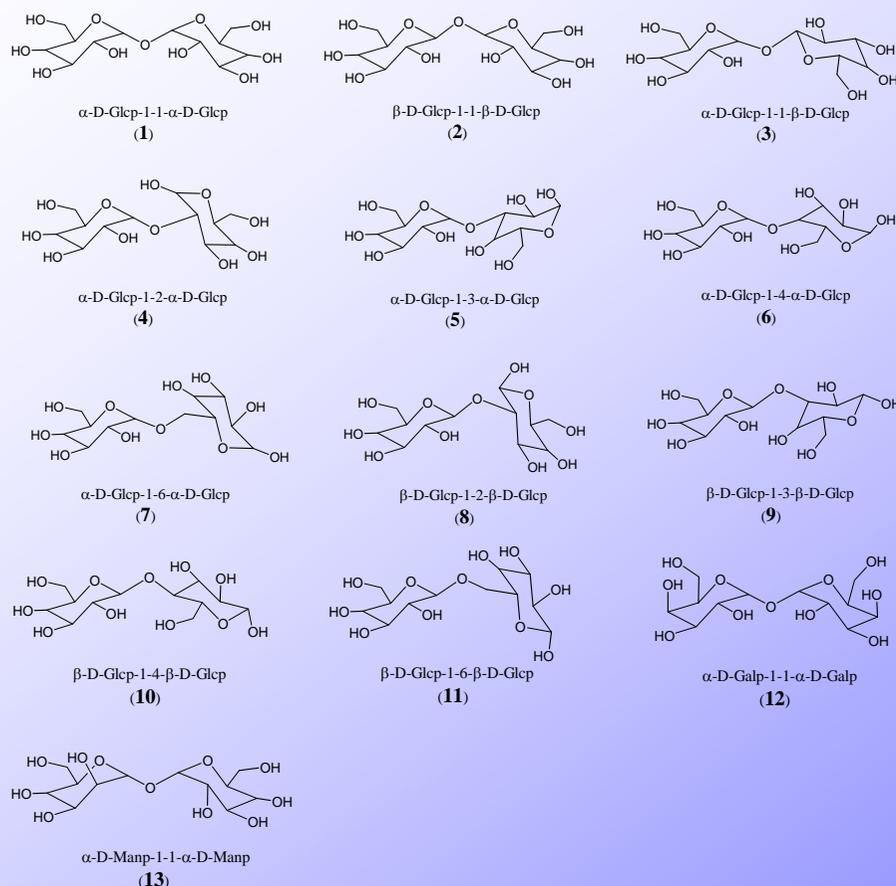
Glc_RNase

Protein + Carbohydrates => Stability Increase



Research Example

Conformation and Hydration of the Series of Sugars



The radial distribution function (RDF) of water molecules around disaccharides. (A) RDF around all oxygen atoms of each disaccharides (B) RDF around glycosidic oxygen of 1, 2, and 3 (C) RDF around glycosidic oxygen of 1, 4, 5, 6, and 7 (D) RDF around glycosidic oxygen of 1, 8, 9, 10, and 11. The RDF of water around whole trehalose is not dissimilar to other sugars. But, the RDF of water around glycosidic oxygen of trehalose is quite dissimilar to other linkage typed disaccharides. Only 1,1-linked trehalose showed anisotropic water distribution among the other 1,2-, 1,3-, 1,4- or 1,6-linked sugars.

Schematic diagrams of the glycosidic linkage model of the sugars studied in this work.

