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Software-As-A-Service for improving Drug Research towards a standardized approach

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Abstract

Software as a Service (SaaS) is one of the most interesting applications of a service-oriented architecture. SaaS spares users the cost of acquiring and maintaining hardware and software. The SaaS business model is very widely appreciated in the economy, because it brings not only financial benefits but also process-optimizing benefits. Drug research is a lengthy, complex and costly process that involves a number of disciplines, from medicine through economics to natural science. Until recently, the standard programs and infrastructure used for data analysis were almost exclusively commercial, proprietary, closed source and expensive. One of the major attractions of the open-source model is to customize the platform to suite the requirements and react faster on changes. There are different proprietary approaches. However there is a gap in knowledge regarding using closed and proprietary infrastructure. The aim of this research is to investigate the impact of an open source SaaS approach on the drug research process.

Keywords: *SaaS; OpenStack; Drug Research; Virtual Screening*

1. Introduction

Drug research and development (R & D) is a complex, time intensive, expensive task and involve many risks. According to general estimates[2], it is assumed that the conception of the "drug to market" has duration of 12 years and cost an average of more than $ 800 million. From this fact technologies developed to reduce the research time and cost. Computer-aided drug design (CADD) is such a modern development[3].

1.1. Software as a Service

Cloud computing is defined by Feuerlicht[4]: It includes computing, data storage and software services, which are accessible through the Internet. Coombe[5] defines cloud

computing as a change of paradigm, which enables scalable execution and storage across distributed and networked systems. Cisco[6] believes that cloud computing has the potential to provide on-demand services available and at lower cost than current options, with less complexity, greater scalability and greater range. Catteddu and Hogben[7] describing that cloud computing provides IT-resources in a new way. Cloud services e.g. software or data storage, processing can immediately make on demand available. Especially in times of rising costs, the growth of cloud services is a ray of hope. Another definition [1] describes SaaS as software that is used as a hosted service and accessed over the Internet via standard web browser. This may include IIS or Apache software, but typically SaaS means the provision of business applications, including collaboration software and industry-specific applications, to companies that need these applications to run their business. Fig. 1. Illustrates how the distribution and operation of SaaS compared to in-house looks like.
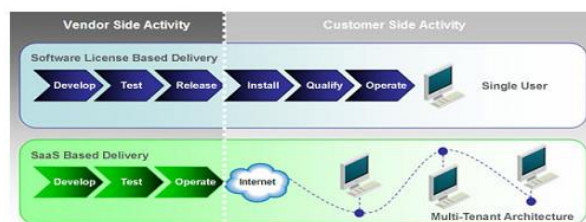

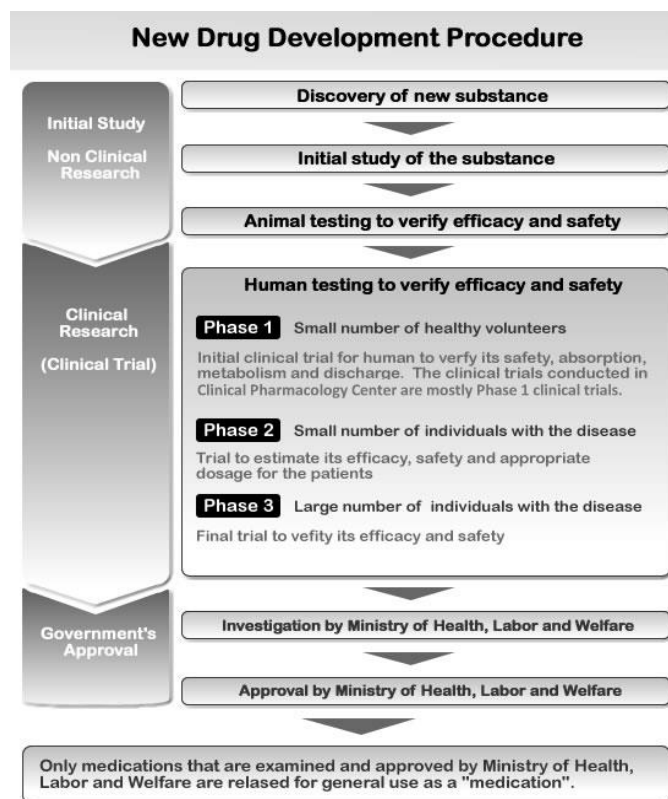Fig. 1 SaaS model vs. traditional Software[8]

Fig. 2 Procedure for developing new drugs [9].

