PC GRID use cases and requirements

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OGF22, Enterprise Grids Requirements RG

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INSTITUTES FOR
BIOMEDICAL RESEARCH

Agenda

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- Overview of Novartis computing
- Scenarios
- Approaches
- Case studies and gap analysis
- Key technical requirements

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Overview of Novartis GRID computing

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Novartis Institutes for Biomedical Research (NIBR) site map

Overview of Novartis GRID computing

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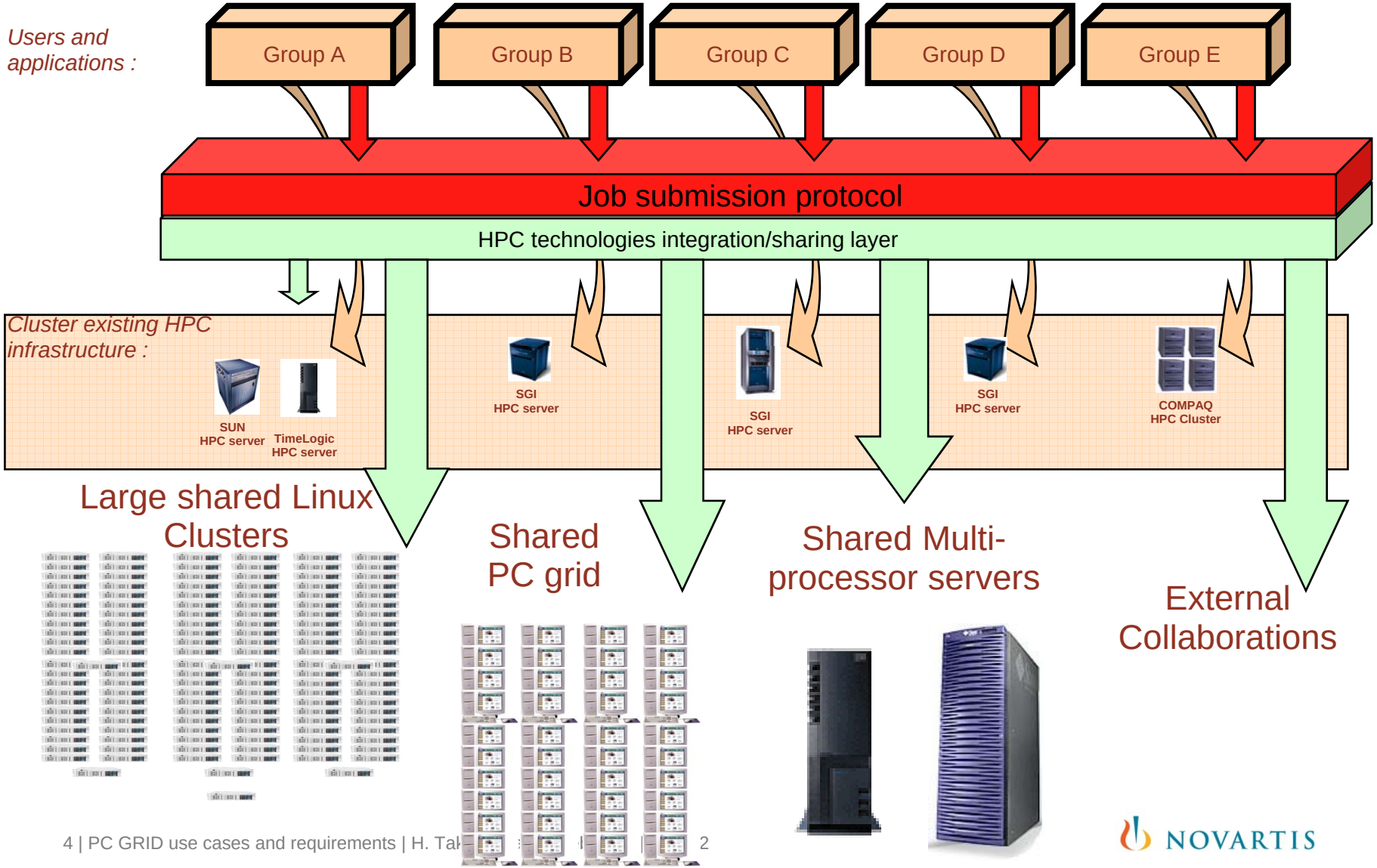

