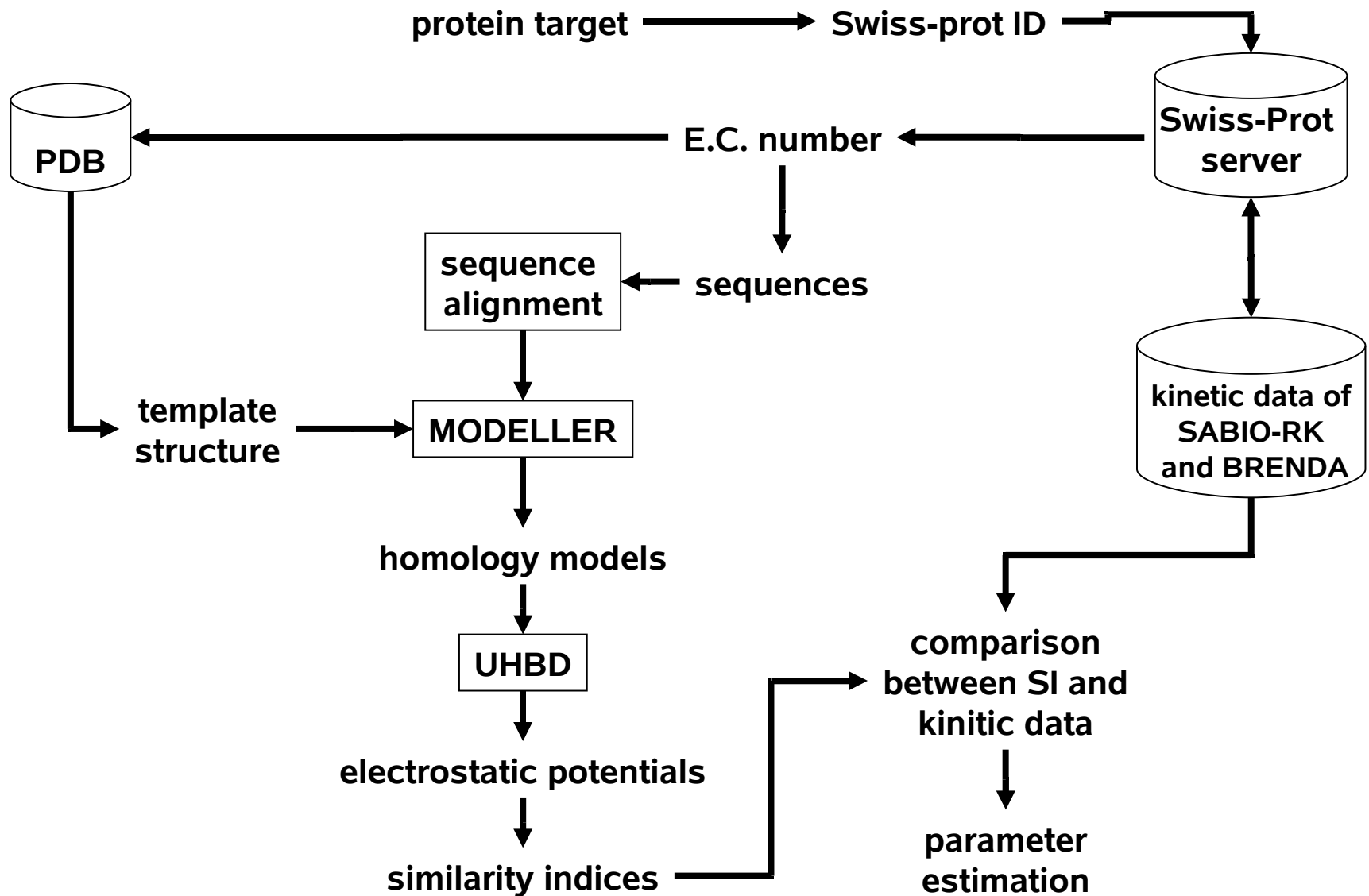


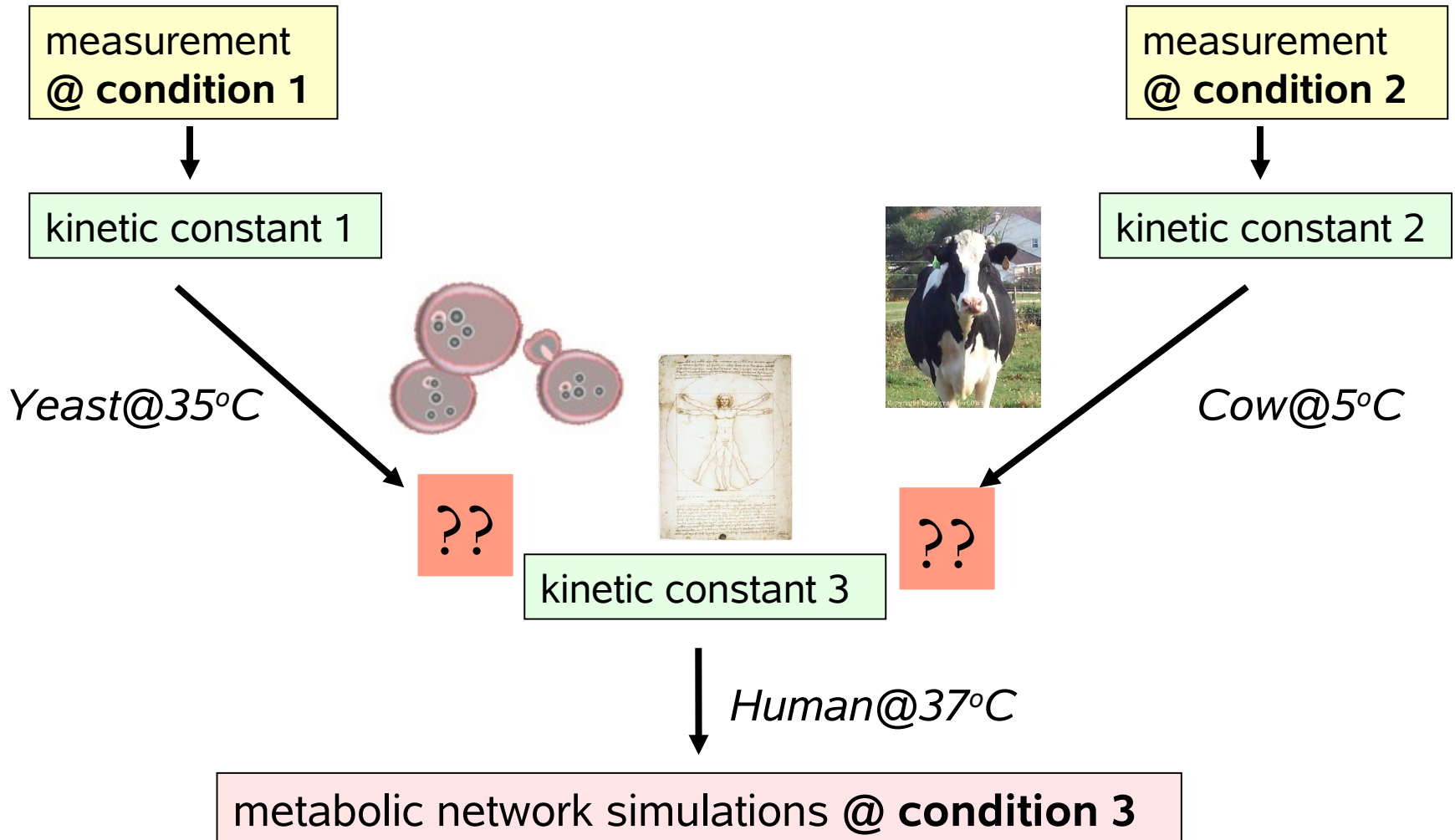
PIPSA

tutorial

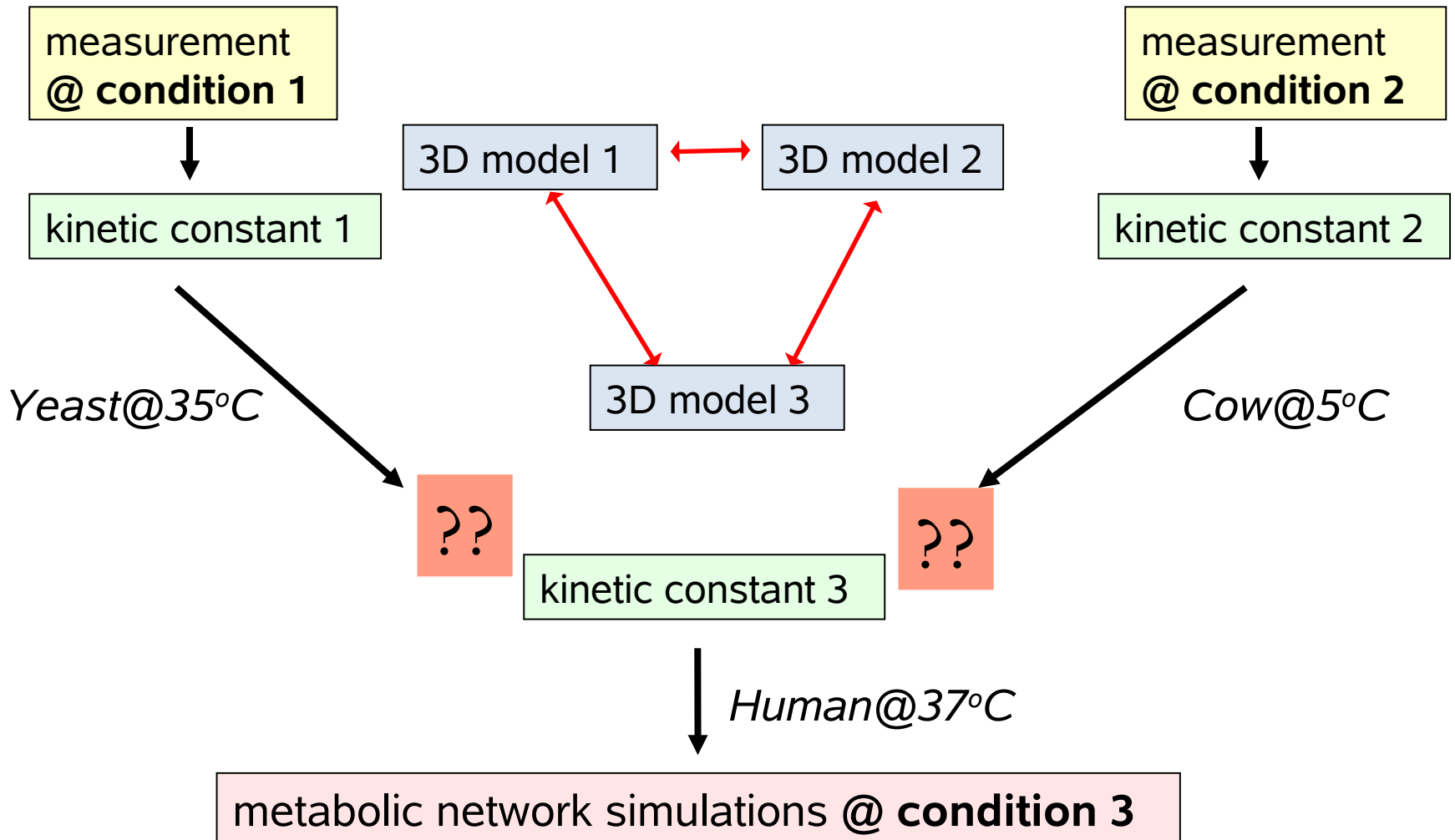
webPIPSA: workflow with homology modeling



Similarity-Based Estimate of Kinetic Constants



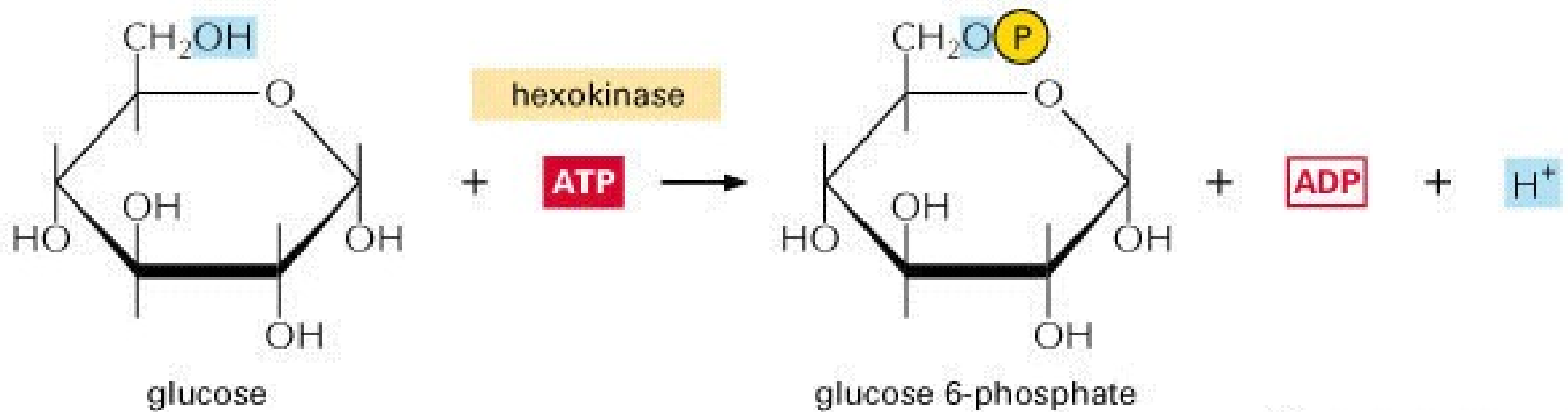
Similarity-Based Estimate of Kinetic Constants



webPIPSA

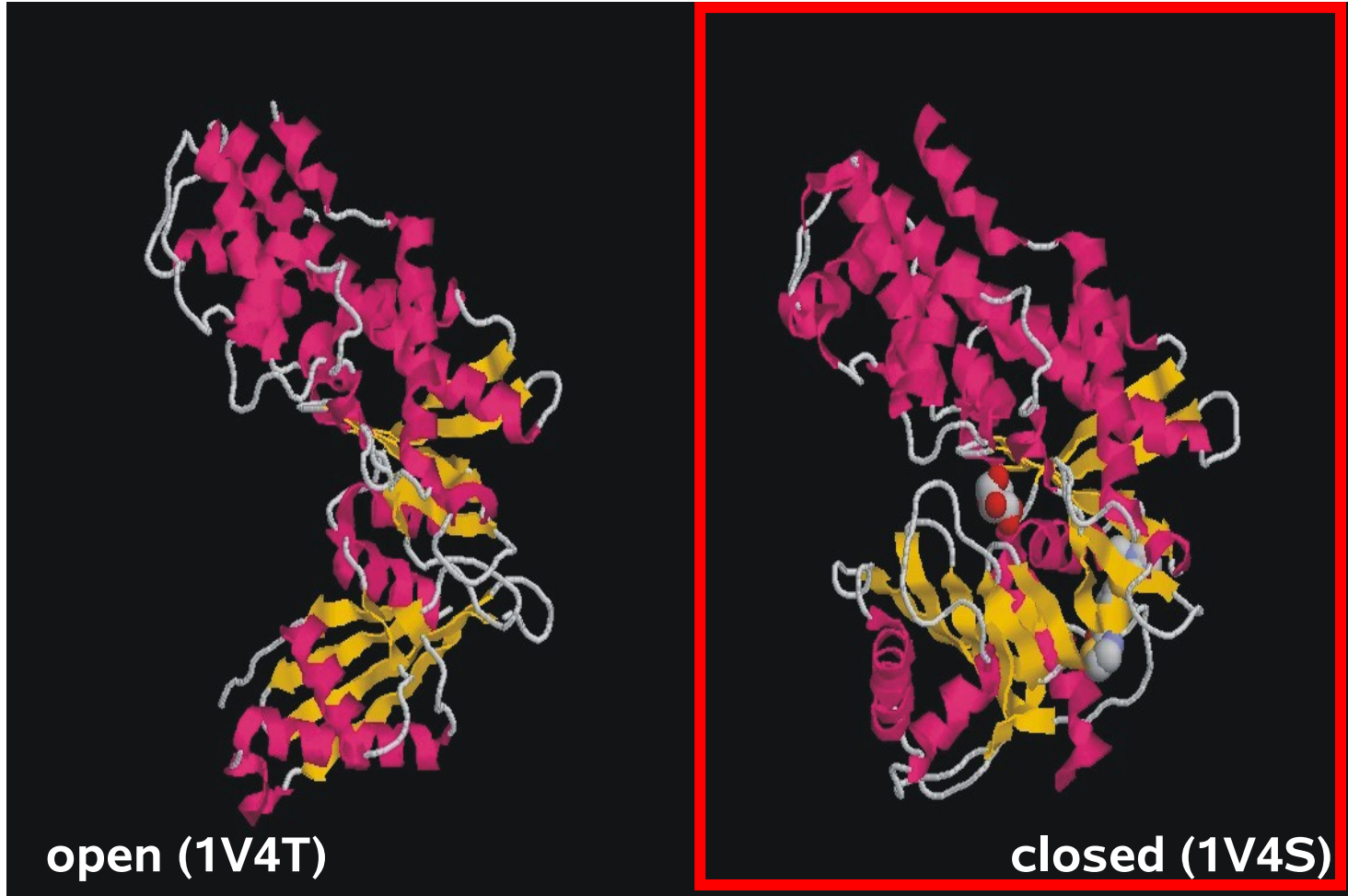
glucokinase (hexokinase)

glucokinase (hexokinase)