1.2. Drug research and development (R & D)

From 10,000 compounds, which were under investigation for a drug, only one ever come to market. Even if a compound reaches the market, only one of three bring their development costs back. Therefore, the development is associated with high risks! Drug development is a scientific challenge that is strictly regulated, because of the legitimate concerns of public health. Fig. 2 shows the procedure for development of a new drug.

Drug development phases: The drug development process can be split up into three phases as seen in Fig. 2. (1) Pre-clinical research and development. (2) Clinical research and development and (3) Government's approval.

2. DRUG DISCCOVERY METHODS

One of the most successful ways to find promising drug candidates is to examine how the target protein interacts with randomly selected compounds that usually are part of libraries. The test is common in so-called high-throughput screening (HTS) facilities. Compound libraries are commercially available with a size of millions of compounds. The most promising compounds from the

screening will come forth, called hits, which are the compounds that exhibit binding activity at the target.

2.1. Virtual Screening

VS is based on the basis of the derived mathematical or simulated real screening. Computational methods can be used to predict or simulate how a particular connection with a specific target protein interacts. These findings are used to help build a hypothesis over chemical properties and in the design of active substances and they can also be used to refine and modify drug candidates. The following three virtual screening or computational methods are used in modern drug development; (A) Molecular Docking, (B) Quantitive Structure-Activity Relationships (QSAR) and (C) Pharmacopeia Mapping.

A. **Molecular Docking:** If the structure of the target is available, usually from x-ray crystallography, molecular docking is the most used VS-method. Molecular docking may also be used to test if the hypothesis is right, before carrying out the expensive laboratory tests. This software can predict how a drug binds to a target protein.

B. **QSAR:** As mentioned above, it is necessary to know the geometrical structure of both the ligand and the target protein in order to use molecular docking. QSAR is an example of a process regardless of whether the structure is known or cannot be applied. QSAR models are used for VS of compounds for investigation to find suitable drug candidates for the target.

C. **Pharmacopeia Mapping:** While QSAR concentrates on a number of descriptors, such as electrostatic and thermodynamic properties. Pharmacopoeia is a geometric mapping approach. A pharmacophore can be thought of a 3D model of the characteristic features of the binding site of the protein under examination (target).

2.2. High-throughput screening

HTS is a method for scientific experimentation especially used in drug discovery and relevant for the areas of biology and chemistry. Robotics, data processing and control software, liquid handling devices and detectors makes HTS available. HTS researcher can quickly perform millions of biochemical, genetic or pharmacological tests. Through this process, one can quickly identify active substances, antibodies or genes, which modulate a particular bimolecular path. The results of these experiments provide starting points for drug design and for understanding the interaction or role of a particular biochemical process in biology.

3. Virtual Screening Software

In this section, AutoDock, VS software will be specifically highlighted. AutoDock is docking software also specifically found in cloud application. AutoDock is a pioneer among the docking programs to model ligand confrontational with full flexibility. The Institute Prof. Arthur J. Olsen Laboratory, the first version (1989-1990) was written in FORTRAN 77 by Dr. David S. Goodsell[10]. (It was almost AutoDoq called because it uses quaternions for rotations, quaternions do not come from the so-called Gymbal lock problem associated with the Euler angles.) AutoDock base algorithm is the so-called Monte Carlo method in combination with genetic algorithm for giving conformations.

3.1. Inhibox

InhibOx[11] focuses on the development and provision of services and technology in computer-aided drug discovery (CADD). Inhibox infrastructure is based upon the Amazon Web Services. InhibOx delivers: Lead identification capabilities, lead optimization and VS capability with a compound database of 110 million synthesized compounds.