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Overview of Novartis GRID computing

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Steve Litster Ph.D, Novartis Institutes for BioMedical Research

Main topic: Storage virtualization

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Scenarios (Business cases)

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- Medicinal chemistry
- Structural biology
- Bioinformatics and knowledge mining

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Scenarios (Business cases)

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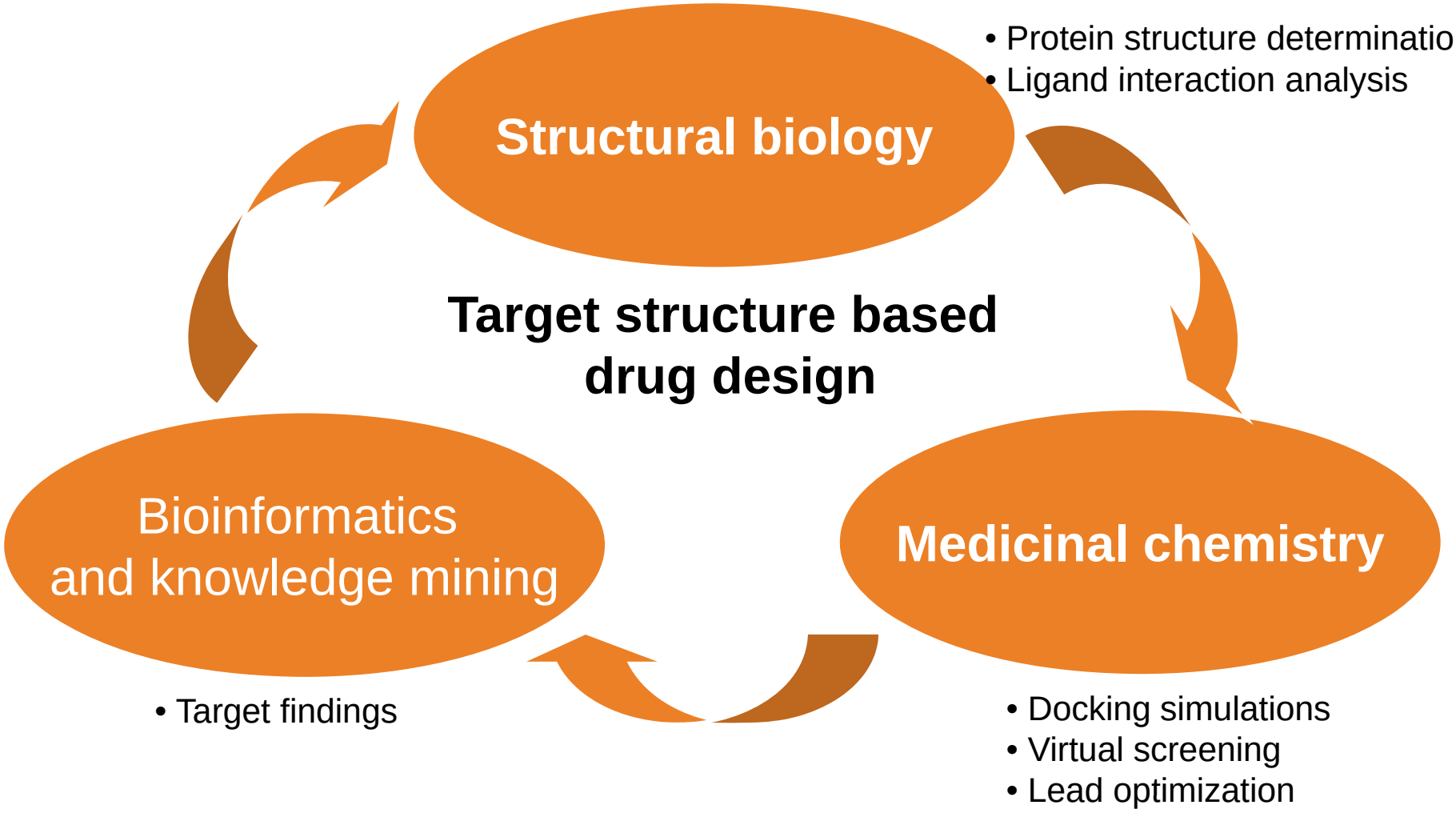