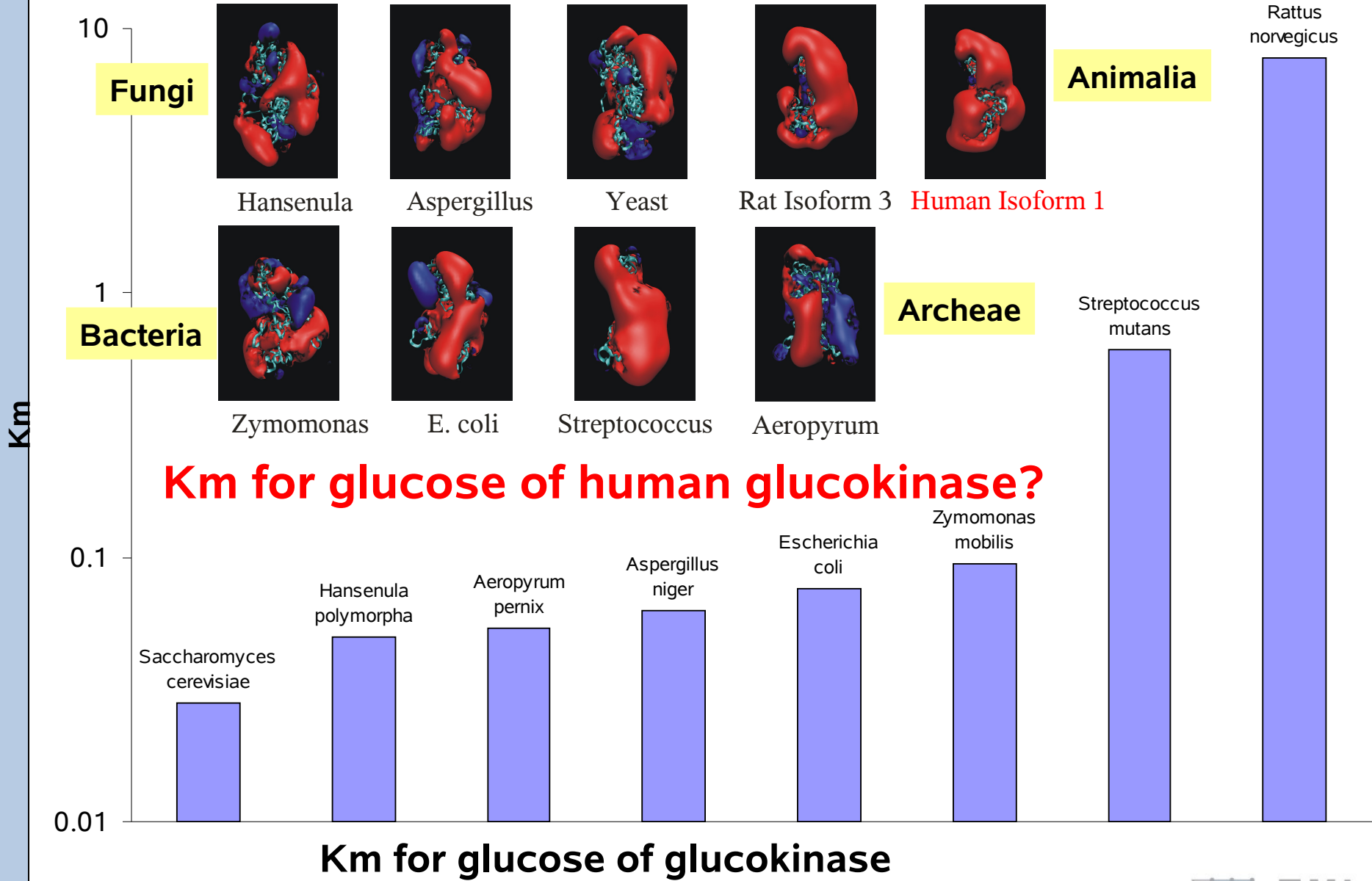
1. Identify Chemical Reaction of Interest

glucokinase (hexokinase)



3. choice of appropriate template
two human glucokinase isoforms
(open and closed form)

glucokinase (hexokinase)



SUCAMORE



SYCAMORE

SYCAMORE is a system that provides you with a facilitated access to a number of tools and methods in order to build models of biochemical systems, view, analyse and refine them, as well as perform quick simulations. SYCAMORE is not intended to substitute for expert simulation and modeling software packages, but might interact with those. It is rather intended to support and guide system biologists when doing computational research.

One important function of SYCAMORE is to allow you to build a draft model of your system of interest in such a way that kinetic expressions and parameters are as close to reality as possible. We want to emphasize that the resulting model still has a draft character and should not be taken as "the final model". However, setting up your model in such a way that parameters etc. are as close to reality as possible on the basis of literature data and computational parameter estimation methods should facilitate any parameter fitting methods that you want to employ later on.

SYCAMORE is a joint project of the Molecular and Cellular Modeling Group (MCM) and Scientific Databases and Visualization Group (SDBV) at [EML Research](#), as well as the department for [Modeling of Biological Processes](#) at the University of Heidelberg. It is supported by the Federal Ministry of Education and Research within the HepatoSys initiative.

Please be aware that this is a prototype release. We are constantly improving the system and would appreciate your comments w.r.t. bugs and improvements of user-friendliness!

(Last updated January 2008)

enter

<http://sycamore.eml.org>



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SYCAMORE

SYCAMORE allows you to build, view and edit models, to analyze and refine them, to perform simulations, sensitivity analysis and parameter estimations. To do so, you may start with one of the following options:

- Build a new model starting from scratch by defining reactions, metabolites, kinetic equations and parameters. [build new model](#)
- Build a new model with the support of SABIORK, a database that stores reactions and their corresponding kinetic parameters. [build SABIORK model](#)
- Load a SBML model from your hard disk. [load model from disk](#)
- Load a SBML model from projects. SYCAMORE offers the possibility to store complete and incomplete models in an internal database as your personal 'projects'. [load model from projects](#)
- Load an example model for testing of SYCAMORE. [load example model](#)
- Additionally, you may perform parameter estimations in order to determine unknown parameter values. [parameter estimation](#)

parameter estimation



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Registration

We request registration because parameter estimations may take between a couple of minutes and - in case of very complex calculations - several days. In addition, because CPU capacity is restricted, all requests are queued, thus it might be that it takes some time even for simple estimations. In any case, you will be notified by email on the result of the estimation(s), therefore an email address is required. Without email registration, parameter calculations will not be performed.

In order to access (load, view, edit, save) your personal models, you must register. In case that you are not registered yet, choose 'new registration'.

Additionally, the workflow for parameter calculations makes use of the program MODELLER, which requires an End-User Software License Agreement. You also need a MODELLER-key for using the program within the parameter estimation workflow.

REGISTERED USERS

Name:

(user name) (password)

[I can't remember user name / password](#)

register:

- user name
- YOUR email address
- password



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qPIPSA Parameter Retrieval and Estimation Module

What this module does?

1. Retrieval of relevant parameters and associated information from [BRENDA](#) and [SABIO-RK](#), as well as protein sequences from [Swiss-Prot](#) and protein structures from [PDB](#), [MODBASE](#) and [SWISSMODEL](#)
2. Parameter estimation using available protein structure information. Currently the [PIPSA](#) method is used to do this. PIPSA analysis can be used to aid the estimation of kinetic parameters from a similarity analysis of the electrostatic potentials of the enzyme for which the parameter is needed and the enzymes for which parameters are already known.

NOTE:

This is an initial beta release. All results generated by this server for PIPSA analysis should be considered preliminary at this stage¹

For more information on the use of this module [click here](#).

Retrieval of parameters and related information

This is based on insertion of a unique protein identifier. Currently a Swiss-Prot accession code must be given. The workflow depends on an [EC](#) annotation in the description line of your Swiss-Prot entry. This EC link is used to search in [BRENDA](#) and [SABIO-RK](#) entries.

Please enter :	
<input type="text"/>	Swiss-Prot accession code (eg. P35557 or P35520) [?]
<input type="text"/>	a valid email address [?]
<input type="button" value="Start search"/>	

In case of unknown or only vaguely known protein functionality ProFAT may assist in detecting protein function and structural homology.

<http://cluster-1.mpi-cbg.de/profat/profat.html>

ProFAT is a tool for the functional annotation of proteins via the detection of weak homologies. Sequence homology is detected with NCBI's PSI-BLAST system. Structural homology is detected with UCL's Threader software. These results are then combined by the use of GenBank annotation and basic text mining.

ProFAT requires the user to submit a keyword list along with the protein sequence. Several pre-made keyword lists are available, however, the system is used optimally with a user defined keyword list consisting of suspected or experimentally determined information.

Bradshaw C. R., Surendranath V., and Habermann B. BMC Bioinformatics 2006, 7:466

¹: Limitations currently are:

- Only single chain protein modelling
- Neglect of protein flexibility

•Swiss-Prot accession code
•YOUR email address



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Work in progress

This page will be reloaded automatically in a few seconds. Please wait.

The time required for a PIPSA analysis depends on several factors:

- the number of structures you submitted for analysis.
- the number of regions you have selected.
- the number of jobs in the request queue (submitted by other users)

Typically a PIPSA analysis takes from 10 min to 2 hours. A qPIPSA analysis requires for the download phase approx. 5-20 min, whereas the analysis requires 30 to 180 minutes.

If you start a [new search](#), the current search will only be accessible via the link in the email you receive.

Your request is being processed. There is 1 job in the request queue.

Here is an overview of the actions done and the advancement of the information retrieval (latest at top):

- Parsing of Swiss-Prot entry P0A6V8 using <http://www.expasy.org/uniprot/P0A6V8.bt> completed.
- Parsing of Swiss-Prot entry Q04409 using <http://www.expasy.org/uniprot/Q04409.bt> completed.
- Parsing of Swiss-Prot entry P17709 using <http://www.expasy.org/uniprot/P17709.bt> completed.
- Parsing of Swiss-Prot entry P21908 using <http://www.expasy.org/uniprot/P21908.bt> completed.
- Parsing of BRENDA entry 2.7.1.2 completed.
- Parsing of Swiss-Prot entry P35557 using <http://www.expasy.org/uniprot/P35557.bt> completed.
- Email sent to stefan.henrich@eml-r.villa-bosch.de

email: PIPSA analysis request



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Parameter Retrieval and estimation

Parameter retrieval: available information

After successful retrieval of kinetic data and structural models, do one of the following:

1. If no information was found, or the information is not suitable, start a new search with a new Swiss-Prot accession code. For this [click here](#).
2. Select a parameter from below and copy/paste it into your SBML model.
3. Assign a parameter based on an average of several retrieved values below and use it in your SBML model.
4. If there is structural information available, select a structural template and do a PIPSA to aid parameter assignment based on calculated electrostatic potentials of the retrieved proteins. The PIPSA analysis can be launched from this page [\[?\]](#).

To start a workflow for PIPSA, do the following:

1. In the section **Protein Structural Information** choose a template protein structure that you consider most suitable for protein structural modeling of your enzyme of interest (**Click on arrow first**). This is going to be used as a structural template in the subsequent homology modeling.
2. In the section **Region selection** below the structural information, you can make selections for Swiss-Prot features of your protein (eg. active site, binding region etc, **click on arrow first**). Additional PIPSA runs will then be performed to restrict the comparison to these regions.
3. In the section **Kinetic data** select Swiss-Prot sequences with relevant kinetic data (by default all sequences are selected).

Please find additional information about the Parameter Retrieval and Estimation on our [help page](#).

On this page, you'll find all the information gathered concerning the Swiss-Prot entry specified. This concerns both structural and kinetic data. There may be a lot of data, so use the triangles to display or hide information.

Here is the information found using the Swiss-Prot accession [P35557](#).

This entry is for the organism *Homo sapiens*.

Calculate electrostatically similar proteins (please first check selected models and sequence below)

At registration you have provided the following

key for MODELLER [\[?\]](#) Please correct if needed. **required MODELLER key**

Use modeller version 8v2

Use modeller version 9v1 (including loop refinement)

Use modeller version 9v1 (including loop refinement using DOPE score, takes longer)

email: Download for analysis of P35557 is complete



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► Structural information

► Region selection

▼ Kinetic data

Kinetic data is retrieved from the SABIO-RK and Brenda databases and concerns information associated with the Swiss-Prot entry given.

▼ Information retrieved from Brenda

The results specific to the query Swiss-Prot entry organism are presented first.

Information retrieved using EC [2.7.1.2](#)

Literature links refer to BRENDA. In case where no PubMed entry is linked in BRENDA, you will get the details of the reference paper.