Youngjin Choi; Kum Won Cho; Karpjoo Jeong; Seunho Jung. Molecular dynamics simulations of trehalose as a 'dynamic reducer' for solvent water molecules in the hydration shell. Carbohydrate Research (2006) vol 341. 1020–1028

Cooperative Simulation

Integrated Environment

DataBase

glycosylation

RNaseA Protein

- Researcher A -

Glycosylation with different position

- Researcher B -

RNaseA Protein

- Researcher C -

RNaseA Protein

Glycosylation with different sugar

Research Community



MGrid

MGrid -PSE	MGrid -CG	MGrid -SDG	MGrid -AG
------------	-----------	------------	-----------

Molecular Model & Simulation Output



- Trajectory File
- Structure File
- Coordinate File
- Restart File
- Velocity File
- Output Log File

Browsing & Searching Similar Research

MGrid Portal

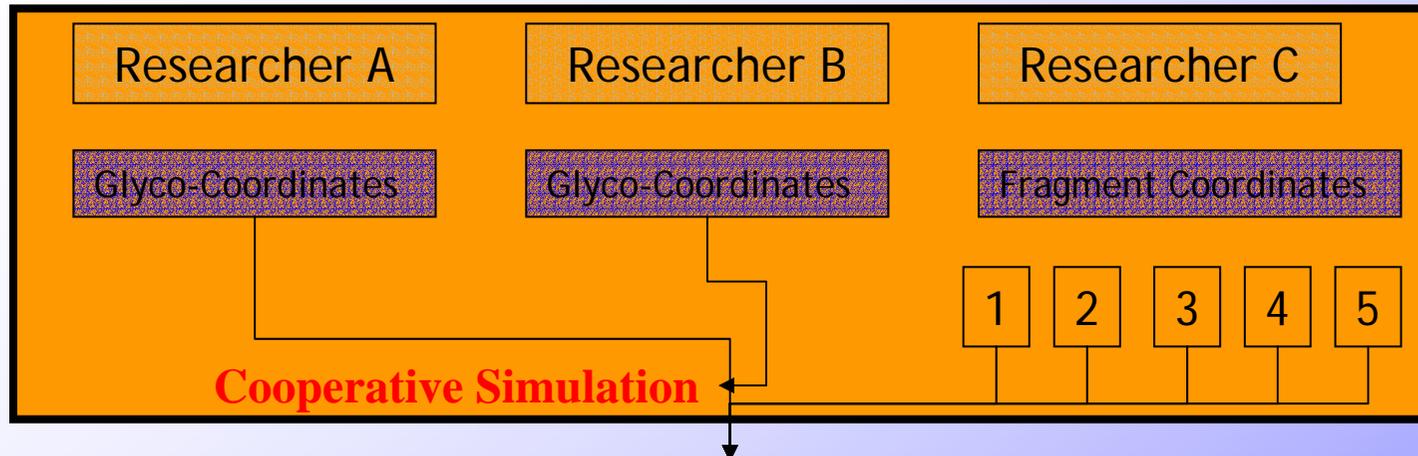