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Approaches (global project: “ENGINE”)

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- Enterprise next generation environment (ENGINE) from 2000 to 2003
  - Globally integrated hardware and platform
    - Windows XP Desktop PC, Laptop PC and Windows 2K/2K3 servers
  - Full Active Directory (AD) implementation

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Approaches (global project: “ENGINE”)

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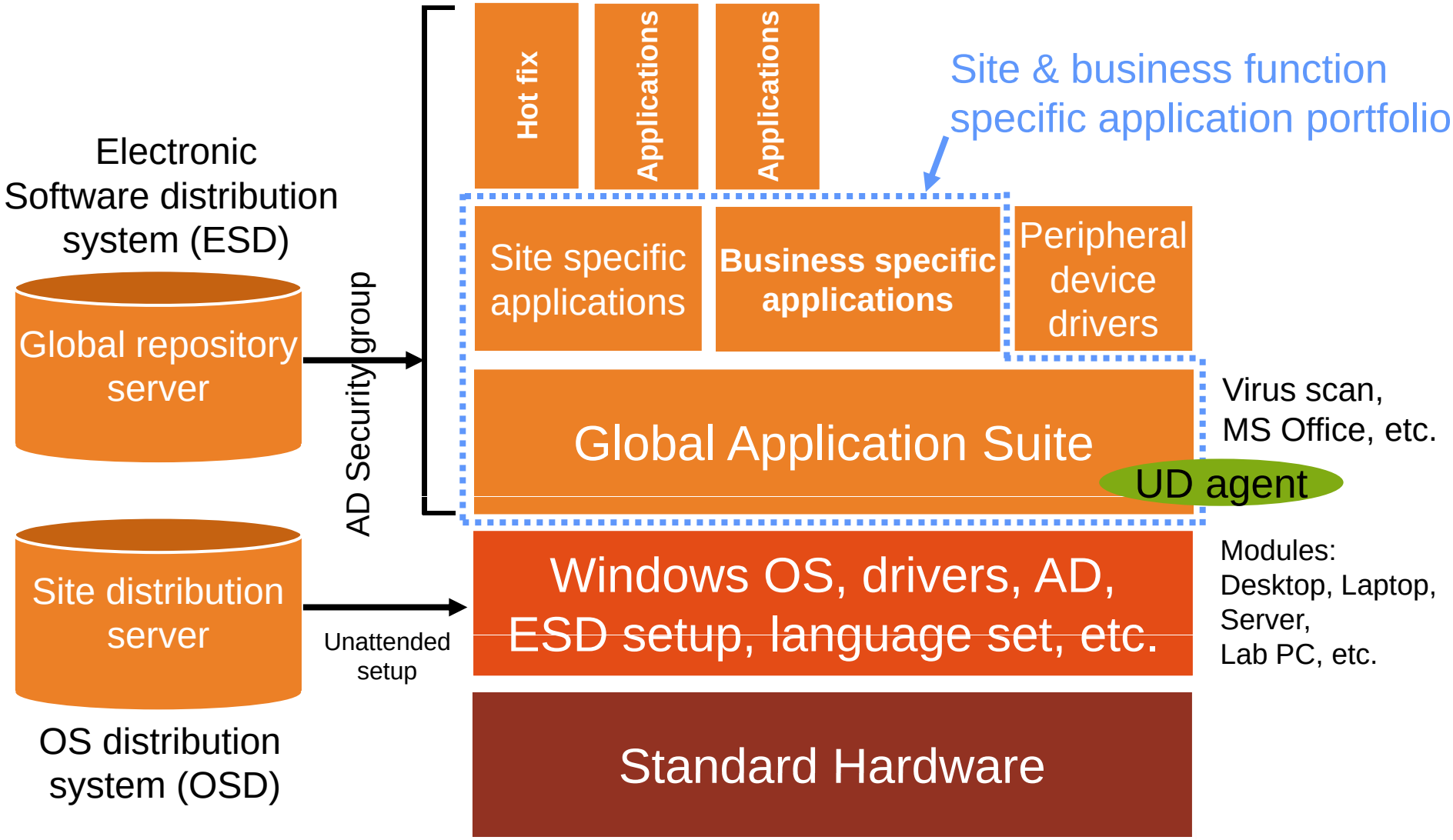