1. Data specific to Swiss-Prot entry *P21908*, sequence derived from organism *Zymomonas mobilis*

▼ Km information						
Km value [mM]	Km value [mM] Maximum	Substrate	Organism	Comment	References	
0.5	-	6-N-(carboxyethyl)ATP	Zymomonas mobilis	-	641063	PubMed
0.55	-	6-N-(carboxymethyl)ATP	Zymomonas mobilis	-	641063	PubMed
0.38	-	6-N-(succinyl)ATP	Zymomonas mobilis	-	641063	PubMed
1.25	-	6-N-[N-(6-aminohexyl)carbamoyl]ATP	Zymomonas mobilis	-	641063	PubMed
0.5	-	ATP	Zymomonas mobilis	-	641063	PubMed
0.8	-	ATP	Zymomonas mobilis	-	641056	PubMed
0.22	-	D-Glucose	Zymomonas mobilis	-	641056	PubMed

1. Data specific to Swiss-Prot entry *P17709,Q04409*, sequence derived from organism *Saccharomyces cerevisiae*

▼ Km information						
Km value [mM]	Km value [mM] Maximum	Substrate	Organism	Comment	References	
0.05	-	ATP	Saccharomyces cerevisiae	-	641066	PubMed
0.028	-	D-Glucose	Saccharomyces cerevisiae	-	641066	PubMed

webPIPSA: hexokinase IV or D (P35557)



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1. Data specific to Swiss-Prot entry Q92407, sequence derived from organism *Aspergillus niger*

Km information						
Km value [mM]	Km value [mM] Maximum	Substrate	Organism	Comment	References	
0.063	-	D-Glucose	<i>Aspergillus niger</i>	-	641066 <small>PubMed</small>	

▼ Information retrieved from Sabio RK

Parameters are grouped per reaction stoichiometry and kinetic law. There may be more than one experiment for each of this group, so some parameters may have different values.

Information retrieved using EC 2.7.1.2

1. Data specific to Swiss-Prot entry P35557, sequence derived from organism *Homo sapiens*

Reaction: ATP + D-Glucose = ADP + D-Glucose 6-phosphate Kinetic Law: [Hill Cooperativity](E*kcat*S^h)/(K+S^h)						
Parameter	Value	Value Maximum	Organism	Comment	References	
Temperature [deg.C]	30	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
D-Glucose (kcat_Km) [1/(mM*sec), cst]	.0089	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
D-Glucose (K) [mM, cst]	840	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
D-Glucose (h) [-, cst]	1.37	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
Temperature [deg.C]	30	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
D-Glucose (kcat_Km) [1/(mM*sec), cst]	3.9	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
D-Glucose (h) [-, cst]	1.97	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
D-Glucose (K) [mM, cst]	18.9	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
Temperature [deg.C]	30	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
ATP (K) [mM, cst]	.65	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
ATP (h) [-, cst]	1.97	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
Temperature [deg.C]	30	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
D-Glucose (K) [mM, cst]	7.7	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
D-Glucose (kcat_Km) [1/(mM*sec), cst]	4.1	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
D-Glucose (h) [-, cst]	1.37	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
Temperature [deg.C]	30	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
ATP (K) [mM, cst]	1.13	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
ATP (h) [-, cst]	1.33	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	
Temperature [deg.C]	30	-	<i>Homo sapiens</i>	-	7961659 <small>PubMed</small>	

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▼ Structural information

▼ Models

Found 5 protein structures. 5 come from PDB.

#	Seq. Max Cov. Max Iden. [?]	Chains (Seq. Cov./ Seq. Iden./ Align. Score) [?]	Details [?]
PDB code: 1GLK			
#1	98%	<input type="radio"/> A P35557 from 1 to 465 (98% / 100% / 1000)	Accession: 1GLK Resolution: NOT APPLICABLE Method: THEORETICAL MODEL
	100%		EC references: ♦ 2.7.1.1 Heteroatoms: ♦ GLUCOSE [GLC]
see alignment			
PDB code: 1V4S			
#2	96%	<input type="radio"/> A P35557 from 13 to 466 (96% / 99% / 990)	Accession: 1V4S Resolution: 2.30 Å Method: X-RAY DIFFRACTION R-factor: 0.232 Organism: HOMO SAPIENS
	99%		Crystallization conditions: PEG1500, HEPES, PH 6.6, VAPOR DIFFUSION, HANGING DROP, TEMPERATURE 293K EC references: ♦ 2.7.1.1 Heteroatoms: ♦ 2-AMINO-4-FLUORO-5-((1-METHYL-1H-IMIDAZOL-2-YL) [MRK] ♦ SODIUM ION [NA] ♦ GLUCOSE [GLC]
see alignment			
PDB code: 1V4T			
#3	91%	<input type="radio"/> A P35557 from 17 to 466 (91% / 100% / 1000)	Accession: 1V4T Resolution: 3.40 Å Method: X-RAY DIFFRACTION R-factor: 0.237 Organism: HOMO SAPIENS
	100%		Crystallization conditions: AMMONIUM SULFATE, BICINE, SODIUM CHLORIDE, PH 8.7, VAPOR DIFFUSION, HANGING DROP, TEMPERATURE 293K EC references: ♦ 2.7.1.1 Heteroatoms: ♦ SODIUM ION [NA] ♦ SULFATE ION [SO4]
see alignment			
PDB code: 1Q18			
#4	91%	<input type="radio"/> A P0AGV8 from 2 to 321 (91% / 100% / 1000)	Accession: 1Q18 Resolution: 2.36 Å Method: X-RAY DIFFRACTION R-factor: 0.206 Organism: ESCHERICHIA COLI
	100%		Crystallization conditions: AMMONIUM SULFATE, BICINE, SODIUM CHLORIDE, PH 8.7, VAPOR DIFFUSION, HANGING DROP, TEMPERATURE 293K EC references: ♦ 2.7.1.1 Heteroatoms: ♦ SODIUM ION [NA] ♦ SULFATE ION [SO4]
see alignment			

1V4S: Homo sapiens, closed form

webPIPSA: hexokinase IV or D (P35557)

T-COFFEE, Version 4.70 (Mon Nov 6 18:05:42 2006)

Cedric Notredame

CPU TIME:0 sec.

SCORE=100

*

BAD AVG GOOD

*

1V4S : 100

P35557 : 100

sequence alignment between
SwissProt sequence P35557
and crystal structure 1V4S

1V4S -----TLVEQILAEFQLQEEDLKKVMRRMQKEMDRGLRLETHEEAS
P35557 MLDDRARMEAAKKEKVEQILAEFQLQEEDLKKVMRRMQKEMDRGLRLETHEEAS

cons *****

1V4S VKMLPTYVRSTPEGSEVGFSLDLGGTINFRVMLVKVGE GEGQWSVKTKHQMY
P35557 VKMLPTYVRSTPEGSEVGFSLDLGGTINFRVMLVKVGE GEGQWSVKTKHQMY

cons *****

1V4S SIPEDAMTGTAEMLFDYISECISDFLDKHKQMKHKKLPLGFTFSFPVRHEDIDKG
P35557 SIPEDAMTGTAEMLFDYISECISDFLDKHKQMKHKKLPLGFTFSFPVRHEDIDKG

cons *****

1V4S ILLNWTKGFKASGAEGNNVVGLLRDAIKRRGDFEMDVVAMVNDTVATMISCYE
P35557 ILLNWTKGFKASGAEGNNVVGLLRDAIKRRGDFEMDVVAMVNDTVATMISCYE

cons *****

1V4S DHQCEVGMIVGTGCNACYMEEMQNVELVEGDEGRMCVNTTEWGAFGDSGELDEFL

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▼Region selection

Features given in the Swiss-Prot entry of P35557 are listed here. You can modify these entries to restrict your analysis to different regions of the protein.

For all features where the key is the same, the region will be centered in the geometric center of all the features of the same key. E.g if you have four keys named 'BINDING', two features describing the binding of one molecule, and two others describing the binding of another molecule, you should rename the binding key to something like 'BINDING_MOL1' and 'BINDING_MOL2'. Please note that spaces in your key will be removed (therefore 'BINDING A' and 'BINDINGA' will result in the same key).

	Key	Description	Residue	
			From	To
<input type="checkbox"/>	BINDING	ATP (Potential)	104	104
<input type="checkbox"/>	CHAIN	Glucokinase	1	465
<input type="checkbox"/>	HELIX		16	20
<input type="checkbox"/>	HELIX		21	23
<input type="checkbox"/>	HELIX		27	45
<input type="checkbox"/>	HELIX		77	100
<input type="checkbox"/>	MUTAGEN	E->K: Small change in activity	177	177
<input type="checkbox"/>	MUTAGEN	E->A: Inactive enzyme	256	256
<input type="checkbox"/>	MUTAGEN	K->A: Small change in activity	414	414
<input type="checkbox"/>	NP_BIND	ATP (Potential)	78	83
<input checked="" type="checkbox"/>	REGION	Glucose-binding (Potential)	145	171
<input type="checkbox"/>	STRAND		58	64
<input type="checkbox"/>	STRAND		72	91
<input type="checkbox"/>	HELIX		332	338
<input type="checkbox"/>	HELIX		346	354
<input type="checkbox"/>	HELIX		361	394
<input type="checkbox"/>	HELIX		411	415

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region selection

select/deselect kinetic data



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▼ Information retrieved from Brenda

The results specific to the query Swiss-Prot entry organism are presented first.

Information retrieved using EC [2.7.1.2](#)

Literature links refer to BRENDA. In case where no PubMed entry is linked in BRENDA, you will get the details of the reference paper.

- 1. Data specific to Swiss-Prot entry *P21908*, sequence derived from organism *Zymomonas mobilis*

▼ Km information						
Km value [mM]	Km value [mM] Maximum	Substrate	Organism	Comment	References	
0.5	-	6-N-(carboxyethyl)ATP	<i>Zymomonas mobilis</i>	-	641063 PubMed	
0.55	-	6-N-(carboxymethyl)ATP	<i>Zymomonas mobilis</i>	-	641063 PubMed	
0.38	-	6-N-(succinyl)ATP	<i>Zymomonas mobilis</i>	-	641063 PubMed	
1.25	-	6-N-[N-(6-aminohexyl)carbamoyl]ATP	<i>Zymomonas mobilis</i>	-	641063 PubMed	
0.5	-	ATP	<i>Zymomonas mobilis</i>	-	641063 PubMed	
0.8	-	ATP	<i>Zymomonas mobilis</i>	-	641056 PubMed	
0.22	-	D-Glucose	<i>Zymomonas mobilis</i>	-	641056 PubMed	

- 1. Data specific to Swiss-Prot entry *P17709,Q04409*, sequence derived from organism *Saccharomyces cerevisiae*

▼ Km information						
Km value [mM]	Km value [mM] Maximum	Substrate	Organism	Comment	References	
0.05	-	ATP	<i>Saccharomyces cerevisiae</i>	-	641066 PubMed	
0.028	-	D-Glucose	<i>Saccharomyces cerevisiae</i>	-	641066 PubMed	

- 1. Data specific to Swiss-Prot entry *P0A6V8,Q1R8X8*, sequence derived from organism *Escherichia coli*

▼ Km information						
Km value [mM]	Km value [mM] Maximum	Substrate	Organism	Comment	References	
0.5	-	ATP	<i>Escherichia coli</i>	-	641064 PubMed	
0.15	-	D-Glucose	<i>Escherichia coli</i>	-	641064 PubMed	

- 1. Data specific to Swiss-Prot entry *Q92407*, sequence derived from organism *Aspergillus niger*

▼ Km information						
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Parameter Retrieval and estimation

Parameter retrieval: available information

After successful retrieval of kinetic data and structural models, do one of the following:

1. If no information was found, or the information is not suitable, start a new search with a new Swiss-Prot accession code. For this [click here](#).
2. Select a parameter from below and copy/paste it into your SBML model.
3. Assign a parameter based on an average of several retrieved values below and use it in your SBML model.
4. If there is structural information available, select a structural template and do a PIPSA to aid parameter assignment based on calculated electrostatic potentials of the retrieved proteins. The PIPSA analysis can be launched from this page [\[?\]](#).

To start a workflow for PIPSA, do the following:

1. In the section **Protein Structural Information** choose a template protein structure that you consider most suitable for protein structural modeling of your enzyme of interest (**Click on arrow first**). This is going to be used as a structural template in the subsequent homology modeling.
2. In the section **Region selection** below the structural information, you can make selections for Swiss-Prot features of your protein (eg. active site, binding region etc, **click on arrow first**). Additional PIPSA runs will then be performed to restrict the comparison to these regions.
3. In the section **Kinetic data** select Swiss-Prot sequences with relevant kinetic data (by default all sequences are selected).

Please find additional information about the Parameter Retrieval and Estimation on our [help page](#).

On this page, you'll find all the information gathered concerning the Swiss-Prot entry specified. This concerns both structural and kinetic data. There may be a lot of data, so use the triangles to display or hide information.

Here is the information found using the Swiss-Prot accession [P35557](#).

This entry is for the organism *Homo sapiens*.

Calculate electrostatically similar proteins (please first check selected models and sequence below)

At registration you have provided the following

key for MODELLER [\[?\]](#) Please correct if needed. **required MODELLER key**

Use modeller version 8v2

Use modeller version 9v1 (including loop refinement)

Use modeller version 9v1 (including loop refinement using DOPE score, takes longer)

start modelling



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Work in progress

This page will be reloaded automatically in a few seconds. Please wait.

The time required for a PIPSA analysis depends on several factors:

- the number of structures you submitted for analysis.
- the number of regions you have selected.
- the number of jobs in the request queue (submitted by other users)

Typically a PIPSA analysis takes from 10 min to 2 hours. A qPIPSA analysis requires for the download phase approx. 5-20 min, whereas the analysis requires 30 to 180 minutes.

If you start a [new search](#), the current search will only be accessible via the link in the email you receive.

Your request is being processed. There is 1 job in the request queue.

Here is an overview of the actions done and the advancement of the information retrieval (latest at top):

- Download of entries from databases complete.
- Parsing of pdb entry 1V4T completed.
- Parsing of pdb entry 1V4S completed.
- Parsing of pdb entry 1SZ2 completed.
- Parsing of pdb entry 1Q18 completed.
- Parsing of pdb entry 1GLK completed.
- Parsing of Swiss-Prot entry Q9CE25 using <http://www.expasy.org/uniprot/Q9CE25.txt> completed.
- Parsing of Swiss-Prot entry Q9YA47 using <http://www.expasy.org/uniprot/Q9YA47.txt> completed.
- Parsing of Swiss-Prot entry P17712 using <http://www.expasy.org/uniprot/P17712.txt> completed.
- Retrieval of SABIO-RK entry 2.7.1.2 completed.
- Parsing of Swiss-Prot entry Q92407 using <http://www.expasy.org/uniprot/Q92407.txt> completed.
- Parsing of Swiss-Prot entry Q1R8X8 using <http://www.expasy.org/uniprot/Q1R8X8.txt> completed.
- Parsing of Swiss-Prot entry P0A6V8 using <http://www.expasy.org/uniprot/P0A6V8.txt> completed.
- Parsing of Swiss-Prot entry Q04409 using <http://www.expasy.org/uniprot/Q04409.txt> completed.
- Parsing of Swiss-Prot entry P17709 using <http://www.expasy.org/uniprot/P17709.txt> completed.
- Parsing of Swiss-Prot entry P21908 using <http://www.expasy.org/uniprot/P21908.txt> completed.

email: Parameter analysis for P35557 is complete

webPIPSA: hexokinase IV or D (P35557)

qPIPSA workflow for P35557 (Glucokinase (EC 2.7.1.2) (Hexokinase type IV) (HK IV) (Hexokinase-4) (HK4) (Hexokinase-D).) completed

start [new search](#)
show [workflow tasks](#)

The result of qPIPSA is a tree-like diagram (dendrogram, which we call an epogram) which puts the electrostatic potential of the query sequence into relation with other enzymes for which kinetic data are available. Additional information about the interpretation of the output can be found in the [STAPAC help](#).