Data Retrieval & Sharing

Statistics & Data Mining

Researcher B and C perform Re-simulation from the results of Researcher A

Comparative Study & Results Sharing

Glyco-Structure Motif Searching Project Scenario



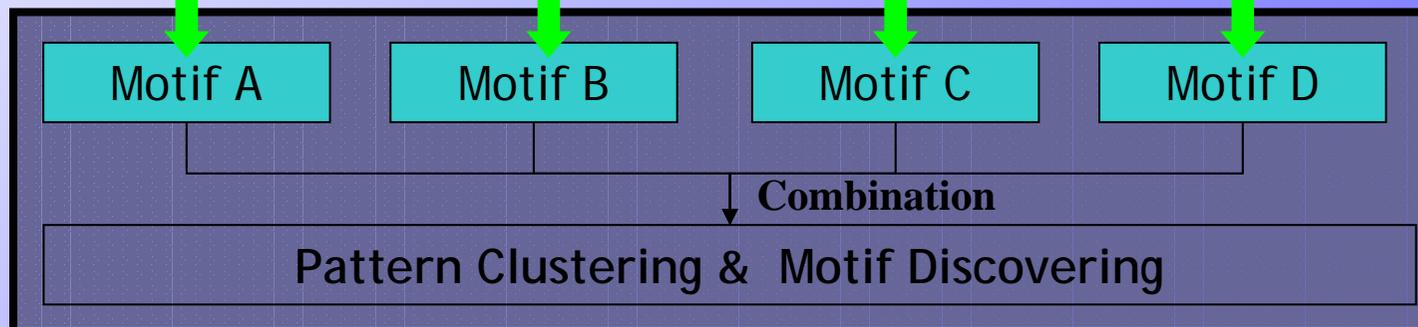
**Research
Community**



**Integrated
Environment**

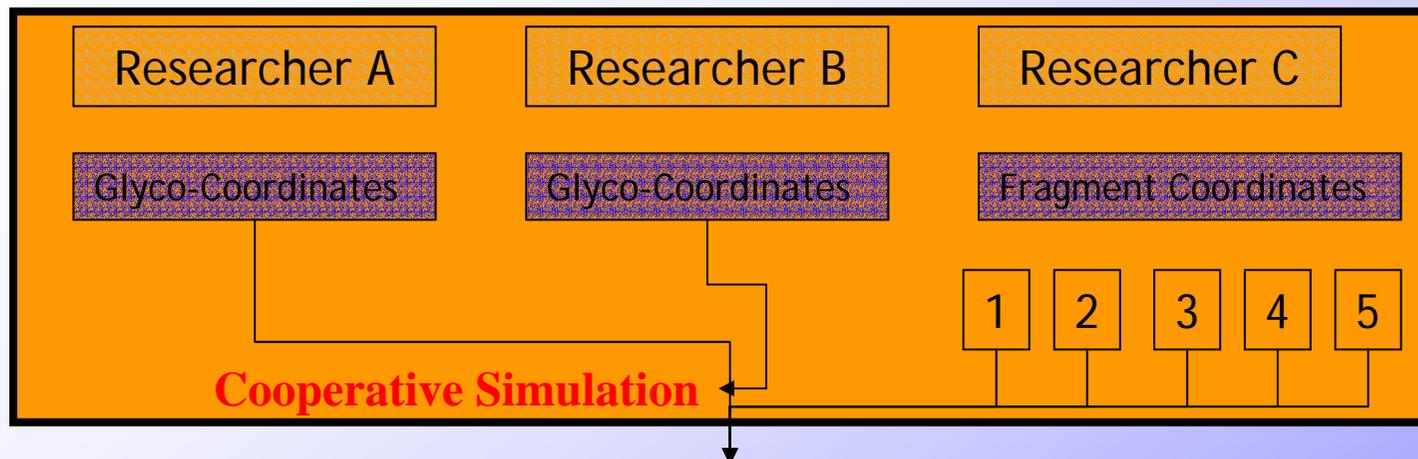


**Comparative
&
Statistical
Study**



**Results
Sharing**

