数学与系统科学研究院

计算数学所学术报告

报告人： **Dr. Dong Xu**

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报告题目：

禽流感病毒的计算机药物设计

Supercomputers Fight against Bird Flu

邀请人： **卢本卓副研究员**

报告时间： **2009 年 1 月 15 日(周四)**

下午 3:00—4:00

报告地点： **科技综合楼三层 311**

计算数学所报告厅

Abstract:

The new highly lethal avian influenza virus strains H5N1 poses a serious pandemic threat. Continuing evolution of influenza viruses through mutations and gene reassortment causes drug resistance and receptor binding specificity switch which may eventually enable efficient human transmission. Development of new anti−viral drugs and rapid binding specificity detection techniques are essential. We employed explicitly and implicitly solvated molecular dynamics (MD) simulations to study the structural flexibility of influenza virus surface proteins Hemagglutinin (HA) and Neuraminidase (NA) that are responsible for the attachment and releasing of viral particles to and from the host cells. The NA simulations revealed remarkable loop flexibility, opening new cavities adjacent to the catalytic active site. Subsequent ensemble−based virtual screening identified top 27 compounds, some of which effectively exploit the expanded binding pocket and may be potent novel inhibitor leads. The

HA simulations examined the topological and energetic characteristics of avian and human receptor analogs in complex with 3 different HA subtypes, avian H3, H5 and swine H9. The findings offer insight to the key HA−glycan interactions and suggest new strategies for drug design and monitoring viral host range selection by different influenza viruses. The absolute binding free energies of Tamiflu bound to N1/N9 and avian and human receptor analogs bound to H3, H5 and H9 were also calculated using Molecular Mechanics, Generalized Born Surface Area (MM−GBSA) scheme and the results trend well with available experimental data.

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