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Approaches (global project: “ENGINE”)

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- Life cycle management for…
  - PC hardware
    - Distribution of hardware specific images (base of SLA)
  - OS and service packs by OSD
    - Version management
  - Applications by ESD with DIPR process (Development, Integration, Productive, Retirement)
    - Global Application Suite and Hot fix
    - Business specific Application portfolio
    - Business applications
- Ownership (roles and responsibilities)
  - Application owner, Application portfolio manager, GRID service manager etc…..

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Approaches (Local build in environments)

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- Linux clusters
  - Site oriented (Basel, Cambridge etc.)
  - Test cluster in Tsukuba
    - 20 Linux PC controlled by Sun Grid Engine (SGE)
    - Logically separated private segments by VPN router

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Approaches (Local build in environments of Tsukuba)

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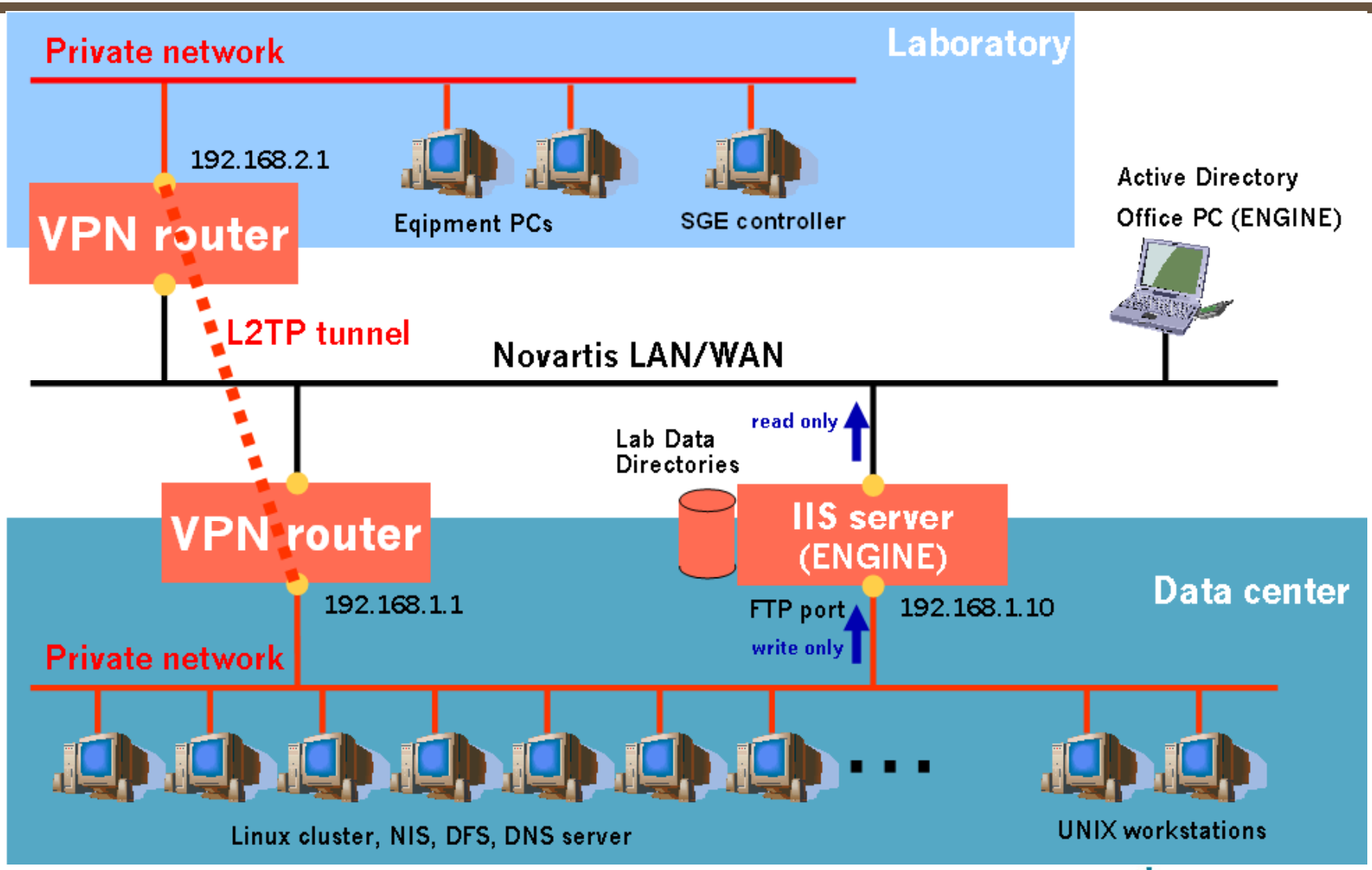