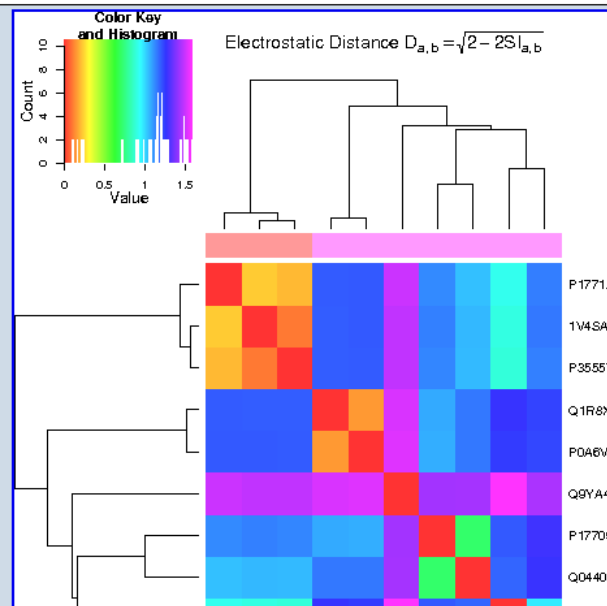
Please click on the tabs to get results based on regions of the protein (in case you have selected regions for analysis before). In case you print this document, all graphs will be shown.

Whole Protein REGION Structure view

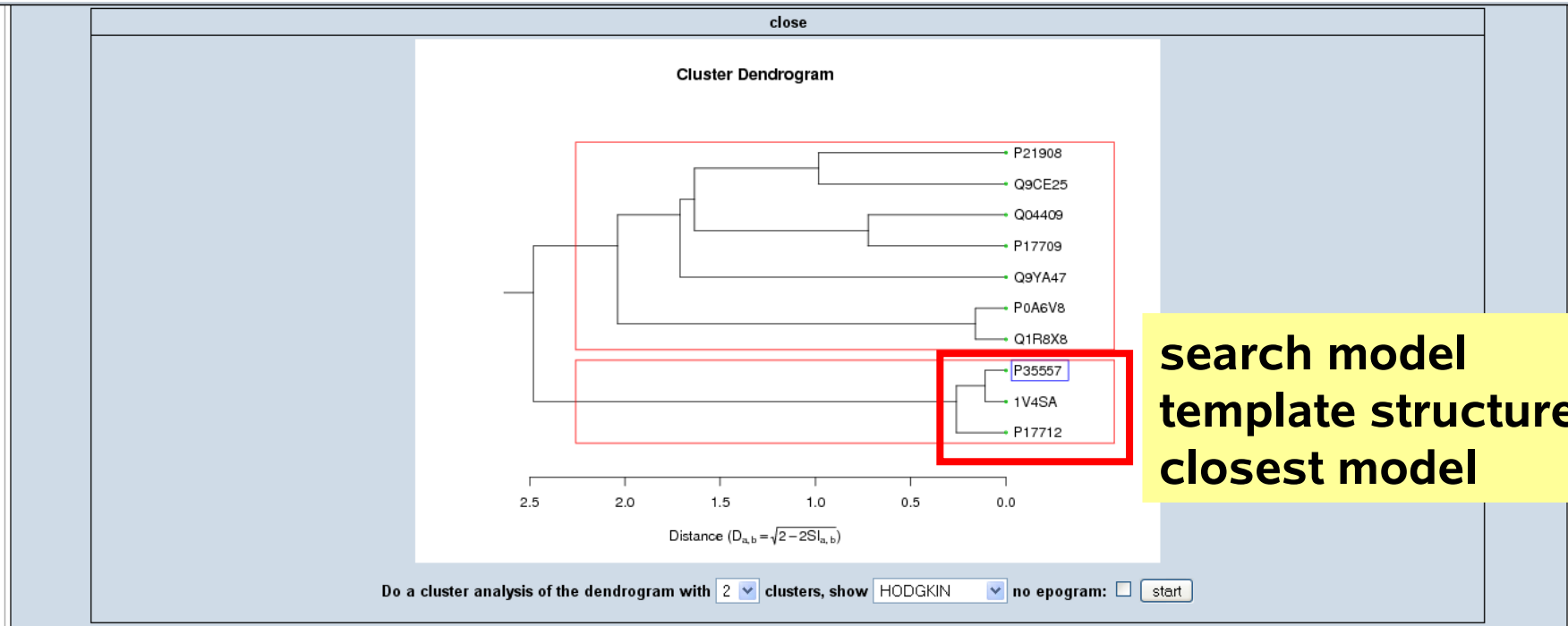
The following graph shows the comparison based on the electrostatic potential around the whole protein:

Distances range from 0.10954 to 1.59185 (maximum range is from 0 to 2)

results



webPIPSA: hexokinase IV or D (P35557)



The proteins sorted according to the similarity of electrostatic potentials to the input sequence are:

No.	Protein	Description	Organism	Kinetic parameter
1	P35557	Glucokinase (EC 2.7.1.2) (Hexokinase type IV) (HK IV) (Hexokinase-4) (HK4) (Hexokinase-D).	Homo sapiens	click here
2	P17712	Glucokinase (EC 2.7.1.2) (Hexokinase type IV) (HK IV) (Hexokinase-4) (HK4) (Hexokinase-D).	Rattus norvegicus	click here
3	Q9CE25	Glucose kinase (EC 2.7.1.2).	Lactococcus lactis subsp	click here
4	P21908	Glucokinase (EC 2.7.1.2) (Glucose kinase).	Zymomonas mobilis	click here
5	Q9YA47	ATP-dependent glucokinase (EC 2.7.1.2).	Aeropyrum pernix	click here
6	Q04409	Glucokinase EMI2 (EC 2.7.1.2) (Glucose kinase) (GLK) (Early meiotic induction protein 2).	Saccharomyces cerevisiae	click here
7	P17709	Glucokinase GLK1 (EC 2.7.1.2) (Glucose kinase) (GLK).	Saccharomyces cerevisiae	click here
8	P0A6V8	Glucokinase (EC 2.7.1.2) (Glucose kinase).	Escherichia coli	click here
9	Q1R8X8	Glucokinase (EC 2.7.1.2) (Glucose kinase).	Escherichia coli	click here

Kinetic parameters for P17712

▼ Information retrieved from Brenda

The results specific to the query Swiss-Prot entry organism are presented first.

Information retrieved using EC [2.7.1.2](#)

Literature links refer to BRENDA. In case where no PubMed entry is linked in BRENDA, you will get the details of the reference paper.

▼ Information retrieved from Sabio RK

Parameters are grouped per reaction stoichiometry and kinetic law. There may be more than one experiment for each of this group, so some parameters may have different values.

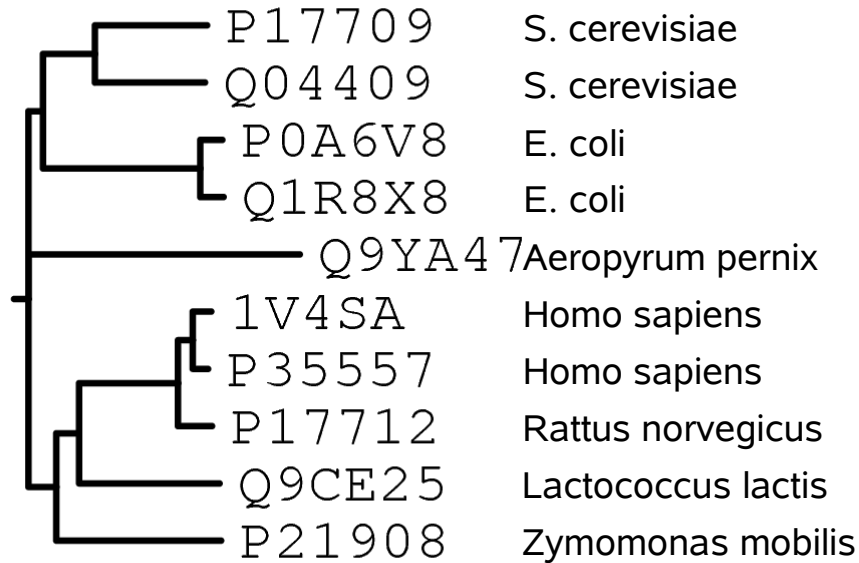
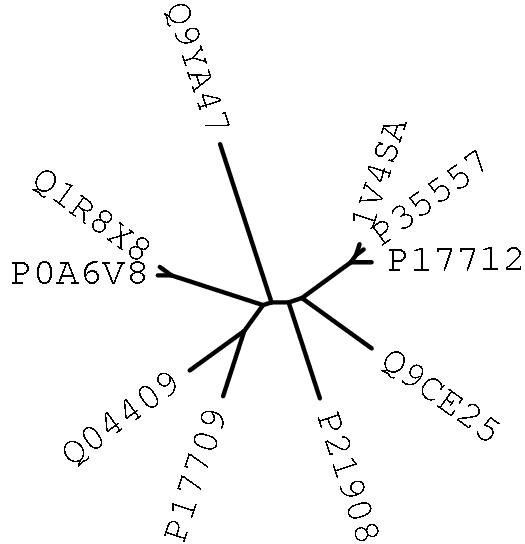
Information retrieved using EC [2.7.1.2](#)

1. Data specific to Swiss-Prot entry P17712, sequence derived from organism *Rattus norvegicus*

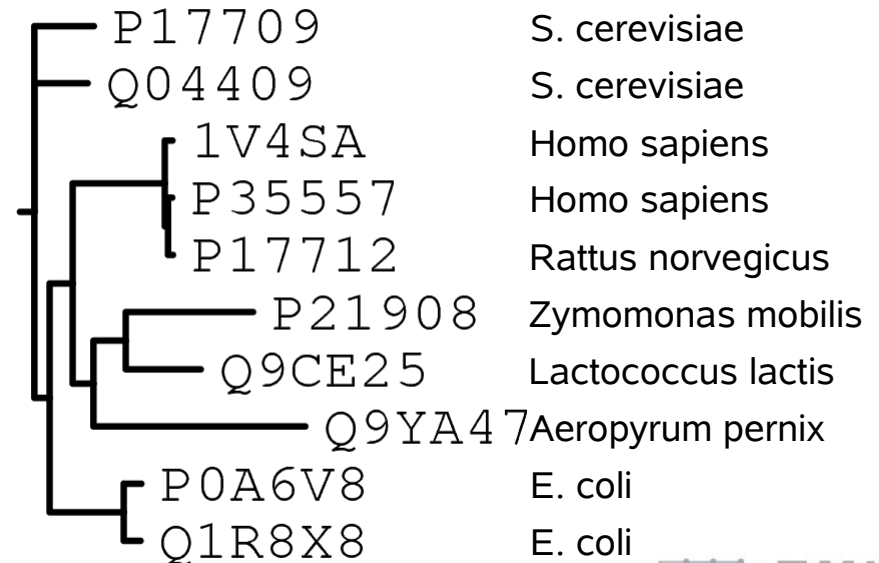
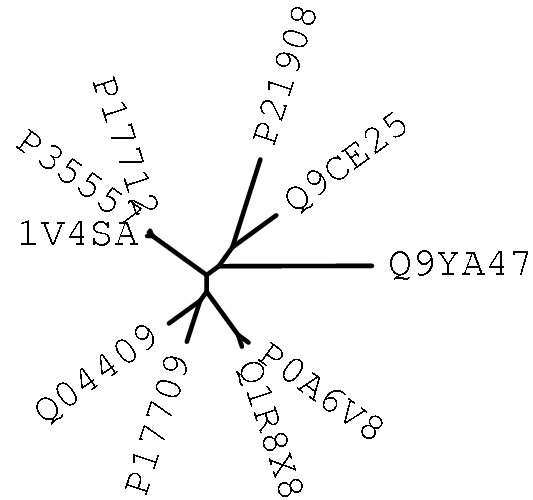
▼ Reaction: D-Glucose + ATP = D-Glucose 6-phosphate + ADP Kinetic Law: [unknown]unknown					
Parameter	Value	Value Maximum	Organism	Comment	References
D-Glucose (Km) [mM, cst]	7.61	-	Rattus norvegicus	-	6296127 <small>PubMed</small>
ATP (Km) [mM, cst]	.55	-	Rattus norvegicus	-	999645 <small>PubMed</small>
Temperature [deg.C]	30	-	Rattus norvegicus	-	999645 <small>PubMed</small>
pH [-]	8	-	Rattus norvegicus	-	999645 <small>PubMed</small>
D-Glucose (Km) [mM, cst]	3	5	Rat	-	1854332 <small>PubMed</small>
pH [-]	7.4	-	Rat	-	1854332 <small>PubMed</small>
pH [-]	7.45	-	Rattus norvegicus	-	8804424 <small>PubMed</small>
ATP (Km) [mM, cst]	.2	-	Rat	-	1854332 <small>PubMed</small>
pH [-]	7.4	-	Rat	-	1854332 <small>PubMed</small>
pH [-]	7.45	-	Rattus norvegicus	-	8804424 <small>PubMed</small>
ATP (Km) [mM, cst]	.2	-	Rat	-	1854332 <small>PubMed</small>
pH [-]	7.4	-	Rat	-	1854332 <small>PubMed</small>
pH [-]	7.45	-	Rattus norvegicus	-	8804424 <small>PubMed</small>
D-Glucose (Km) [mM, cst]	8	10	Rat	-	1854332 <small>PubMed</small>
pH [-]	7.4	-	Rat	-	1854332 <small>PubMed</small>

webPIPSA: hexokinase IV or D (P35557)