Disease-Related Glycan Modeling Project Scenario



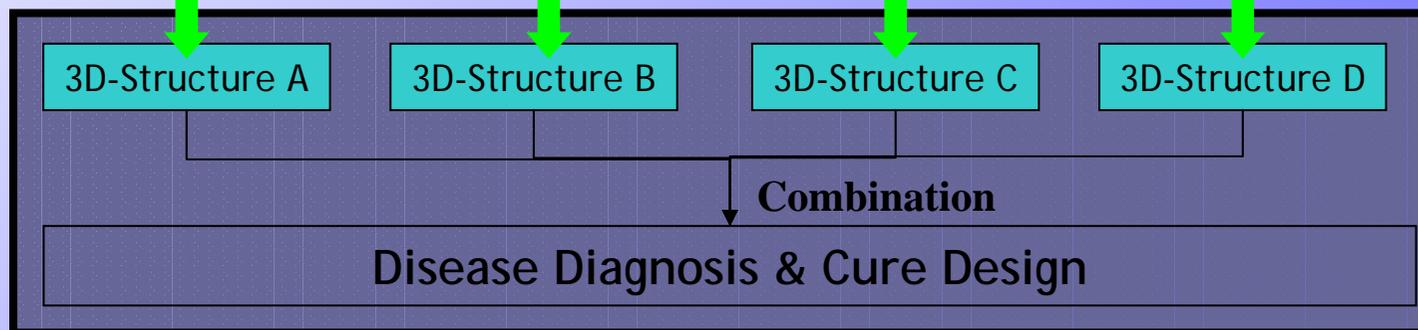
**Research
Community**



**Integrated
Environment**

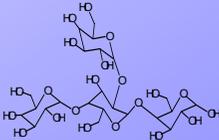
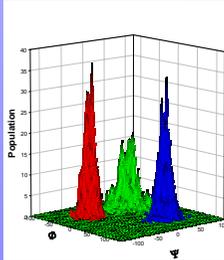
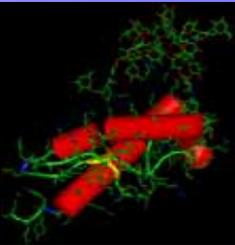


**Comparative
&
Statistical
Study**



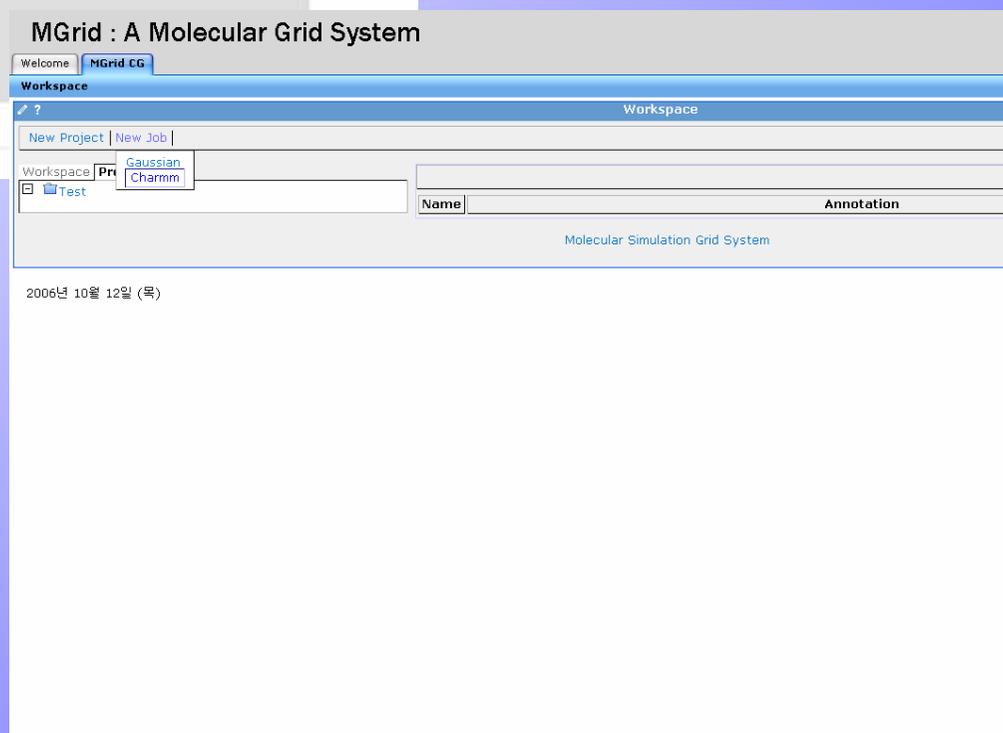
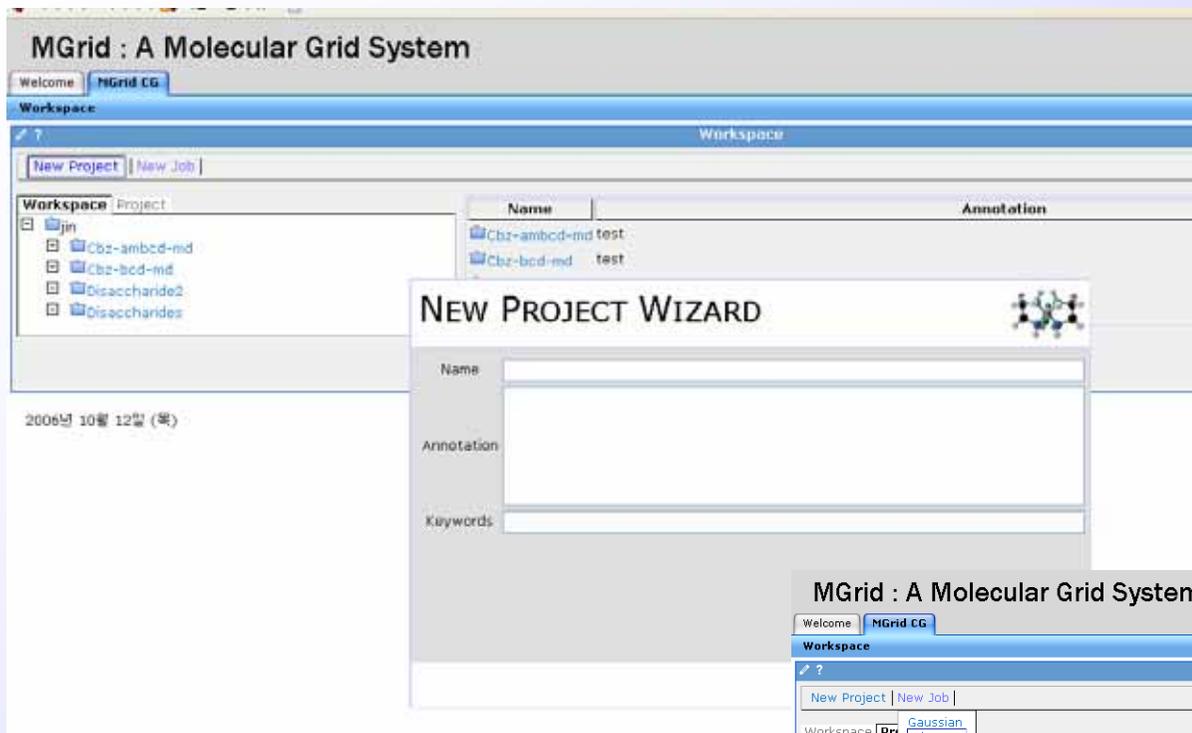
**Results
Sharing**