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Case studies and gap analysis

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- High-Throughput Docking for *in silico* screening
- Protein structure determination
- Vector/Parallel/Distributed jobs bench marks

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Case Study 1: High-Throughput Docking for *in silico* screening

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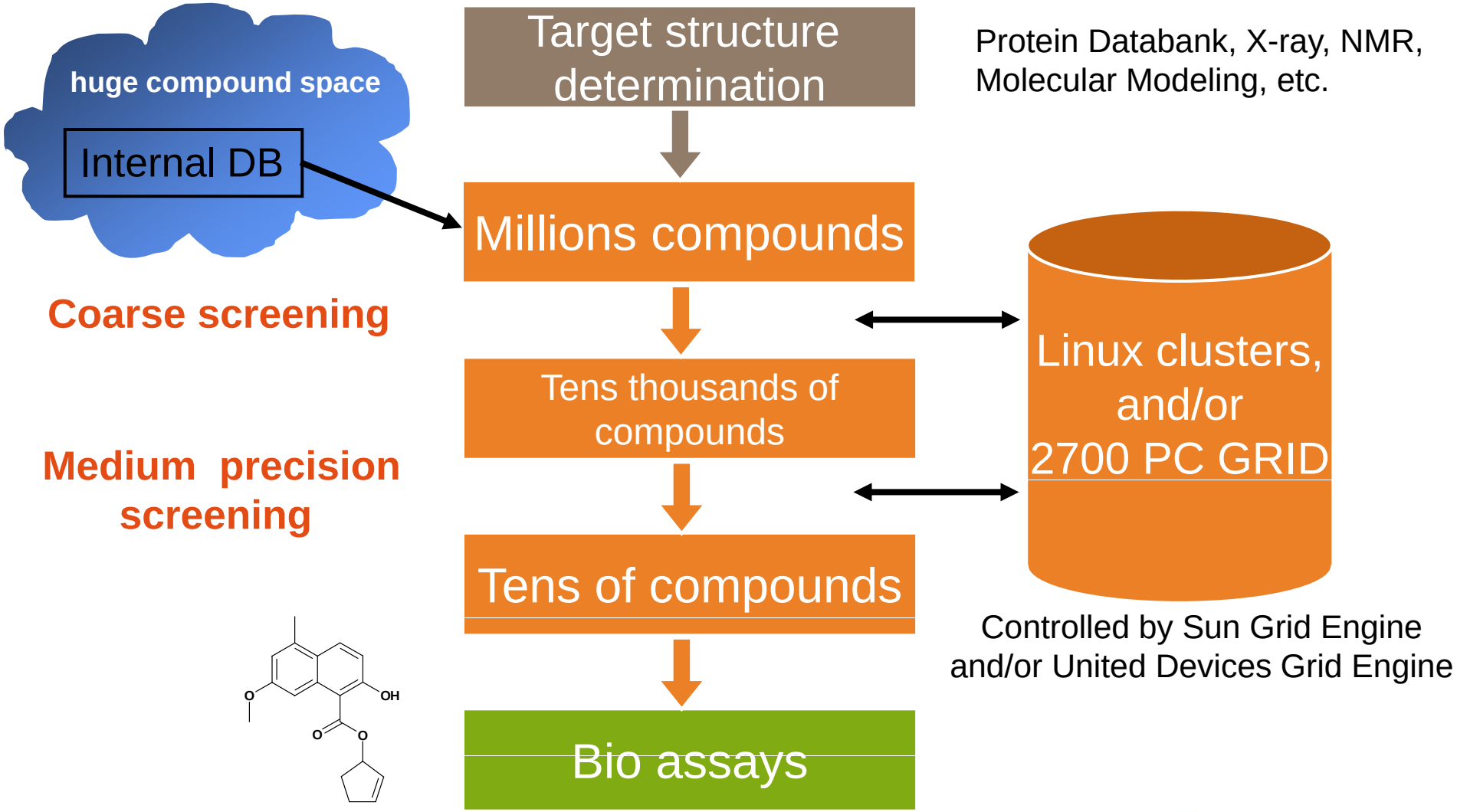

