VIROLAB

A Virtual Laboratory for Decision Support in Viral Disease Treatment

www.virolab.org

Peter Sloot[1], Charles Boucher[2], Marian Bubak[3,4], Alfons Hoekstra[1], Pawel Plaszczak[5], Alice Posthumus[6], David van de Vijver[2], Stefan Wesner[7], Alfredo Tirado-Ramos[1]

[1]Universiteit van Amsterdam, The Netherlands
[2]Institute Universitair Medisch Centrum Utrecht, The Netherlands
[3]Institute of Computer Science AGH, Kraków, Poland
[4]Academic Computer Centre CYFRONET, Kraków, Poland
[5]Gridwise Technologies, Kraków, Poland
[6]Virology Education B.V., The Netherlands
[7]Universitaet Stuttgart, Germany
sloot@science.uva.nl, A.K.GroeninxvanZoelen@uva.nl

Motivation

The main objective of the ViroLab project is to develop a Virtual Laboratory for Infectious Diseases that facilitates medical knowledge discovery and decision support for, e.g., HIV drug resistance. Large, high quality in-vitro and clinical patient databases have become available which can be used to relate genotype to drug-susceptibility phenotype. Relevant data has two main characteristics: it spans all temporal and spatial scales from the genome up to the clinical data, and it is inherently distributed over various sources (virological-, clinical- and drugs-databases) that change dynamically over time.
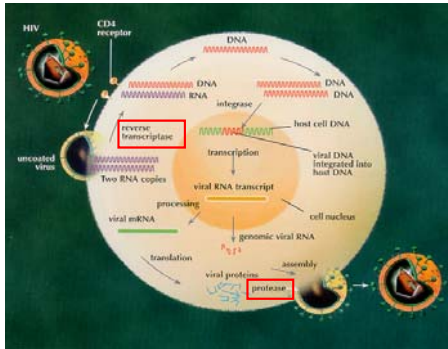
HIV Farmacology

Such data comes also from a considerable proportion of patients for whom drugs fail to completely suppress the virus resulting in the rapid selection of drug-resistant HIV and loss of drug efficacy. To avoid the rapid selection of drug-resistance, HIV-1 replication should be completely suppressed, in order to delay the destruction of the immune system by inhibiting the depletion of CD4+ cells. Genotypic assays, based on nucleic acid sequencing of the viral reverse-transcriptase and protease genes are widely used to determine drug resistance and identify mutations associated with resistance to antiretroviral drugs.
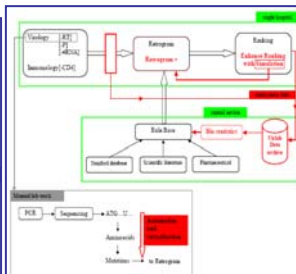
Approach

At the core of the ViroLab Virtual Laboratory is a rule-based ranking system, like Retrogram. Because Retrogram is currently a monolithic program, we separate and virtualize its components to use it in a Grid environment. Using a Grid-based service oriented architecture, we vertically integrate the biomedical information from viruses (proteins and mutations), patients (e.g. viral load) and literature (drug resistance experiments), resulting in a rule-based decision support system for drug ranking.


Interpretation tools VL

Decision Support Functional Architecture

Grid Architecture

The Grid-based Virtual Laboratory supports tools for statistical analysis, visualization, modeling and simulation, to predict the temporal virological and immunological response of viruses with complex mutation patterns to drug therapy. It provides the medical doctors with a decision support system to rank drugs targeted at patients, and the virologists with an advanced environment to study trends on an individual, population and epidemiological level.
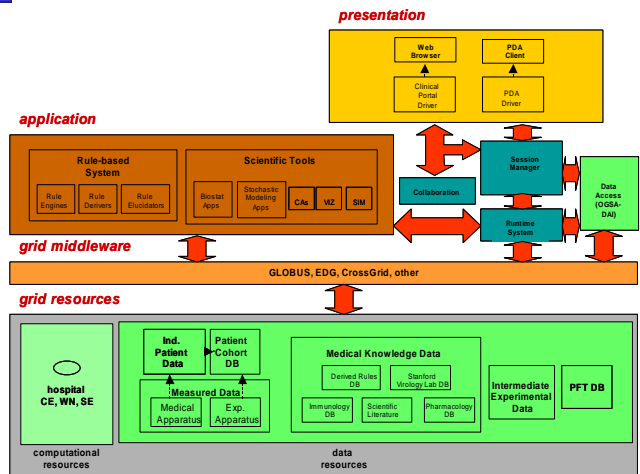
ViroLab Component Perspective

Conclusions

By virtualizing the hardware, compute infrastructure and databases, the ViroLab virtual laboratory is a user friendly environment, with tailored workflow templates to harness and automate such diverse tasks as data archiving, data integration, data mining and analysis, and modeling and simulation. HIV drug resistance is one of the few areas in medicine where genetic information is widely used for a considerable number of years. Large numbers of complex genetic sequences are available, in addition to clinical data. ViroLab offers a unique opportunity as a blueprint for the potentially many diseases where genetic information becomes important in future years.

References

[1] VIROLAB - EU IST STREP Project027446 http://www.virolab.org/
[2] De Luca A, Cingolani A, Di Giambenedetto S, Trotta MP, Baldini F, Rizzo MG et al. Variable prediction of antiretroviral treatment outcome by different systems for interpreting genotypic human immunodeficiency virus type 1 drug resistance. J Infect Dis 2003: 187(12):1934-1943
[3] VL-e: Virtual Laboratory for e-sciences, Dutch research program funded by the Ministry of Science and Education and by the Royal Academy of Sciences and by the Ministry of Economic Affairs. http://www.vl-e.nl
[4] P.M.A. Sloot; A.V. Boukhanovsky; W. Keulen; A. Tirado-Ramos and C.A. Boucher: A Grid-based HIV Expert System, Journal of Clinical Monitoring and Computing, (in press) 2005.