3.2. Accelrys HEOS

HEOS[12] was a development and a starting point for neglected diseases collaborations. HEOS was able to manage information, which was generated by more than 400 users across the world. HEOS is hosting over 90 drug research projects and has a library with over 600,000 chemical compounds.

3.3. eScience Central

e-Science Central[13] is another SaaS provider on the VS market. It is a solution working 100% in the cloud and needs only a web browser for running studies. They offer working with total privacy or in collaboration with trusted partners. One of the most important key features of e-science central is to analyze data and not only share them in the cloud like other collaboration solutions does. The infrastructure is Windows Azure. The difference is that e-science central is Platform as a Service provider and deliver a complete platform to run specific applications like AutoDock or similar.

4. Conclusions and Future Work

Virtual screening services are currently offered as web services. They are accessible for interactive use or batch processing of entire library of compounds with transparent
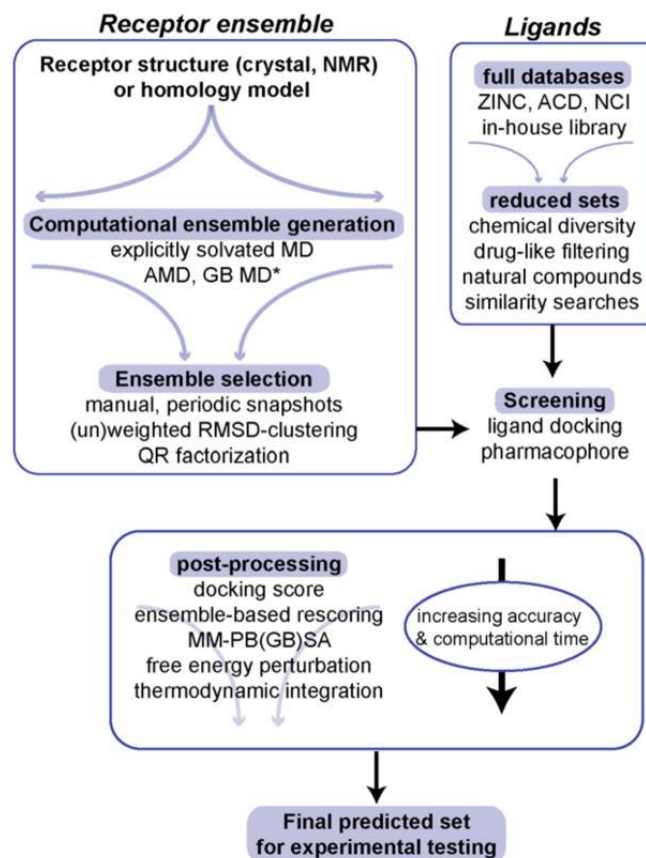

Fig. 3 General workflow for ensemble-based virtual screen experiment [15]

access to cloud or cluster resources[14]. The systems will be available as a computational workflow (see Fig.3) and be easily accessible to a much wider audience. Commercial offers, like Accelrys Pipeline Pilot provides a complete solution for academic research in computer-aided drug design. Increasingly, both academic and commercial enterprises rely on cloud-based virtual screening services that are completely transparent to the end user. Research, such as the World Community Grid use the idle time of computers and provide another venue for virtual screening represents. Better theories and efficient numerical Procedure to allow selection of the most relevant conformations of ligand binding* in a predictive manner are still needed. New algorithms, like Iterated Local Search global optimizer[16] and multi threading optimized algorithms, used in AutoDock Vina present with 10 to 100 times faster compared to AutoDock with equal or better performance. In summary, make the further acceleration by algorithmic and hardware improvements, utility computing and cloud-based virtual screening make it accessible to a wider audience, and its further validation and optimization. Algorithmic acceleration is an important point, because results

delivered faster without increasing hardware power. Further research will be done in running AutoDock Vienna in a standardized environment using OpenStack. Openstack[17] is a cloud operating system based on standardized programs. Results will be compared with proprietary alternatives like Amazon Web Services or Microsoft Azure.

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