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Case Study 1: High-Throughput Docking for *in silico* screening

Enterprise Grids Requirements RG

Discovery of a Potent and Selective Protein Kinase CK2 Inhibitor by High-Throughput Docking
Vangrevelinghe, E., Zimmermann, K., Schoepfer, J., Portmann, R., Fabbro, D., and Furet, P. (2003) *J. Med. Chem.* **46**, 2656-2662.

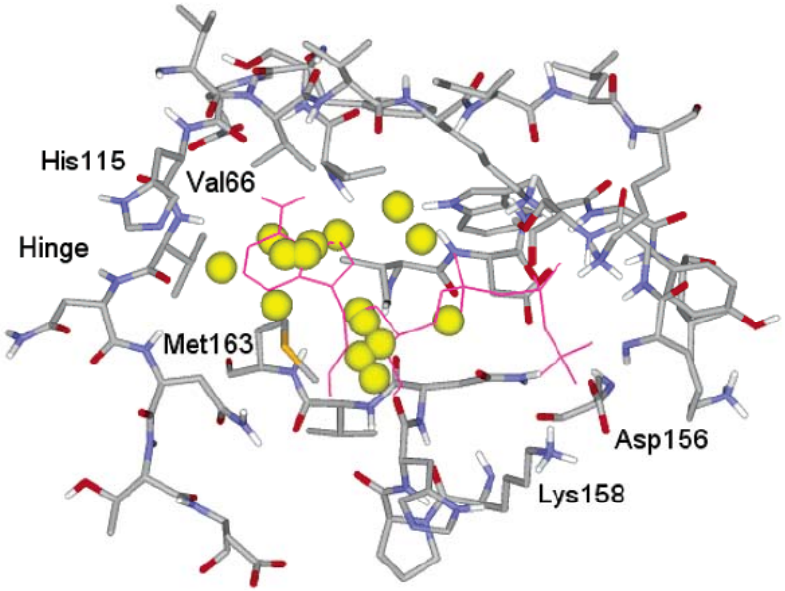

Figure 2. Overlay of the docking site points used (yellow spheres) and the ATP analogue extracted from the crystallographic template structure 1DAW (magenta) inside the active site of the homology model of human CK2α.

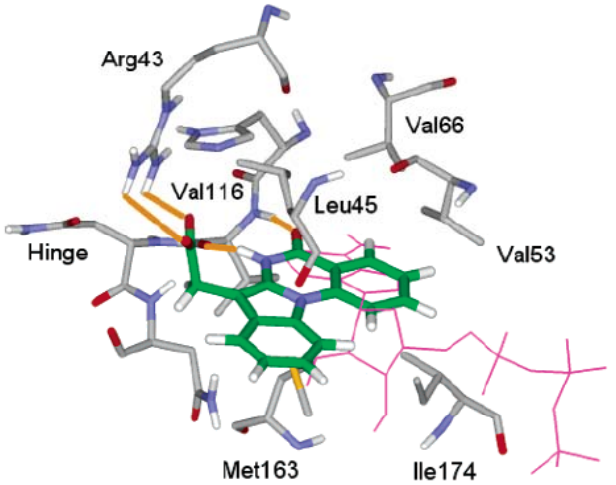

Figure 3. Relative binding modes of compound **4** (green) and the ATP analogue extracted from the crystallographic template structure 1DAW (magenta) in the human CK2α active site. The hydrogen bonds formed with Arg 43 and Val 116 are indicated as orange lines.