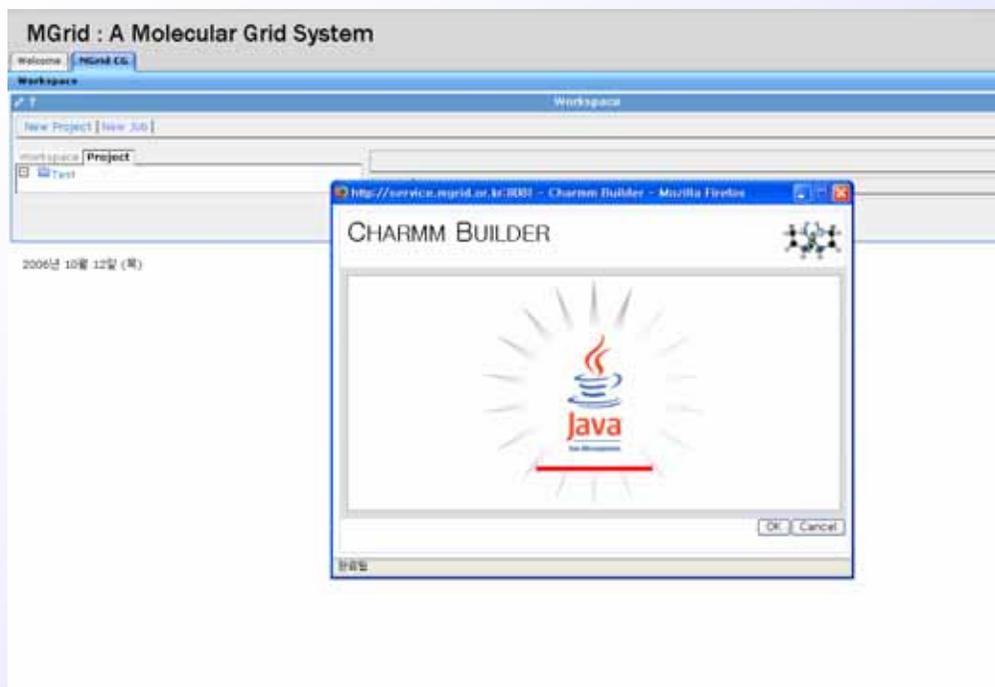
Current-Status of Glyco-MGrid Project

Glyco-compounds	Research Project	Job Details	Analyses
Glycan	Branching	Branching effect on the glycan conformation	
	Glycan Core	Calculation of biological core glycan structure	
Sugar compounds	Glycosidic Linkage	Glycosidic angle map of each glycosidic linkage	
Poly-saccharide	Microbial Carbohydrates	MC and MD conformational searching of bacterial carbohydrates	
	Cyclic Carbohydrates	Conformational characteristics of cyclic carbohydrates	
Glycoprotein	Unfolding	Unfolding simulations for the stability and conformations of glycosylated proteins	
	Folding	Folding simulations for the conformational effects of glycosylation	
	Function	MD simulations for the biological function of glycoproteins	

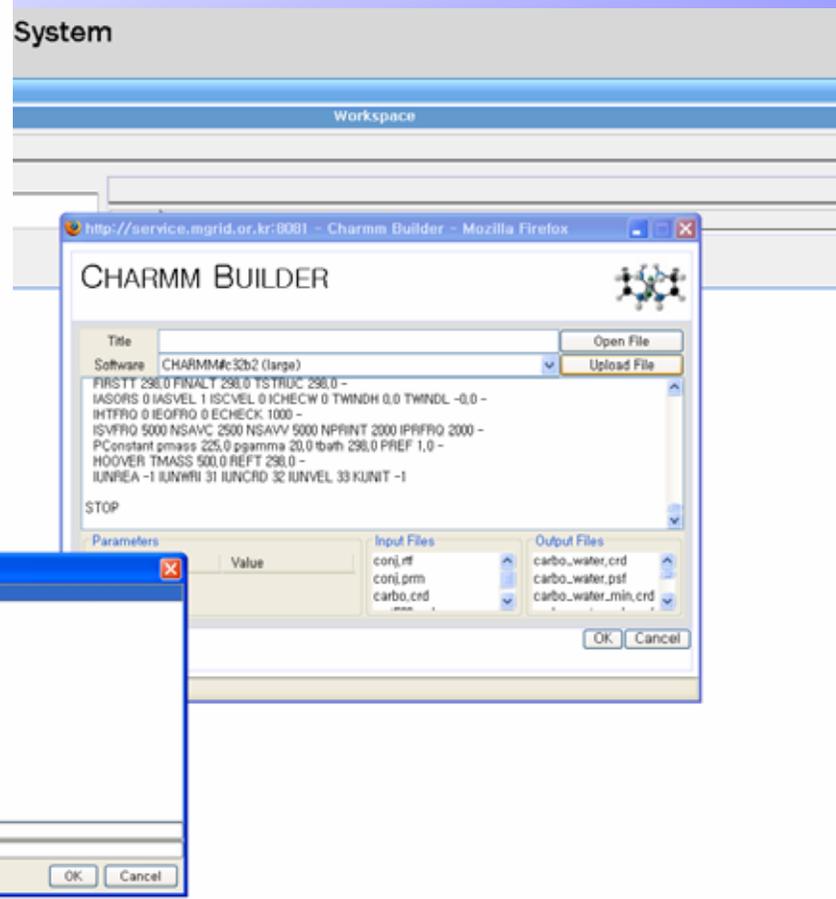
Use on the MGrid

1. Project & CHARMM Job





2. CHARMM Input Script & File Upload



MGrid : A Molecular Grid System

Welcome | MGrid EG

Workspace

New Project | New Job

Workspace | Project

Test

2006년 10월 12일 (목)