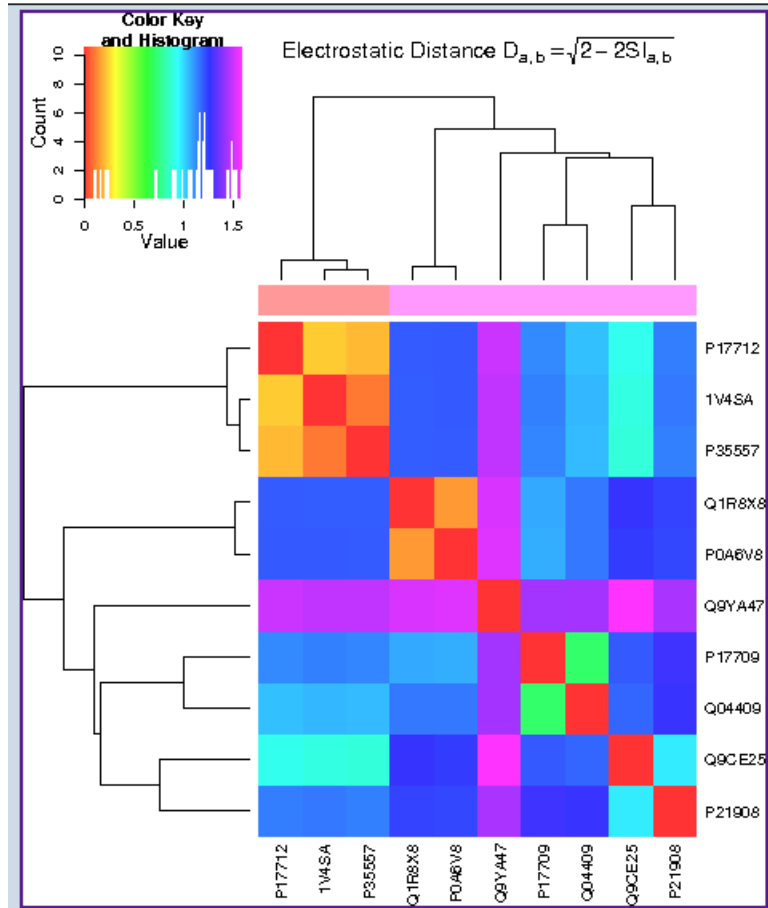
whole protein



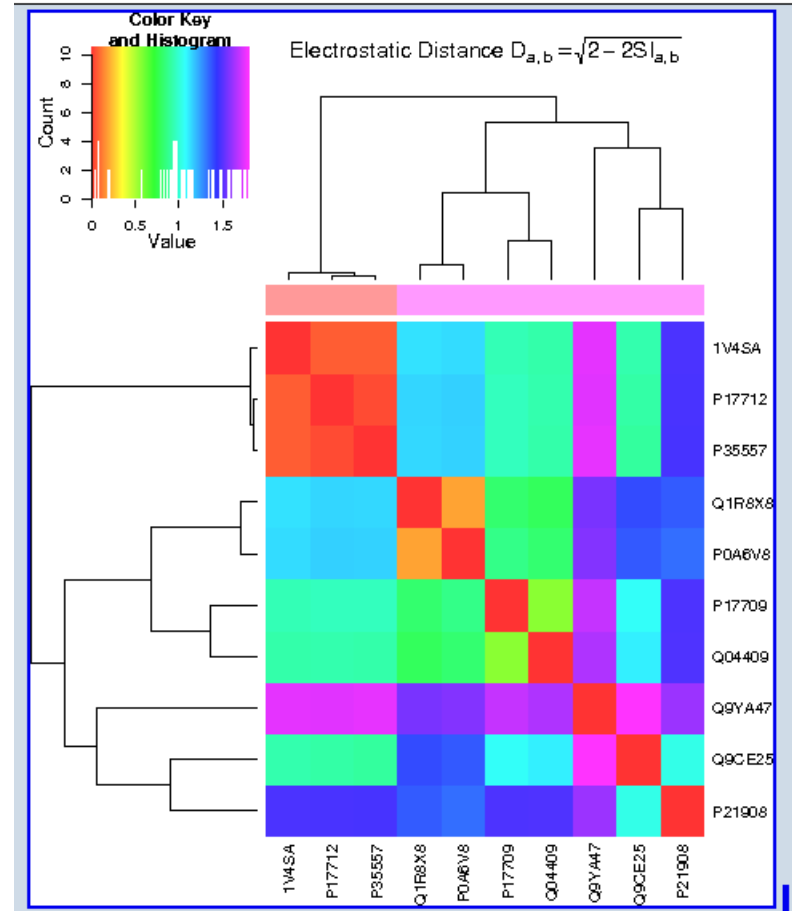
glucose binding region



whole protein



glucose binding region

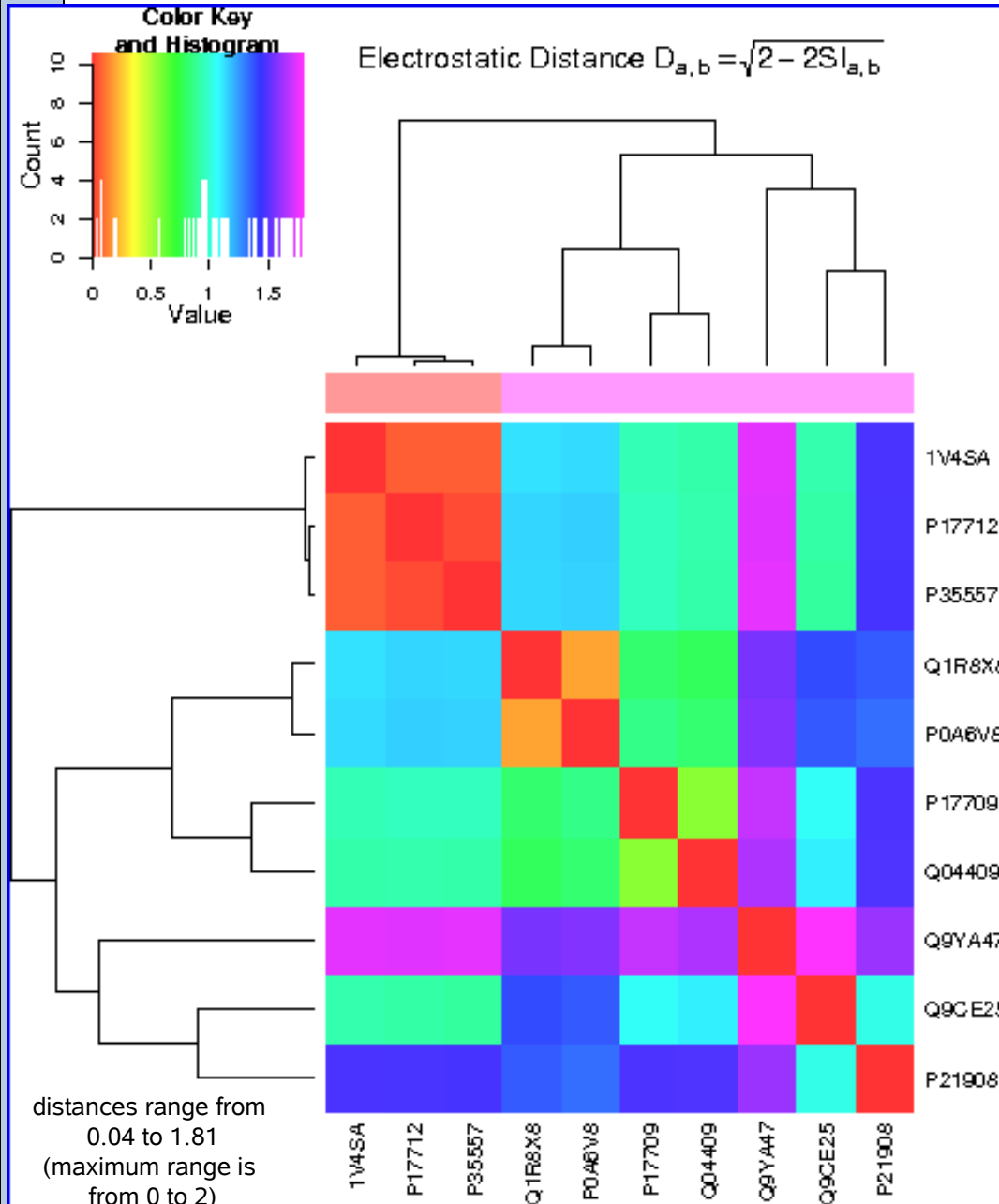


distances range from (maximum range is from 0 to 2)

0.11 to 1.59

0.04 to 1.81

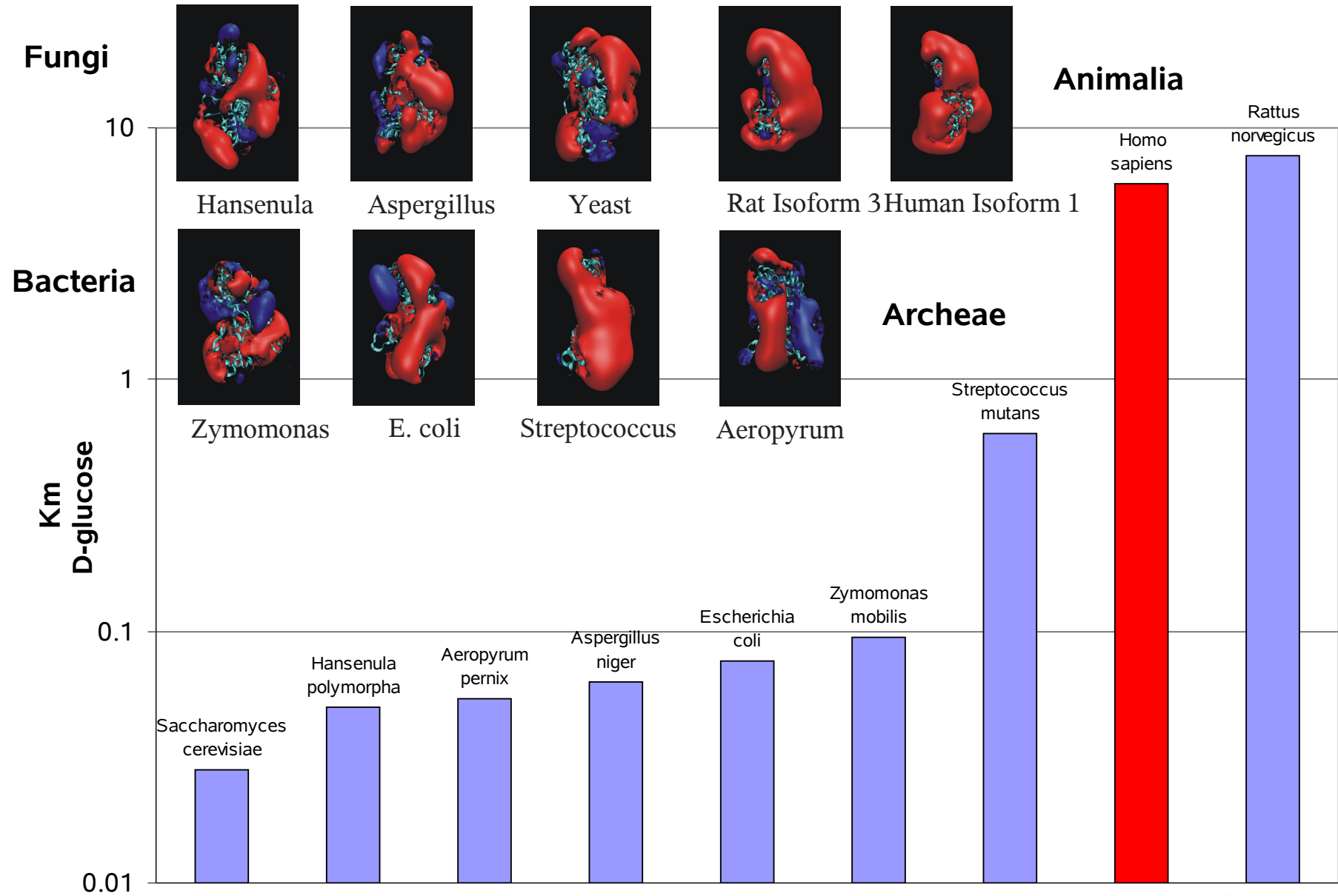
webPIPSA: hexokinase IV or D (P35557)



hexokinase IV glucose binding region

- 1V4SA Homo sapiens (template)
- P17712 Rattus norvegicus
- P35557 Homo sapiens
- Q1R8X8 Escherichia coli
- P0A6V8 Escherichia coli
- P17709 Saccharomyces cerevisiae
- Q04409 Saccharomyces cerevisiae
- Q9YA47 Aeropyrum pernix
- Q9CE25 Lactococcus lactis subsp
- P21908 Zymomonas mobilis

glucokinase (hexokinase)



webPIPSA: hexokinase IV or D (P35557)

Whole Protein

REGION

Structure view



Controls Help

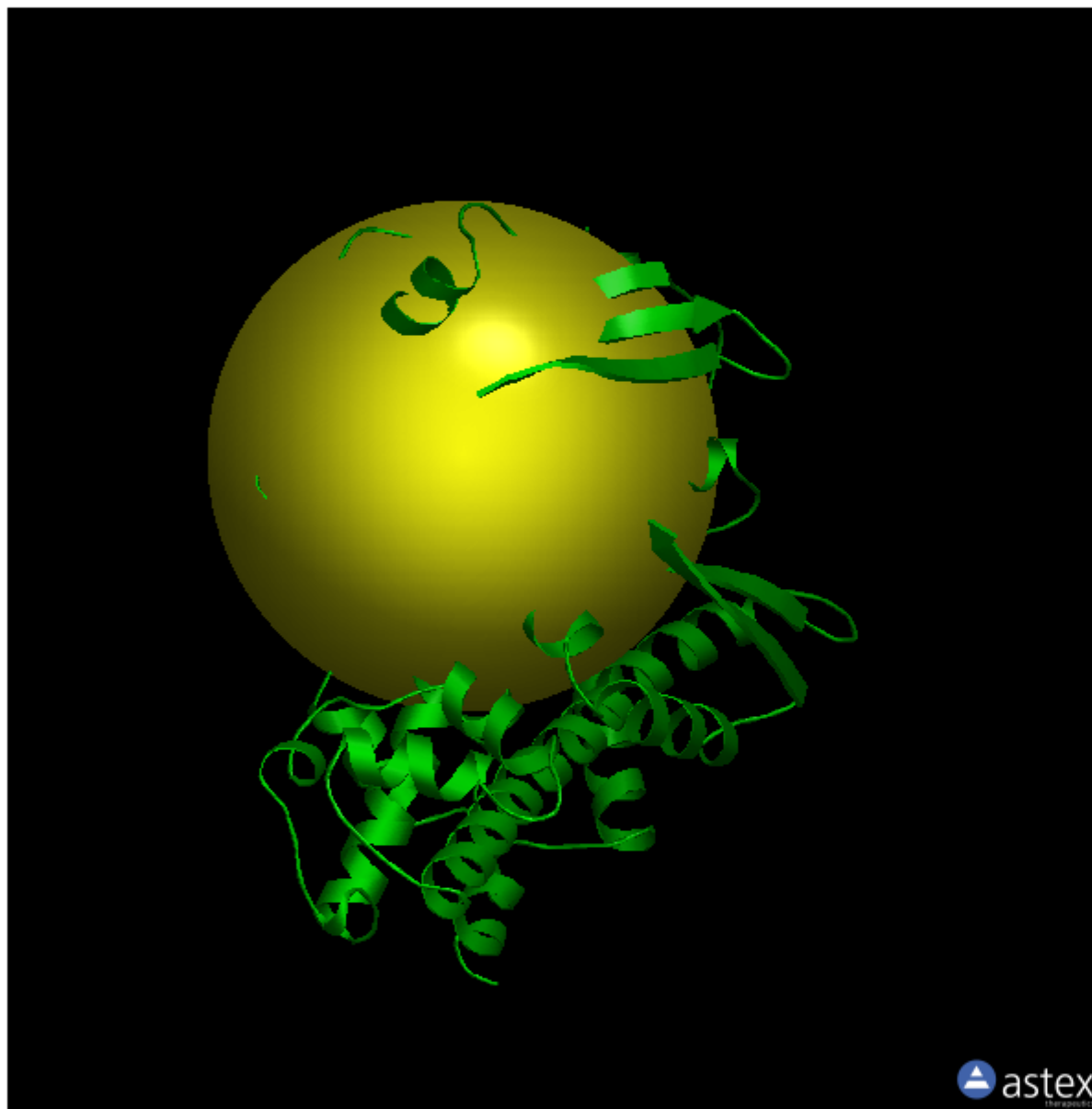
- Q1R8X8_1V4SA (schematic)
- P17712_1V4SA (schematic)
- Q9YA47_1V4SA (schematic)
- Q9CE25_1V4SA (schematic)
- Q92407_1V4SA (schematic)
- P17709_1V4SA (schematic)
- 1V4SA (schematic)
- P21908_1V4SA (schematic)
- Q04409_1V4SA (schematic)
- P35557_1V4SA (schematic)
- P0A6V8_1V4SA (schematic)
- 1V4SA_REGION (atomic)
- Region REGION for PIPSA
- Protein surface 255

webPIPSA: hexokinase IV or D (P35557)

Whole Protein

REGION

Structure view



Controls Help

- Q1R8X8_1V4SA (schematic)
- P17712_1V4SA (schematic)
- Q9YA47_1V4SA (schematic)
- Q9CE25_1V4SA (schematic)
- Q92407_1V4SA (schematic)
- P17709_1V4SA (schematic)
- 1V4SA (schematic)
- P21908_1V4SA (schematic)
- Q04409_1V4SA (schematic)
- P35557_1V4SA (schematic)
- P0A6V8_1V4SA (schematic)
- 1V4SA_REGION (atomic)
- Region REGION for PIPSA
- Protein surface 255

webPIPSA: hexokinase IV or D (P35557)