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Case Study 2: Protein structure determination

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- X-ray
- NMR
- Electron microscopy
- Computer modeling

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Case Study 2: Protein structure determination

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Experimental data

Protein sample preparation,
NMR experiments, Data analysis

Initial structures

huge
conformational space

Energy minimized
structures

**Molecular Dynamics
calculations**

Refined structures

Linux clusters
20 CPUs

Controlled by Sun Grid Engine

Protein Databank,
Medicinal chemistry

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Case Study 2: Protein structure determination

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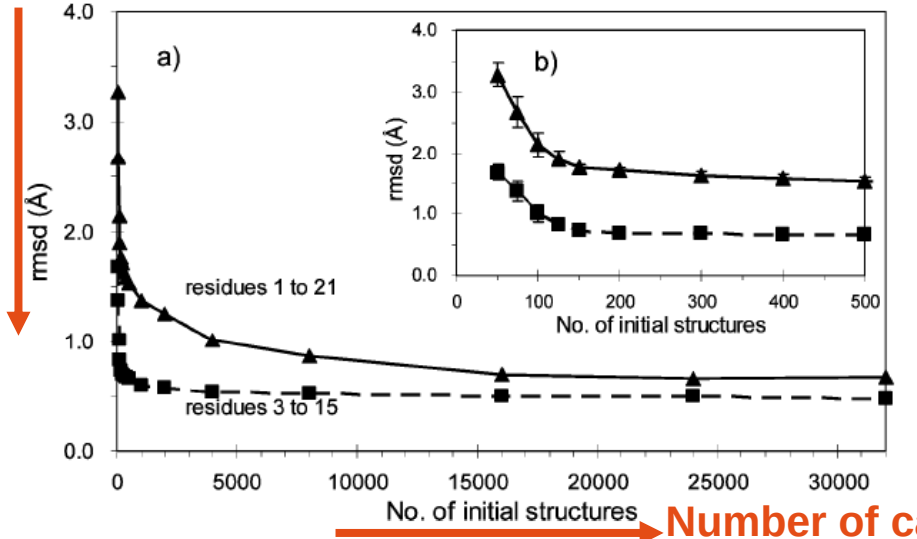
Distributed Computing and NMR Constraint-Based High-Resolution Structure Determination: Applied for Bioactive Peptide Endothelin-1 to Determine C-terminal Folding.
Takashima, H., Mimura, N., Ohkubo, T., Yoshida, T., Tamaoki, H., and Kobayashi, Y. (2004) *J.Am.Chem.Soc.* **126**, 4504-4505.

Structural precision



Number of calculations

Figure 1. (a) The pairwise averaged rmsd values of all backbone atoms of ET-1 have been elucidated for 20 minimum energy structures out of various numbers of calculated structures with 80-ps simulated annealing at initial temperature 5000 K. (▲) Overlay for all residues from 1 to 21. (■) Overlay for residues 3 to 15. (b) The same plot as (a), expanding the horizontal axis.

