# A Distributed Decision Support System for Viral Disease Treatment

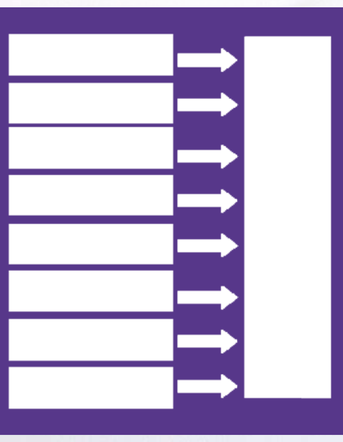
## Motivation

**“Understanding the dynamics of infectious-diseases demands a holistic approach”**
Neil Ferguson, Nature Vol. 446, 12 April 2007

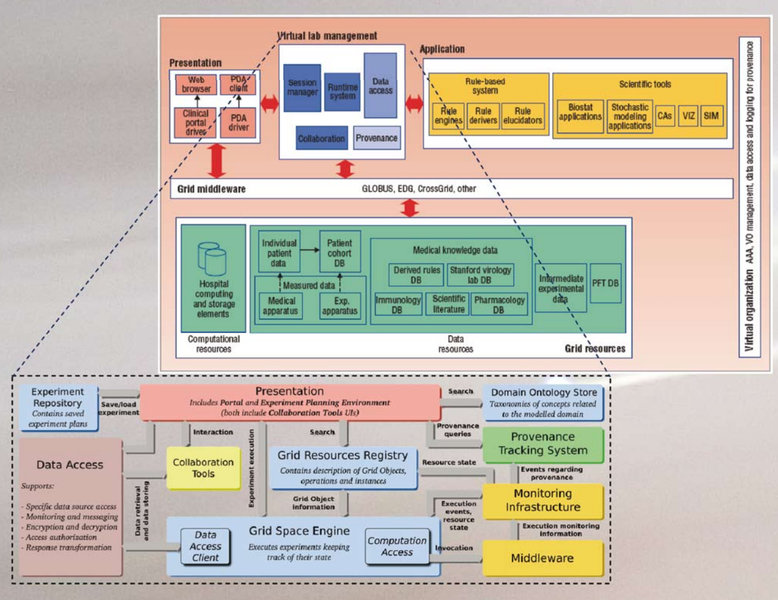
During the past decade, researchers have made significant progress in treating patients with viral diseases. The objective of the Virolab project is to develop a virtual distributed decision support system for infectious diseases that facilitates medical knowledge discovery. This virtual laboratory for researchers and clinicians functions as a user-friendly decision support system for HIV drug-resistance testing and treatment, as well as for reliably predicting drug susceptibility and virological response at individual and epidemiological levels.

## Approach

ViroLab facilitates medical knowledge discovery and decision support for drug resistance by ranking drugs targeted at patients by virtualizing the hardware, computing infrastructure, and data repositories using tailored workflow templates to harness and automate such diverse tasks as data archiving, integration, and mining, complex modeling and simulation, and the integration of biomedical information from viruses (proteins and mutations), patients (viral load), and literature (drug-resistance experiments).



### System Architecture and Virtual Laboratory

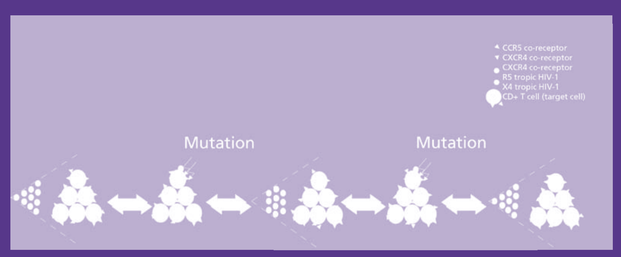



### Enhancements to the Drug Susceptibility Interpretation System

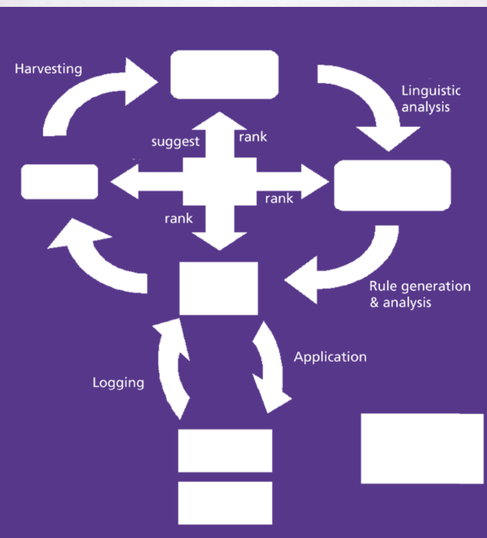
For instance, we developed a parameterized Complex Network (CN) model describing the dynamics of HIV spreading “on top of it”. The model has some distinctive features: It takes into consideration all the existing kinds of HIV spreading. Homosexual and heterosexual spreading is described by a scale-free network, drug users spreading is described with the assumption of homogeneous mixing inside the exposure group. All the network parameters have been aken from medicine literature and didn’t change during numerical experiments.

Sexual contact networks over a one year period. (left) - hetrosexual network; right - MSM(men having sex with men) network. The network structure is scale free, with $P(k)=\kappa^{\gamma}$ and $2<\gamma<3$ and $\kappa$ the number of outgoing links per node.

On the other hand, early infection with human immunodeficiency virus (HIV) is characterized by the predominance of CCR5-tropic (R5) virus. However, over the course of infection CXCR4-tropic (X4) virus appears in the later stage of the infection in approximately 50% of the infected individuals and usually precedes an accelerated CD4+ T cell depletion with rapid disease progression. We investigate the interaction between HIV-1 quasi-species population and the changes in the target cell co-receptor designation in the disease course.




One more approach we use is Bayesian hierarchical modeling to make predictive distributions in the presence of uncertainty, used in two ways: as posterior inferences summarizing uncertainties about predictive quantities, as well as within the decision analysis in multistage decision trees. The full chain of analysis will combine Bayesian hierarchical modeling with probabilistic decision analysis based on utility attribution and/or multi-objective optimization of such quantities as cost, chance and duration of survival or quality-adjusted life years.




## Conclusion

The increasing availability of genetic information and extensive patient records allow researchers to study diseases from the DNA level all the way up to medical responses. Resolving the long-standing challenges of individual-based, targeted treatments is coming within reach. ViroLab’s enhancements to the state-of-the-art genotypic resistance interpretation tools and their integration into the virtual laboratory are based on research initiatives to explore novel ways of providing data, evidence and knowledge for enhancing the Virolab HIV drug-susceptibility interpretation system and to evaluate their feasibility.


P. M. A. Sloot[1], A. Tirado-Ramos[1], G. Ertaylan[1], Breanndan O Nuallain[1], D. van de Vijver[2], C. Boucher[2], M. Bubak[3]
(1) Section Computational Science, University of Amsterdam, The Netherlands, (2) Utrecht University Medical Center, The Netherlands, (3) AGH University of Science and Technology, Poland



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