Whole Protein REGION Structure view



- Controls Help
- Q1R8X8_1V4SA (schematic)
 - P17712_1V4SA (schematic)
 - Q9YA47_1V4SA (schematic)
 - Q9CE25_1V4SA (schematic)
 - Q92W07_1V4SA (schematic)
 - P17709_1V4SA (schematic)
 - 1V4SA (schematic)
 - P21908_1V4SA (schematic)
 - Q04409_1V4SA (schematic)
 - P35557_1V4SA (schematic)
 - P10698_1V4SA (schematic)
 - 1V4SA_REGION (atomic)
 - Region REGION for PIPSA
 - Protein surface ■ 255

Example cases of PIPSA

DHFR

- compare Dihydrofolate Reductase (DHFR) of different species
- starting with human DHFR sequence (P00374)
- choose template structure: Homo sapiens (1u72)
- define DHF and NADPH binding region
- run modelling
- check models
- estimate parameters

human DHFR (1u72)

crystal structures of DHFR
pink: human (1u72)

green: cofactor NADPH

blue: inhibitor MTX



superposition of crystal structures

crystal structures of DHFR

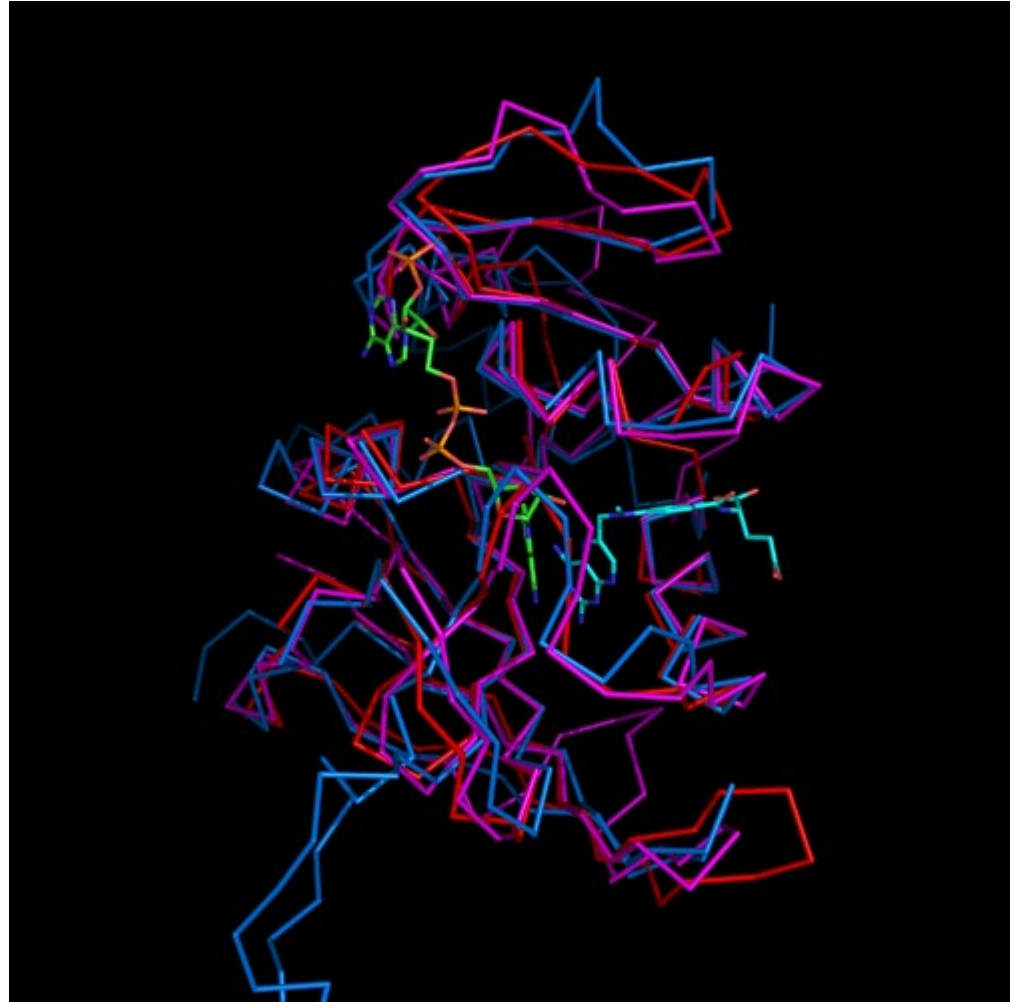
pink: human (1u72)

blue: Plasmodium falciparum
(1j31)

red: E. coli (1rh3)

green: cofactor NADPH

blue: inhibitor MTX



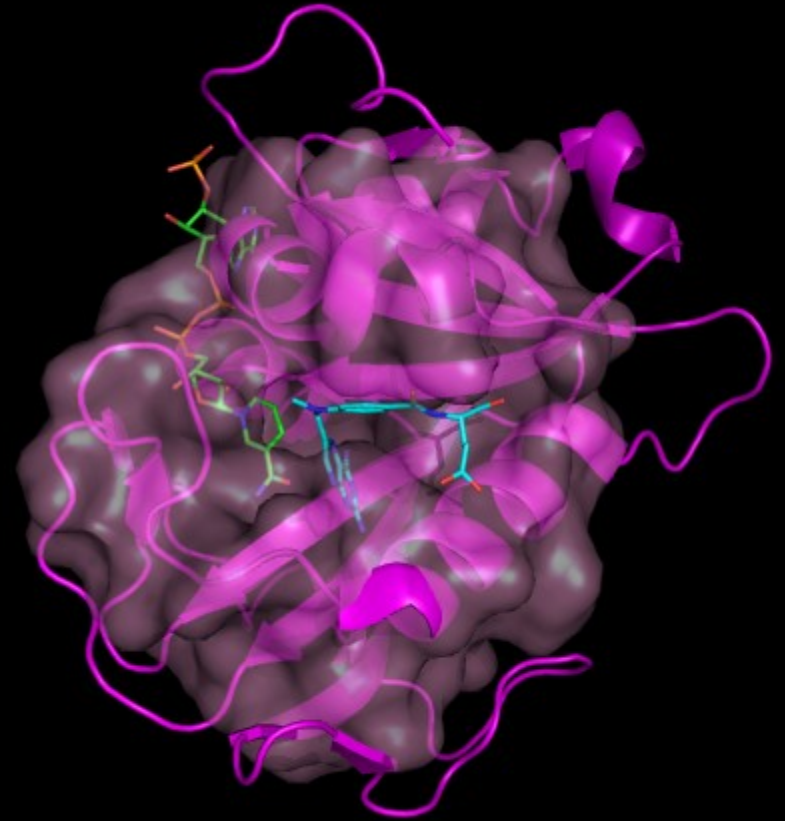
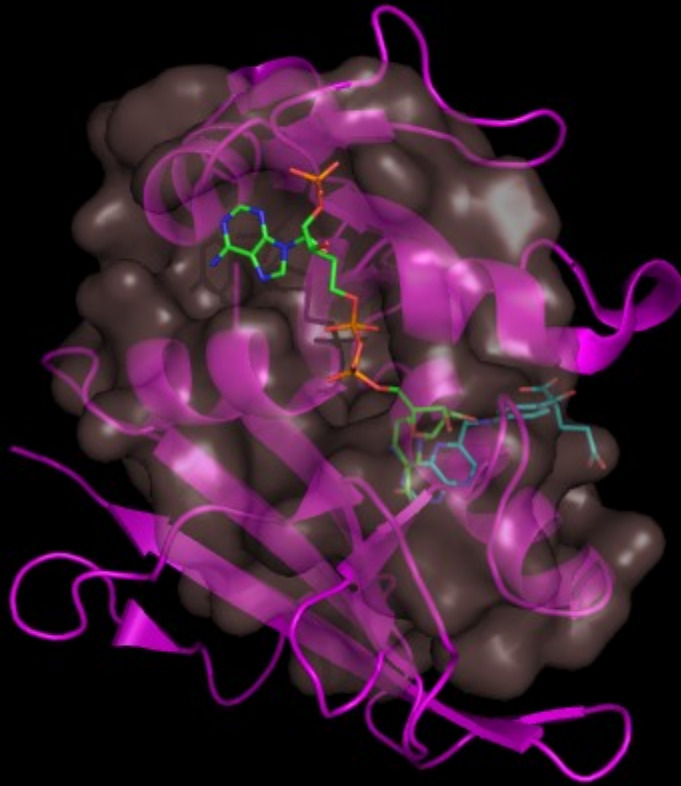
human DHFR (1u72)

crystal structures of DHFR
pink: human (1u72)

green: cofactor NADPH

blue: inhibitor MTX





focus on cofactor binding region

focus on substrate binding region

DHFR: region selection

▼Region selection

Features given in the Swiss-Prot entry of P00374 are listed here. You can modify these entries to restrict your analysis to different regions of the protein.

For all features where the key is the same, the region will be centered in the geometric center of all the features of the same key. E.g if you have four keys named 'BINDING', two features describing the binding of one molecule, and two others describing the binding of another molecule, you should rename the binding key to something like 'BINDING_MOL1' and 'BINDING_MOL2'. Please note that spaces in your key will be removed (therefore 'BINDING A' and 'BINDINGA' will result in the same key).

	Key	Description	Residue	
			From	To
<input checked="" type="checkbox"/>	DHF	Dihydrofolate binding region	23	23
<input checked="" type="checkbox"/>	DHF	Dihydrofolate binding region	35	35
<input checked="" type="checkbox"/>	DHF	Dihydrofolate binding region	57	57
<input checked="" type="checkbox"/>	DHF	Dihydrofolate binding region	61	62
<input checked="" type="checkbox"/>	DHF	Dihydrofolate binding region	68	68
<input checked="" type="checkbox"/>	DHF		116	116
<input checked="" type="checkbox"/>	DHF		136	137
<input checked="" type="checkbox"/>	NADPH		9	9
<input checked="" type="checkbox"/>	NADPH		23	23
<input checked="" type="checkbox"/>	NADPH		56	56
<input checked="" type="checkbox"/>	NADPH		76	76
<input checked="" type="checkbox"/>	NADPH		94	94
<input checked="" type="checkbox"/>	NADPH		115	115
<input checked="" type="checkbox"/>	NADPH		119	119
<input checked="" type="checkbox"/>	NADPH		121	121
<input type="checkbox"/>	STRAND		146	148

DHF:

23, 35, 57, 61-62, 68, 116, 136-137

NADPH:

9, 23, 56, 76, 94, 115, 119, 121

Whole Protein | DHF | NADPH | Structure view



Controls Help

- P78218_1U72A (schematic)
- P00377_1U72A (schematic)
- P22906_1U72A (schematic) **C. albicans**
- Q59397_1U72A (schematic)
- P00381_1U72A (schematic)
- P05794_1U72A (schematic)
- P00382_1U72A (schematic)
- P00378_1U72A (schematic)
- P07807_1U72A (schematic)
- P00384_1U72A (schematic)
- P27422_1U72A (schematic)
- P00374_1U72A (schematic) **H. sapiens**
- P0ABQ4_1U72A (schematic)
- P00383_1U72A (schematic)
- Q59408_1U72A (schematic)
- Q23695_1U72A (schematic)
- 1U72A (schematic)
- P04174_1U72A (schematic)
- P0ABQ7_1U72A (schematic)
- P00375_1U72A (schematic)
- Q04515_1U72A (schematic)
- Q9U8B8_1U72A (schematic)
- P51820_1U72A (schematic)
- P00376_1U72A (schematic)
- P12833_1U72A (schematic)
- P11731_1U72A (schematic)
- Q920D2_1U72A (schematic)
- 1U72A_NADPH (atomic) **NADPH region**
- Region NADPH for PIP...
- 1U72A_DHF (atomic) **DHF region**



Whole Protein DHF NADPH Structure view



Controls Help

- P78218_1U72A (schematic)
- P00377_1U72A (schematic)
- P22906_1U72A (schematic)
- Q59397_1U72A (schematic)
- P00381_1U72A (schematic)
- P05794_1U72A (schematic)
- P00382_1U72A (schematic)
- P00378_1U72A (schematic)
- P07807_1U72A (schematic)
- P00384_1U72A (schematic)
- P27422_1U72A (schematic)
- P00374_1U72A (schematic)
- P0ABQ4_1U72A (schematic)
- P00383_1U72A (schematic)
- Q59408_1U72A (schematic)
- Q23695_1U72A (schematic)
- 1U72A (schematic)
- P04174_1U72A (schematic)
- P0ABQ7_1U72A (schematic)
- P00375_1U72A (schematic)
- Q04515_1U72A (schematic)
- Q9U8B8_1U72A (schematic)
- P51820_1U72A (schematic)
- P00376_1U72A (schematic)
- P12833_1U72A (schematic)
- P11731_1U72A (schematic)
- Q920D2_1U72A (schematic)
- 1U72A_NADPH (atomic)
- Region NADPH for PIP...
- 1U72A_DHF (atomic)

E. coli

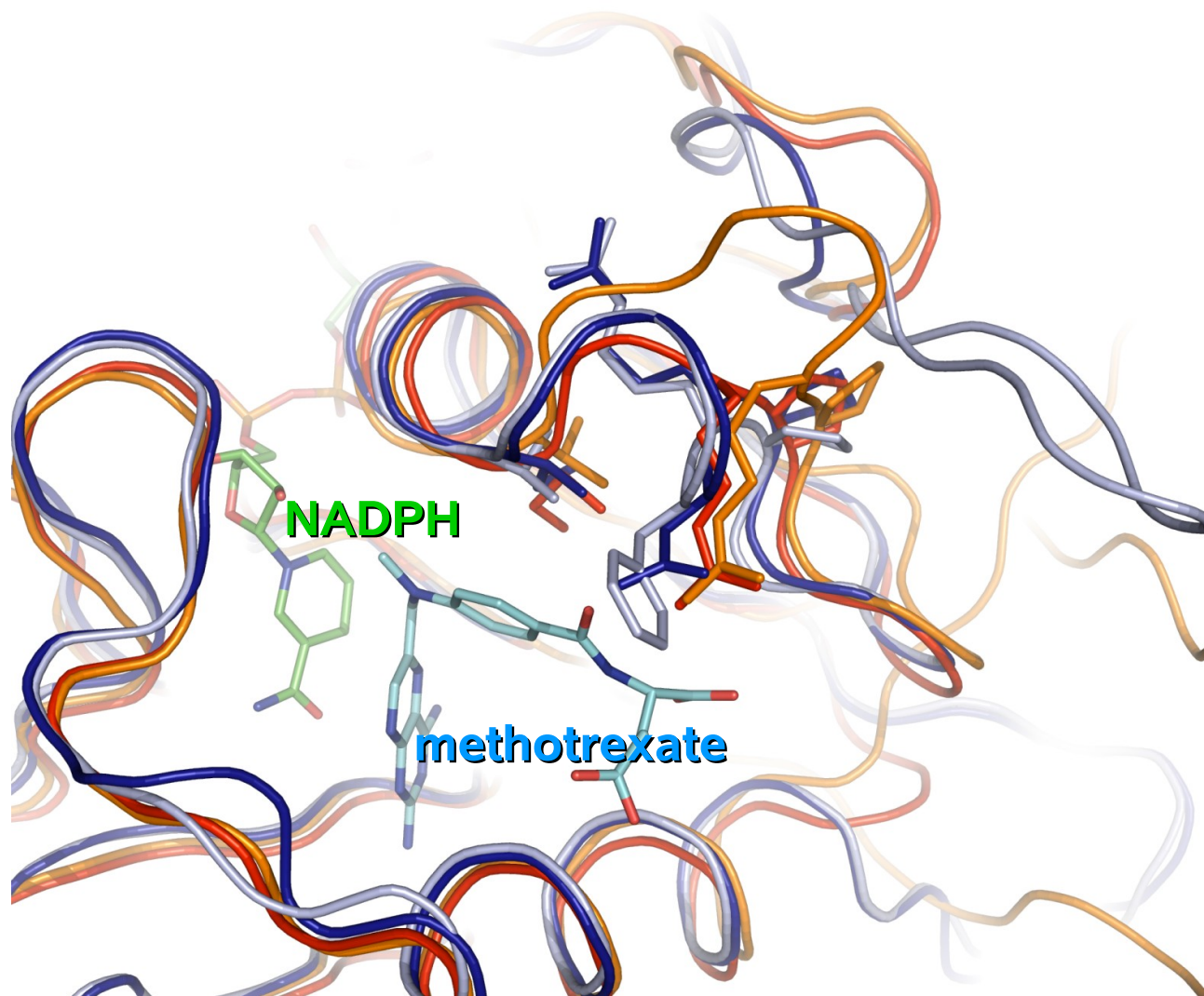
H. sapiens

NADPH region

DHF region







crystal structure
DHFR of
human (1u72)
E. coli (1rh3)