http://service.mgrid.or.kr:8081 - New Folder - Mozilla Firefox

CHARMM BUILDER

Successfully job submitted.
Click 'Close' and then reloading your project tree and list.

Close

3. CHARMM Job Running

Logout
Welcome, Youngjin, Choi

space

Test MD
Charmm Builder v0.1

MD Analysis

Output Files	Parameters
stdout.log stderr.log carbo_water.crd carbo_water.psf carbo_water_min.crd carbo_water_min.psf heat.rst carbo_wmd_heat.dcd produ.rst carbo_wmd.dcd	

Script.

```

.....
• b-D-GalNac-(1-2)-a-D-GalNac CONJ topology file
• By Youngjin Choi (Konkuk University, Seoul, Korea). 2005
•
boas -l

open read unit 10 card name "conj.rtf"
read rtf unit 10 card
close unit 10

OPEN READ UNIT 11 CARD NAME "conj.prm"
READ PARA UNIT 11 CARD
CLOSE UNIT 11

read sequence ADGL 1
generate GADD setup warn

read sequence EDGA 1
generate GND1 setup warn

read sequence EDGA 1
generate GND2 setup warn

```


5. Post-Processing of the Trajectory

Microsoft Excel - TKE.csv

파일(F) 편집(E) 보기(V) 삽입(I) 서식(O) 도구(T) 데이터(Q)

A5 -6864.9681

	A	B	C	D	E
1	-6907.18				
2	-6901.48				
3	-6890.53				
4	-6878.01				
5	-6864.96				
6	-6854.13				
7	-6840.67				
8	-6826.52				
9	-6813.09				
10	-6801.75				
11	-6783.82				
12	-6769.74				
13	-6757.72				
14	-6744.86				
15	-6724.59				
16	-6709.73				
17	-6692.56				
18	-6690.48				
19	-6666.63				
20	-6646.7				
21	-6642.99				
22	-6626.47				
23	-6601.98				
24	-6592.2				
25	-6579.92				
26	-6580.14				
27	-6570.05				
28	-6566.19				
29	-6540.09				
30	-6516.43				
31	-6514.68				
32	-6495.81				
33	-6471.82				
34	-6465.12				
35	-6446.11				
36	-6438.78				
37	-6423.99				
38	-6409.19				
39	-6387.03				
40	-6382.15				
41	-6364.19				
42	-6338.03				
43	-6311.68				
44	-6298.65				
45	-6293.32				
46	-6281.81				
47	-6263.61				
48	-6246.76				

\\TKE/ 준비

MGrid : A Molecular Grid System

Welcome MGrid CG

Logout
Welcome, Youngjin, Choi

Workspace

New Project | New Job

Workspace Project

- Test
- Test MD

Test MD(SUCCESS)
Chamm Builder v0.1

MENU Delete | MD Analysis

Input Files	Output Files	Parameters
conj.rtf conj.prm	stdout.log stderr.log carbo_water.crd carbo_water.psf carbo_water_min.crd carbo_water_min.psf heat.rst carbo_wmd_heat.dcd produ.rst carbo_wmd.dcd	

TKE.csv TKE.png TPE.csv TPE.png Temperature.csv Temperature.png

TPE.png

Total Potential Energy

Interaction energy

0 500 1000 1500

0 500 1000 1500

Trajectory Frames

read sequence BDGA I
generate GNDI setup warn
read sequence BDGA I