

Cursos de verano 2011

Universidad de Alcalá

Taller de *docking* y cribado virtual:
uso de herramientas computacionales en el diseño de fármacos

La plataforma VSDMIP

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VSDMIP

(plataforma integrada para el manejo de datos de cribado virtual)

Plataforma informática orientada al descubrimiento de nuevos fármacos a través de la técnica de cribado virtual de quimiotecas

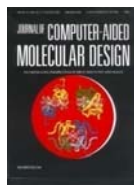
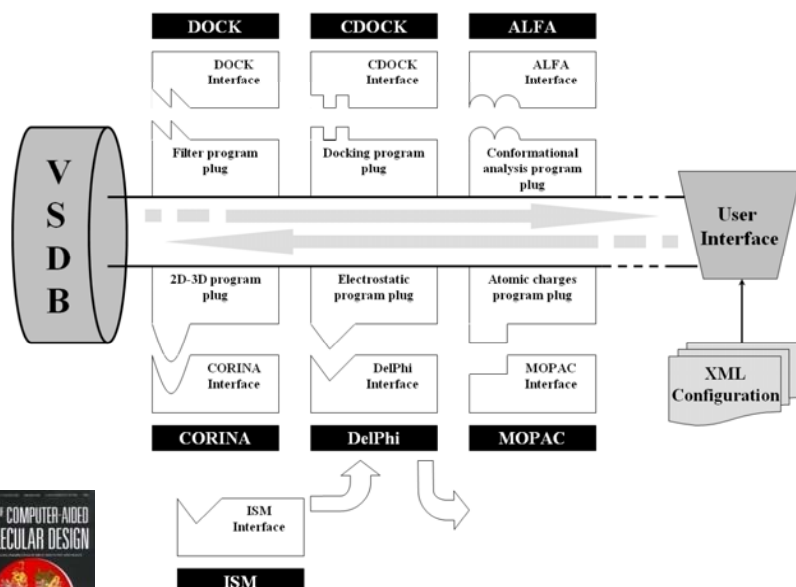
V
S
D
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1 artículo metodológico (2005-2009)
3 artículos de aplicación
4 patentes depositadas
1 Tesis Doctoral (Rubén Gil-Redondo)
Colaboraciones
Estancias cortas de investigadores