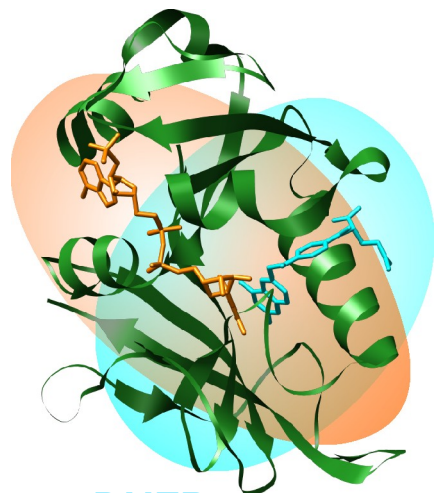
Modelled DHFR
of *Leishmania*
major (P07382)
human (1u72)-
based
E. coli (1rh3)-
based

Henrich et al.,
ChemMedChem, 2008

webPIPSA: clustering

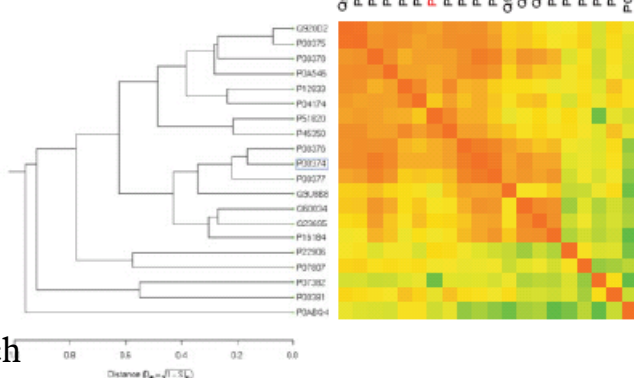
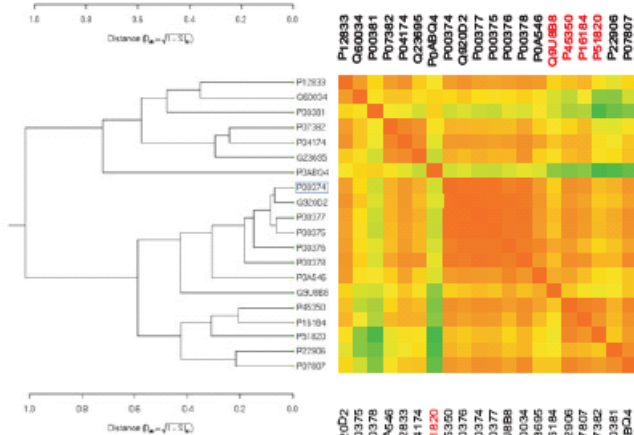
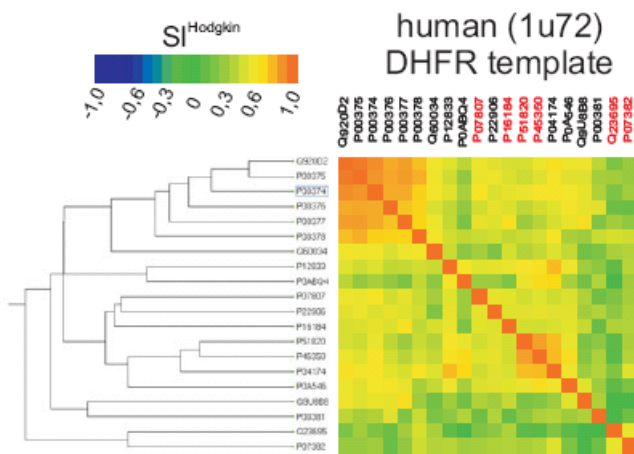
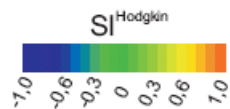
dihydrofolate reductases (DHFR) from 20 species

NADPH binding region

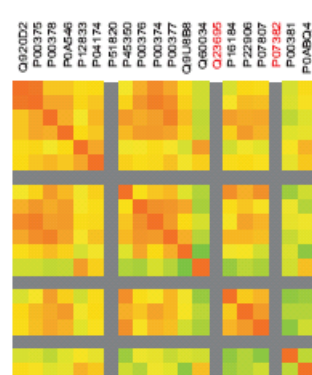
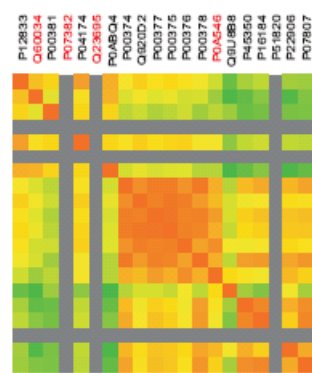
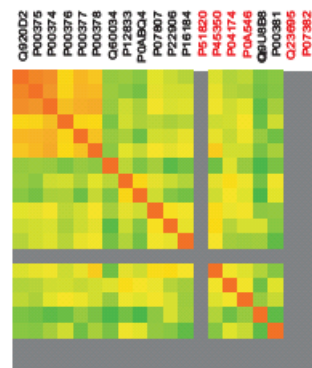


DHFR binding region

Henrich et al., ChemMedChem, 2008



C. albicans (1aoe) DHFR template



whole protein

- Rattus norvegicus
- Mus musculus
- Homo sapiens
- Bos taurus
- Sus scrofa
- Gallus gallus
- Thermotoga maritima
- Salmonella typhimurium
- Escherichia coli
- Saccharomyces cerevisiae
- Candida albicans
- Pneumocystis carinii
- Glycine max
- Daucus carota
- Neisseria gonorrhoeae
- Mycobacterium tuberculosis
- Heliothis virescens
- Lactobacillus casei
- Crithidia fasciculata
- Leishmania major

DHF region

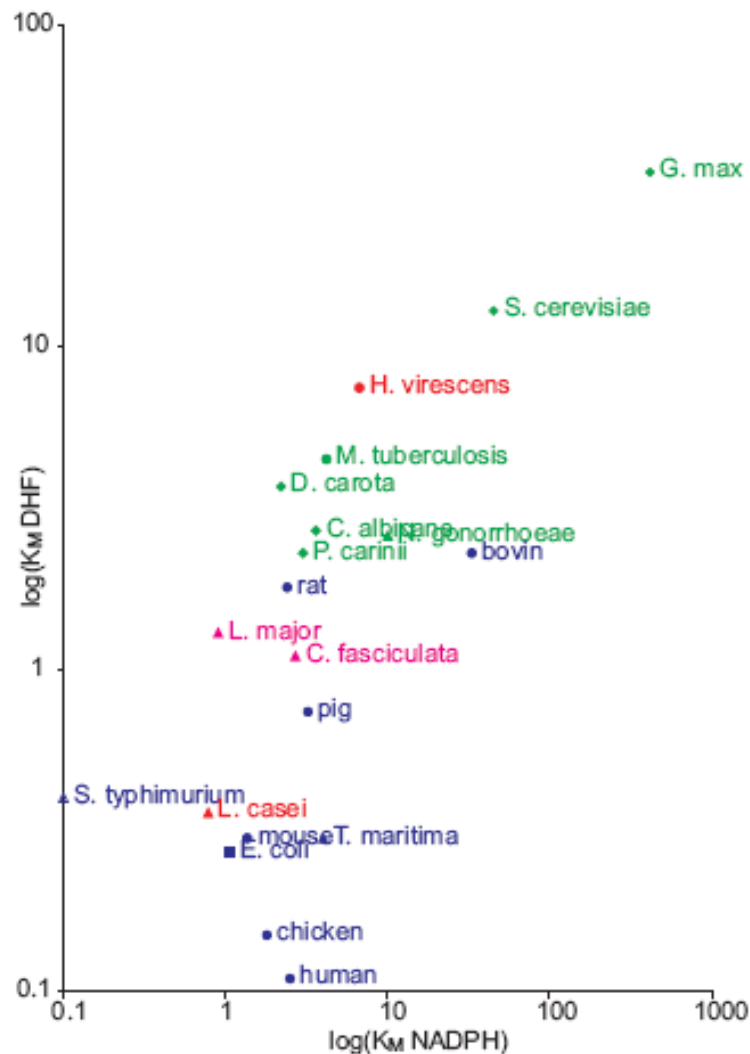
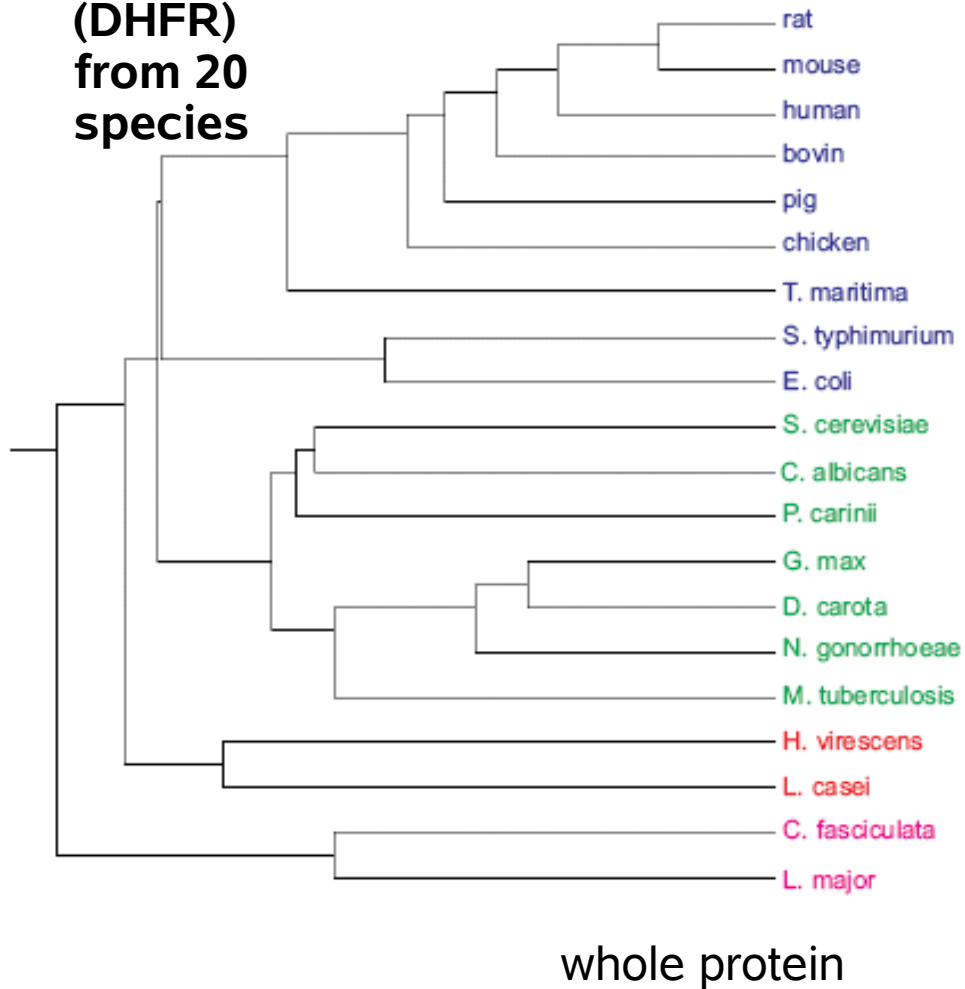
- Salmonella typhimurium
- Thermotoga maritima
- Lactobacillus casei
- Leishmania major
- Neisseria gonorrhoeae
- Crithidia fasciculata
- Escherichia coli
- Homo sapiens
- Rattus norvegicus
- Sus scrofa
- Mus musculus
- Bos taurus
- Gallus gallus
- Mycobacterium tuberculosis
- Heliothis virescens
- Daucus carota
- Pneumocystis carinii
- Glycine max
- Candida albicans
- Saccharomyces cerevisiae

