Chapter 11

Virtual Screening: An Emergent, Key Methodology for Drug Development in an Emergent Continent—A Bridge Towards Patentability

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ABSTRACT

The universe of known organic chemical compounds has grown exponentially during the last 50 years, which greatly increases the probability of finding chemotherapeutic agents which interact selectively with any given molecular target. Traditional systematic pharmacological screening of available drug-like compounds has, however, can not keep the pace with the uninterrupted growth of the chemical space. The last 20 years have thus witnessed the emergence of novel high throughput screening technologies conceived to explore the vast chemical universe in an efficient manner, among them, virtual or in silico screening.

In this chapter, the authors analyze virtual screening advantages and the classification of virtual screening approaches. They also discuss the current and potential importance of virtual screening for drug development in Latin America. Finally, they present a brief overview on virtual screening perspectives.

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INTRODUCTION

The advances in Organic Chemistry and in technologies related to chemical synthesis have resulted in a tremendous increase in the rate of development of new chemical entities. The number of known chemical compounds has been growing exponentially during the last four decades. In 2009, the Chemical Abstract Service (http://www.cas.org), a subsidiary of the American Chemical Society responsible for the most comprehensive collection of disclosed chemical substance information in the world (from both patent and journal literature), announced the record of its 50 millionth substance. The 40 millionth compound had been registered just nine months before. In contrast, the 10 millionth chemical was not registered until 1990. Pubchem Substance (http://pubchem.ncbi.nlm.nih.gov), a chemical database oriented to small chemical compounds, includes to the day more than 17 million records of substances. This is a promising scenario for the pharmaceutical sector: in this virtual infinite universe of chemicals it is highly probable to find compounds that selectively interact with any given molecular target of interest. Nevertheless, as Kubinyi has once and again described, the drug discovery process is, in this background, quite equivalent to the proverbial search for a needle in a haystack (Kubinyi, 2002; the reader may also see Professor Kubinyi’s website and conferences therein, http://www.kubinyi.de/). Exploring this vast chemical space in an exhaustive manner (through systematic pharmacological screening of all known chemical entities against all possible biological targets) is no longer feasible (nor rational) in terms of time and resources that ought to be invested. Instead, Medicinal Chemists have developed alternative approaches to explore the haystack in a cost and time-efficient manner. High Throughput Screening (HTS), for example, merges microarrays and robotics to test small samples of a series of compounds against a wide range of in vitro tests (Pereira & Williams, 2007). Instead of asking a researcher to carefully analyze each element of the haystack until the unique properties of the needle are revealed to the experienced eye, HTS replaces (to some extent) the human ingredient by automated technologies relying on robotics, controlling software and sensitive detectors. On the other hand there is Virtual Screening (VS): a heterogenic set of computational techniques to explore digital representations of chemical entities recorded in chemical databases, in order to indentify potential candidates gathering an array of structural constrains or requisites that are somehow linked to certain biological and/or chemical properties. The use of VS has been progressively increasing since the first campaigns in the early 1990s, as illustrated in Figure 1.

In this chapter we will analyze the advantages and types of VS and we will discuss the opportunities linked to the use of this approach in Latin America, related to potential patenting of research and development (R&D) on new drugs and possible collaborations between the academic and the industrial sectors. We will also include a short section on perspectives of VS.

BACKGROUND

Advantages of Virtual Screening

Among the advantages of VS one might mention:

- **Time-efficiency.** Today, the fastest approaches can today easily handle a collection of several millions of chemical structure in a few weeks period (Muegge & Olof, 2006). The ever-growing processor speed of computers may allow attaining this time-efficiency when more complex approaches are involved, in the near future.

- **Cost-efficiency.** Once a lab has acquired (or developed in-house) a chemical database and the necessary hardware and software to apply a given methodology, the