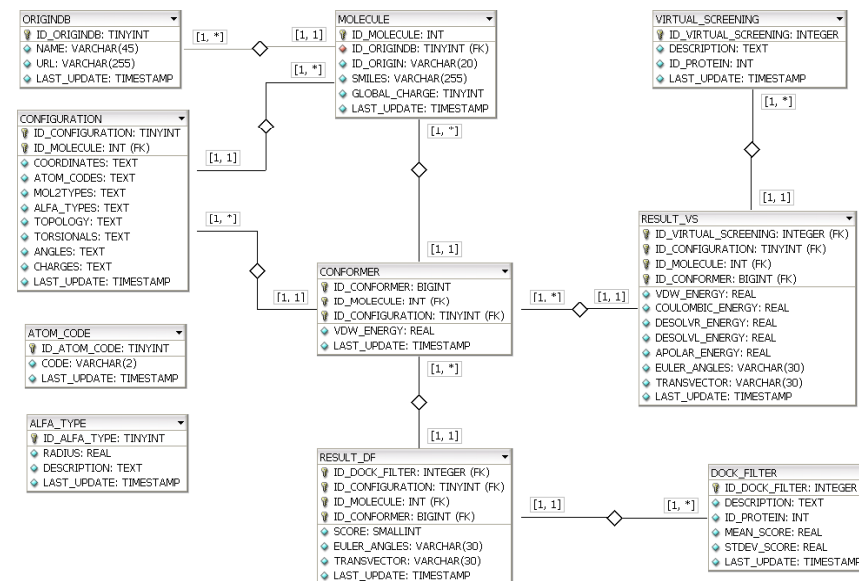
Versión 1.0 SBDD

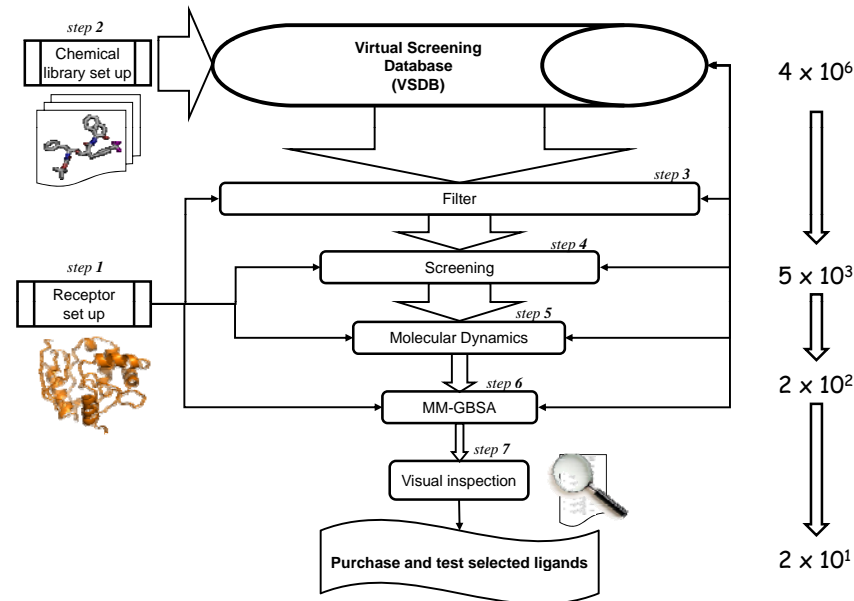
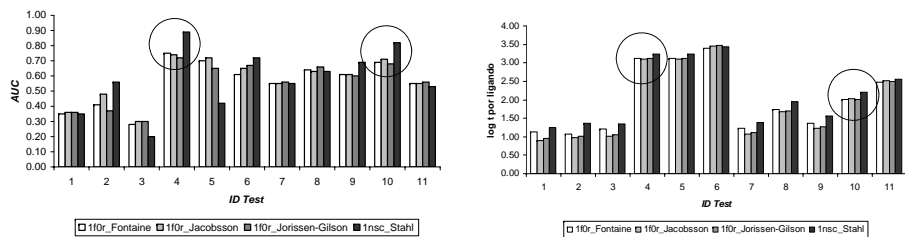
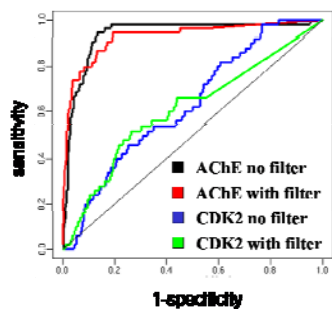
Versión 1.5 SBDD & LBDD + GUI

Versión 2.0 servidor web (largo plazo, 3-4 años)

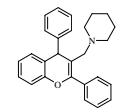


J Comput.-Aided Mol. Des. 2009, 23, 171-184



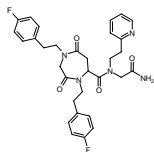


Immunosupresores

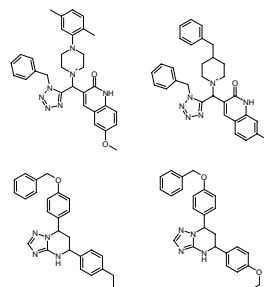
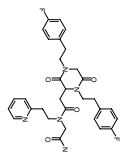


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Reparación de ADN



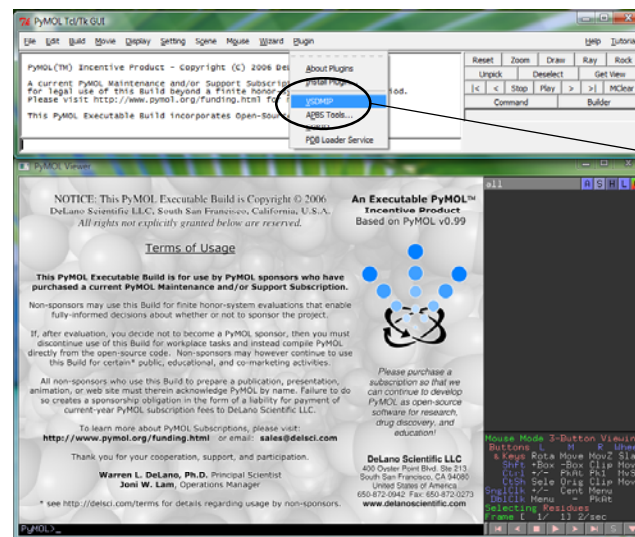
P200700120



P200702958

VSDMIP 1.5

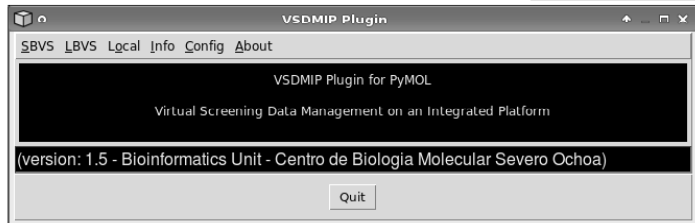
Creación de una interfaz gráfica para VSDMIP en forma de *plugin* para pymol