NADPH region

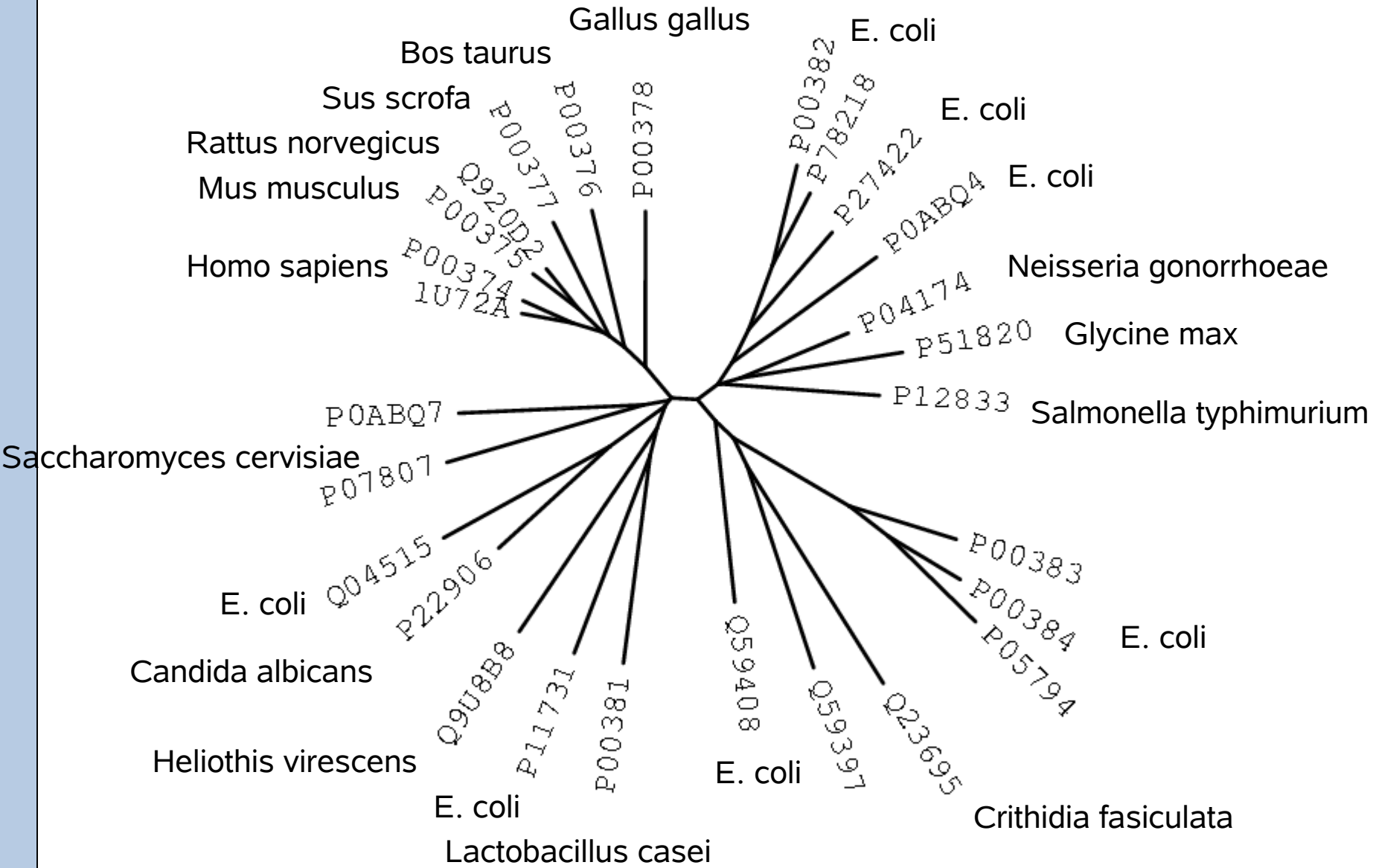
- Rattus norvegicus
- Mus musculus
- Gallus gallus
- Mycobacterium tuberculosis
- Salmonella typhimurium
- Neisseria gonorrhoeae
- Glycine max
- Daucus carota
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- Pneumocystis carinii
- Candida albicans
- Saccharomyces cerevisiae
- Leishmania major
- Lactobacillus casei
- Escherichia coli

webPIPSA: clustering and relation to K_m values

dihydrofolate
reductases
(DHFR)
from 20
species



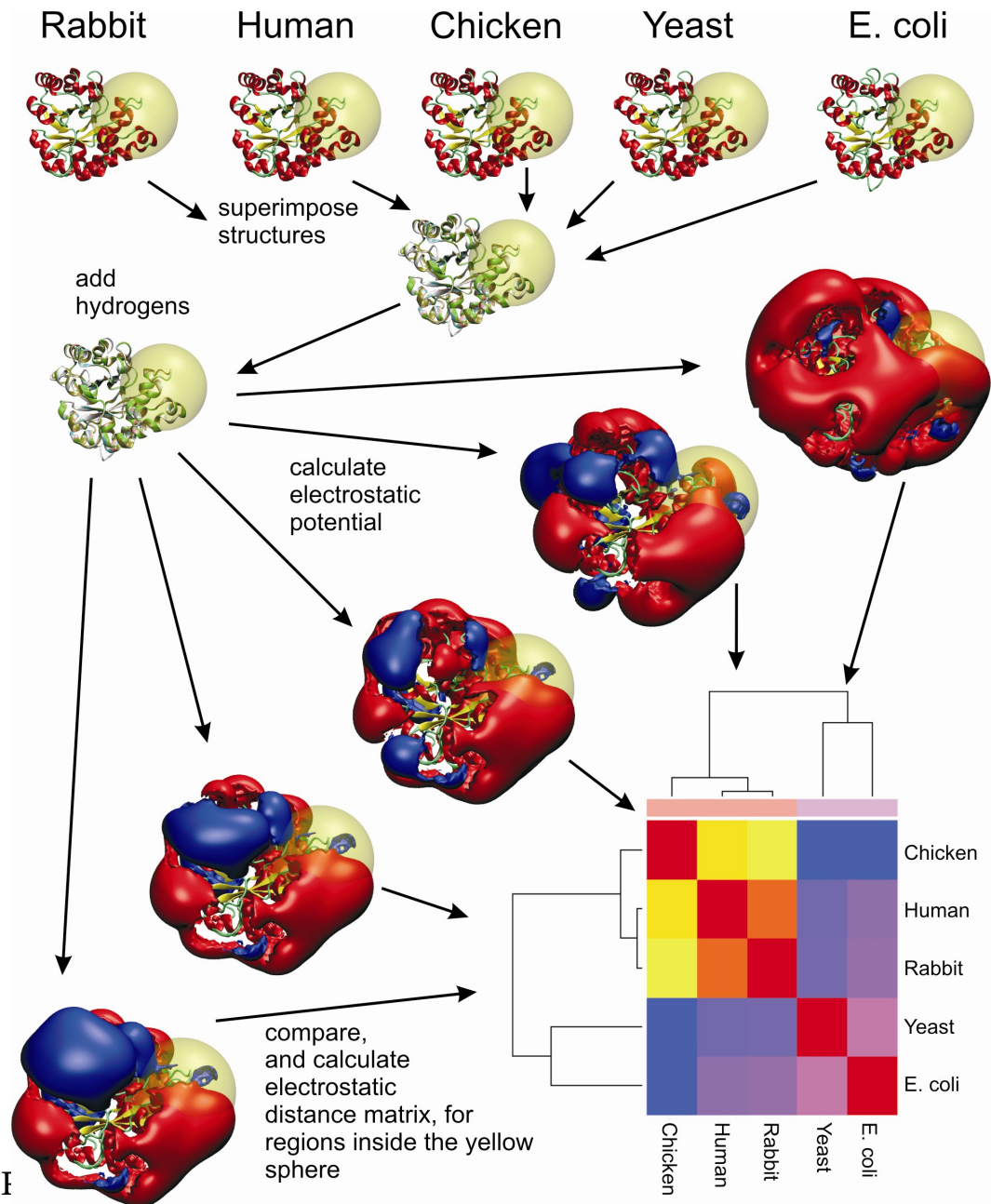
Henrich et al.,
ChemMedChem, 2008

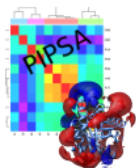


webPIPSA:
pipasa.embl.org

triosephosphate
 isomerase

Richter et al.,
Nucleic Acids Research, 2008





Protein Interaction Property Similarity Analysis

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Introduction

This PIPSA service is provided for the comparison of the electrostatic interaction properties of proteins. It permits the classification of proteins according to their interaction properties. PIPSA may assist in function assignment, the estimation of binding properties and enzyme kinetic parameters. See [References](#) for details.

Method

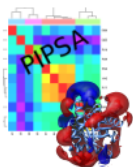
To perform PIPSA on this webserver, you need to upload a set of related protein structures in PDB format. After calculation of the protein electrostatic potentials, the server will calculate similarity indices for all pairs of proteins based on the electrostatic similarity. These indices will be computed for complete protein 'skins' or for a user defined region. The similarity indices are then converted to electrostatic 'distances'. The electrostatic potential distance matrix is displayed in color coded form (heat map) and as a tree (epogram).

[Start a PIPSA analysis \(input PDB format coordinate files\).](#)

[Start a PIPSA analysis \(input SWISSPROT entries with EC annotation\)*.](#)

* This type of analysis involves a protein structural modelling step utilizing [Modeller](#). Therefore this part is subject to the [Modeller license conditions](#). Please obtain a [Modeller license](#) to use this service.

<http://pipsa.eml.org>



Protein Interaction Property Similarity Analysis

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PIPSA analysis with input of protein structures in PDB format.

Enter the file names of the coordinates of the proteins to be analyzed. The pdb files can be selected either from your local disk (left panel) or by entering pdb identifiers (e.g. 1hti 1dkw 1b9b 1ci1 1i45 1tim, right panel). The selected pdb files/entries will be shown in a list and can be removed if necessary.

Input protein structures

Select local PDB files [*]	Specify PDB IDs from the RCSB .
<div style="border: 1px solid black; height: 100px;"></div> <div style="display: flex; justify-content: space-around;">Browse...Upload</div>	<div style="border: 1px solid black; height: 100px;"></div> <div style="display: flex; justify-content: space-around;">ImportZurücksetzen</div>

^{*}Files names will be cut after 23 characters

Please upload at least two, better more PDB files before proceeding!

<http://pipsa.eml.org>

PyMOL Tcl/Tk GUI

File Edit Build Movie Display Setting Scene Mouse Wizard Plugin Help Tutorial

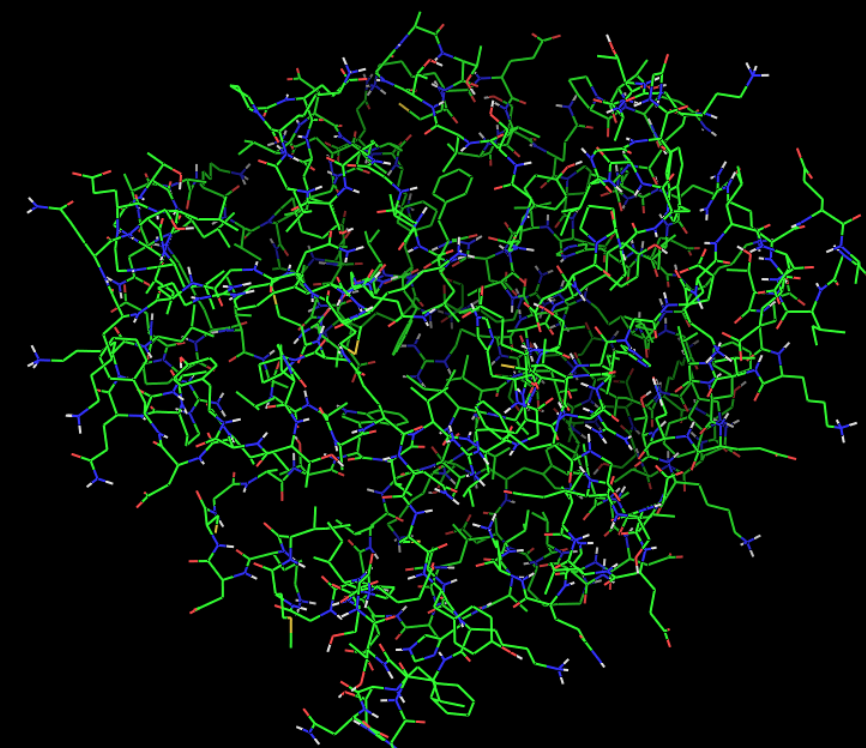
```

COMPND DUMMY
ObjectMolecule: Read crystal symmetry information.
Symmetry: Found 1 symmetry operators.
CmdLoad: "C:/Daten/PIPSA/examples/TPI/TPIC_SPIOL.pdb" loaded as "TPIC_SPIOL".
PyMOL>load_sep C:/Daten/PIPSA/examples/TPI/*pdb
HEADER TPIS of Homo sapiens
COMPND DUMMY
ObjectMolecule: Read crystal symmetry information.
Symmetry: Found 1 symmetry operators.
CmdLoad: "C:/Daten/PIPSA/examples/TPI/TPIS_HUMAN.pdb" loaded as "TPIS_HUMAN".
    
```

PyMOL Viewer

```

/TPIS_HUMAN 121 126 131 136 141 146 151 156 161 166 171 176 181 186 191 196 201 206 211 216 221 226 231 236 241 246
IGQKVAAHALAEGLVIAICIGEKLDEREAGITEKVVFEQTKVIADNVKDWKSVLAEYEPVWAIIGTKTATPQQAQEVHEKLRGWLKSNVSDAVAAQSTRIIYGGSVTGATCKELASQPDVDGFLVGGASLKPEFVDIINAK_CTRM_Q
    
```



all TPIS_HUMAN (select)

Mouse Mode 3-Button Viewing
 Buttons L M R Wheel
 & Keys Rota Move MovZ Slab
 Shft +Box -Box Clip MovS
 Ctrl +/- PkAt Pk1 MvSZ
 CtSh Sele Drig Clip MovZ
 SnglClk +/- Cent Menu
 DbClk Menu - PkAt
 Selecting Residues
 Frame [1 / 1] 2/sec

PyMOL>_

74 PyMOL Tcl/Tk GUI

File Edit Build Movie Display Setting Scene Mouse Wizard Plugin Help Tutorial

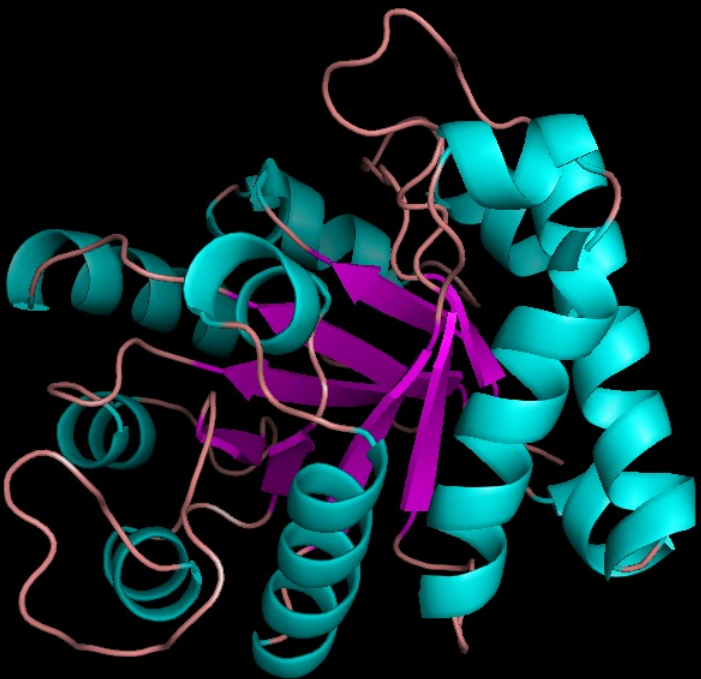
```

COMPND DUMMY
ObjectMolecule: Read crystal symmetry information.
Symmetry: Found 1 symmetry operators.
CmdLoad: "C:/Daten/PIPSA/examples/TPI/TPIC_SPIOL.pdb" loaded as "TPIC_SPIOL".
PyMOL>load_sep C:/Daten/PIPSA/examples/TPI/*pdb
HEADER TPIS of Homo sapiens
COMPND DUMMY
ObjectMolecule: Read crystal symmetry information.
Symmetry: Found 1 symmetry operators.
CmdLoad: "C:/Daten/PIPSA/examples/TPI/TPIS_HUMAN.pdb" loaded as "TPIS_HUMAN".
    
```

PyMOL Viewer

```

/TPIS_HUMAN 121 126 131 136 141 146 151 156 161 166 171 176 181 186 191 196 201 206 211 216 221 226 231 236 241 246
IGQKVAAHALAEGLVGIACIGEKLDEREAGITEKVVFEQTKVIADNVKDWKWLAYEPVVAIGTGKTATPQQAQEVHEKLRGWLKSNVSDAVAQSTRIIYGGSVTGATCKELASQPDVDGFLVGGASLKPEFVDIINAK CTRM Q
    
```



all TPIS_HUMAN

```

Mouse Mode 3-Button Viewing
Buttons L M R Wheel
& Keys Rota Move MovZ Slab
Shft +Box -Box Clip MovS
Ctrl +/- PKAt PK1 MovS2
CtSh Sele Orig Clip MovZ
SnglClk +/- Cent Menu
DblClk Menu - PKAt
Selecting Residues
Frame t 1/ 11 15/sec
    
```

PyMOL>_