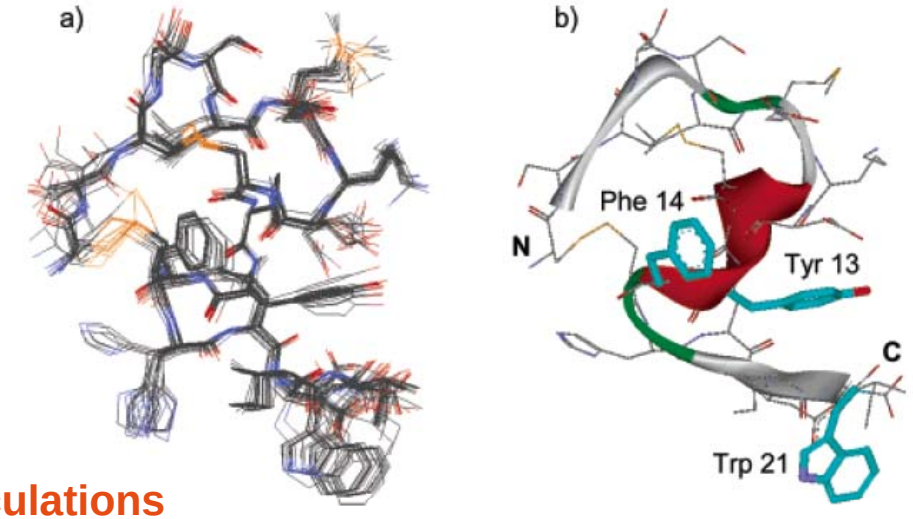


Figure 2. (a) Overlay of 20 minimum energy structures of ET-1, pairwise backbone rmsd 0.58 ± 0.28 Å. (b) The lowest energy structure of (a) with ribbon drawing, schematically representing α-helix and β-turns in red and green, respectively.

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Case Study 2: Protein structure determination

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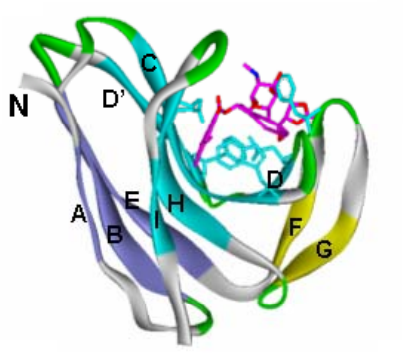
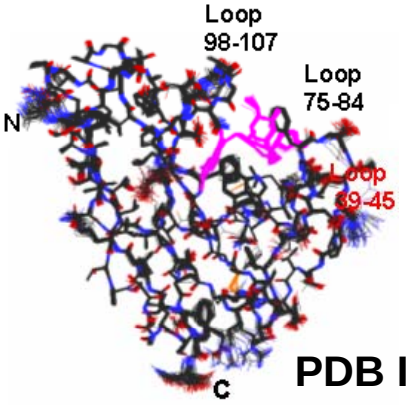
Solution NMR Structure Investigation for Releasing Mechanism of Neocarzinostatin Chromophore from the Holoprotein.
Takashima, H., Yoshida, T., Ishino, T., Hasuda, K., Ohkubo, T., and Kobayashi, Y.
(2005) *J. Biol. Chem.* **280**, 11340-11346.

High-Resolution Protein Structure Determination by NMR
Takashima, H. (2006) in *Annual Reports on NMR Spectroscopy* **59**, 235-273. printed by Elsevier Ltd., London

Structure of Cytocrome c552 from a Moderate Thermophilic Bacterium, Hydrogenophilus thermoluteolus: Comparative study on the thermostability of cytochrome c.
Nakamura, S., Ichiki, S., Takashima, H., Uchiyama, S., Hasegawa, J., Kobayashi, Y., Sambongi, Y., and Ohkubo, T. (2006) *Biochemistry* **45**, 6115-6123.





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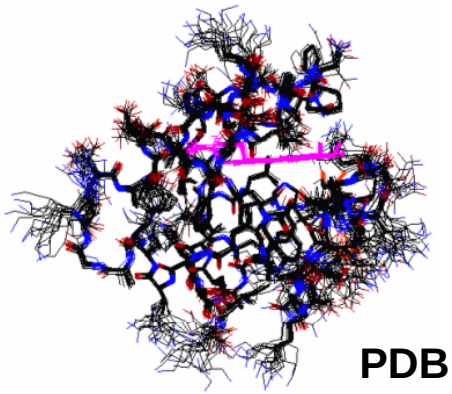

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Key technical requirements

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- Limitation as is
  - Difficult license management
    - Number of CPUs is limited by software licenses
  - Scientific application platform
    - Unix/Linux base to Windows base software
  - Network performance
    - Especially at remote sites
  - Overhead of parallel calculations
  - Calculation precisions
    - With or without induced fitting, Free energy calculations, Protein dynamics Force fields, Solvent and more……

Key technical requirements

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- Requirements to be
  - Precision as high as possible (depending on computer power)
    - Expand available applications
    - Real time simulations
  - More computer power on demand (from user's point of view)
  - Software license virtualization

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Thank you for your collaboration!

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