acceso a
VSDMIP

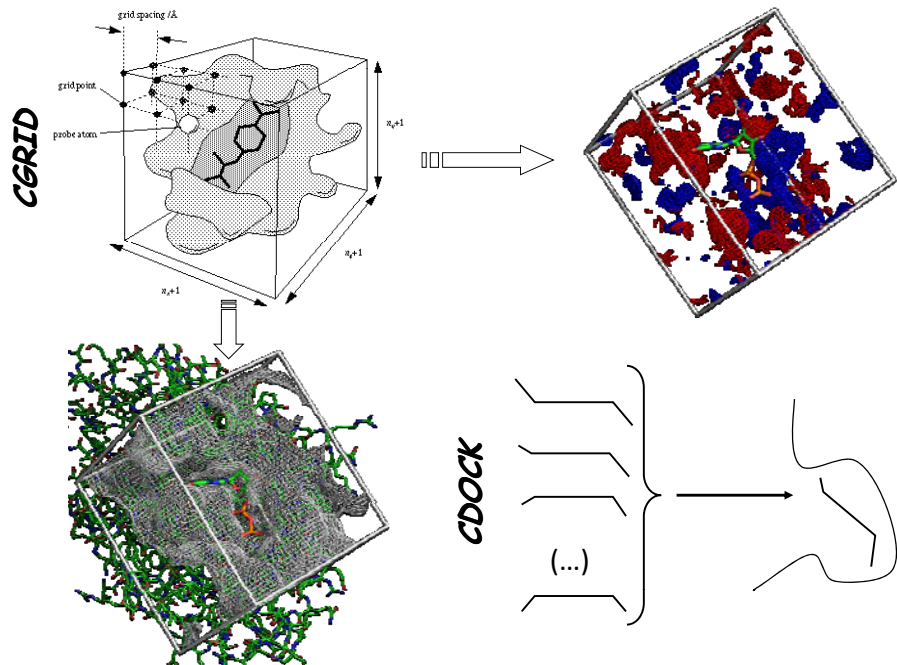
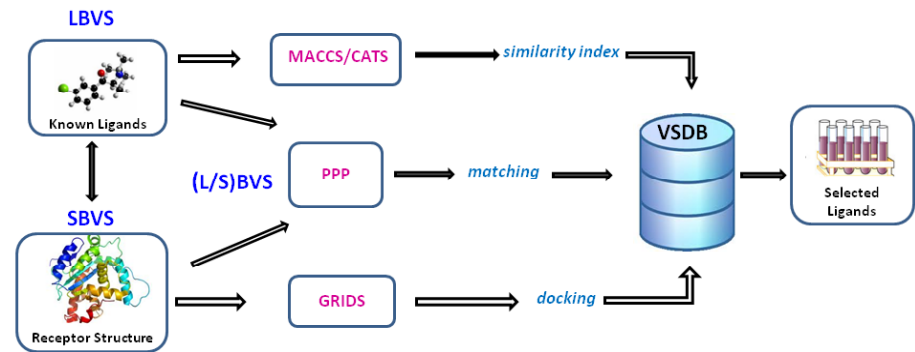
- SBVS**
- Insert new molecules
 - Run Virtual Screening
 - Get Results from Screening
 - Receptor preparation
 - Set up Molecular dynamics

- LBVS**
- Generate 2D Fingerprints
 - Generate 3D Fingerprints
 - Insert 2D Fingerprints
 - Simple search
 - Advanced search
 - 3D Pharmacophores



- Lgcal**
- Options
 - Ligand set up
 - CGRID
 - View Grids
 - CDOCK
 - Docking Results Visualization

- Info**
- Show sources of molecules
 - Show Virtual Screening catalog
 - Remote process



Scoring function

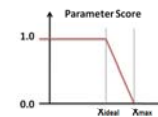
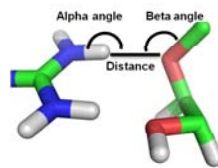
$$\Delta G_{LR}^{binding} = E_{LR}^{vdW} + \Delta G_{LR}^{ele} + \Delta G_{LR}^{non-ele} + \Delta G_{corr}^{(HB)}$$

$$E_{LR}^{vdW} \rightarrow \sum_i^{lig} \sum_j^{prot} \left[\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^6} \right]$$

$$\Delta G_{LR}^{ele} \rightarrow \sum_{i=1}^{N_L} \sum_{j=1}^{N_R} \frac{q_i q_j}{D_s(r_{ij}) r_{ij}} + \frac{1}{2} \sum_{i=1}^{N_L + N_R} q_i^2 \left[\left(\frac{1}{D_s(R_s^c) R_s^c} - \frac{1}{D_s(R_s^u) R_s^u} \right) + \left(\frac{1}{R_s^u} - \frac{1}{R_s^c} \right) \right]$$

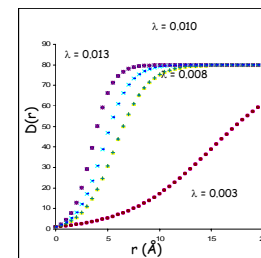
$$\Delta G_{LR}^{non-ele} \rightarrow a + \sum_i^{atoms} b \times SASA_i$$

$$\Delta G_{corr}^{(HB)} \rightarrow E_{HB}(x) = \prod_{x=1}^3 p * score(x)$$



$$score(x) = \begin{cases} 1 & si \quad x \leq x_{ideal} \\ 1 - \frac{x - x_{ideal}}{x_{max} - x_{ideal}} & si \quad x_{ideal} \leq x \leq x_{max} \\ 0 & si \quad x \geq x_{max} \end{cases}$$

Sigmoidal dielectric function



$$\epsilon(r) \approx D(r) = \frac{\epsilon_w + 1}{1 + k \exp[-\lambda(\epsilon_w + 1)r]} - 1$$