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NICS

Simulations of Influenza Neuraminidase In Search of the Next Generation of Flu Drugs

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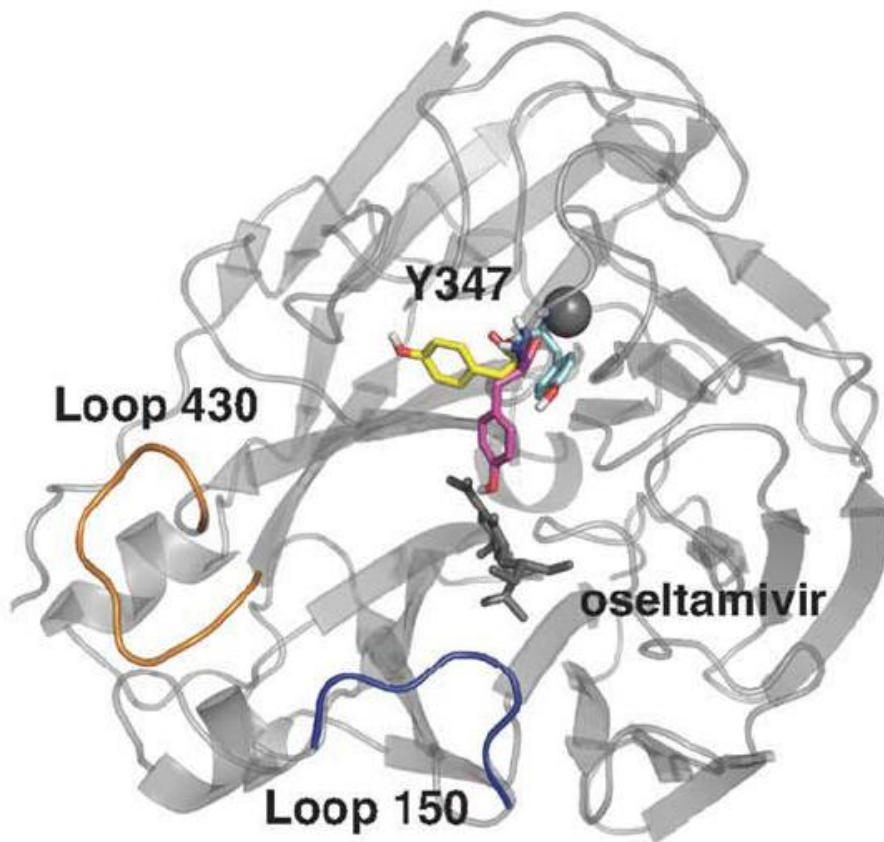
University of Florida

Ross C. Walker

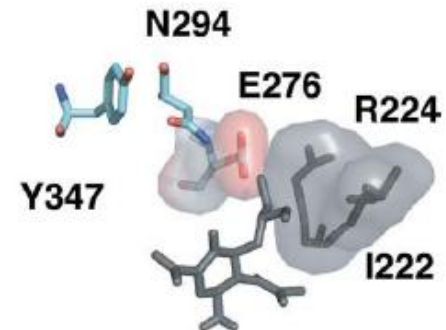
San Diego Supercomputer Center



Impact of Calcium on N1 influenza neuraminidase dynamics and binding free energy



Calcium ion required for proper ligand binding conformation and free energy



2009 pandemic N1 reveals an open cavity

NATURE COMMUNICATIONS | ARTICLE OPEN

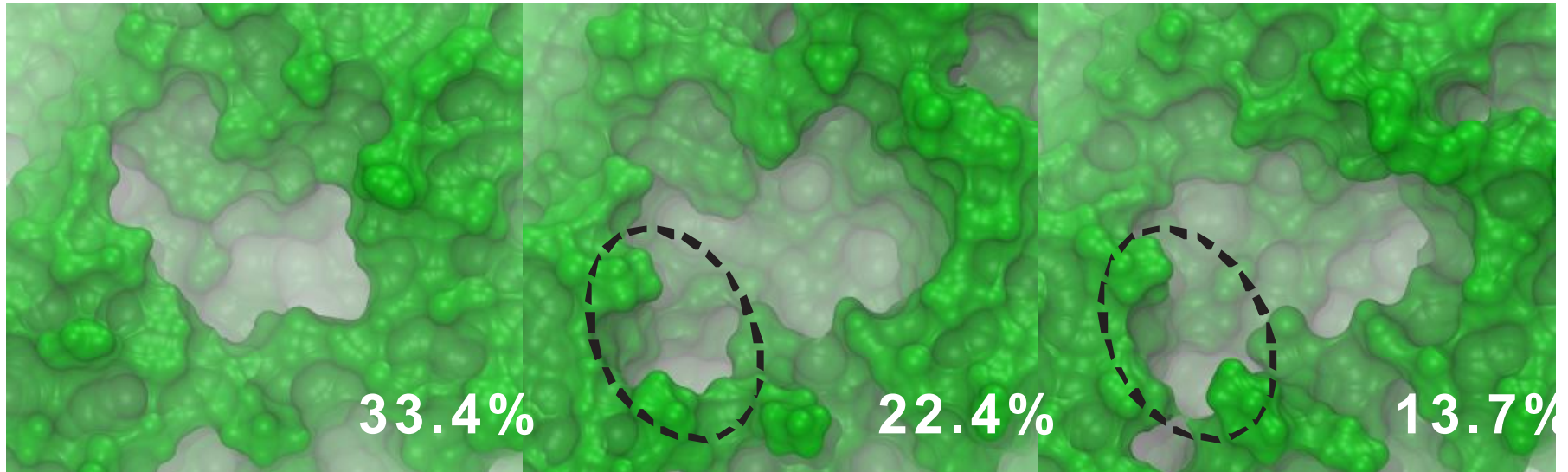
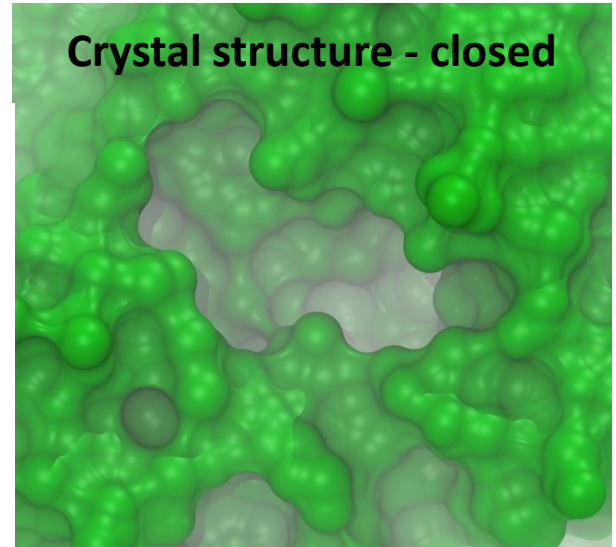
Mechanism of 150-cavity formation in influenza neuraminidase

Rommie E. Amaro, Robert V. Swift, Lane Votapka, Wilfred W. Li, Ross C. Walker & Robin M. Bush

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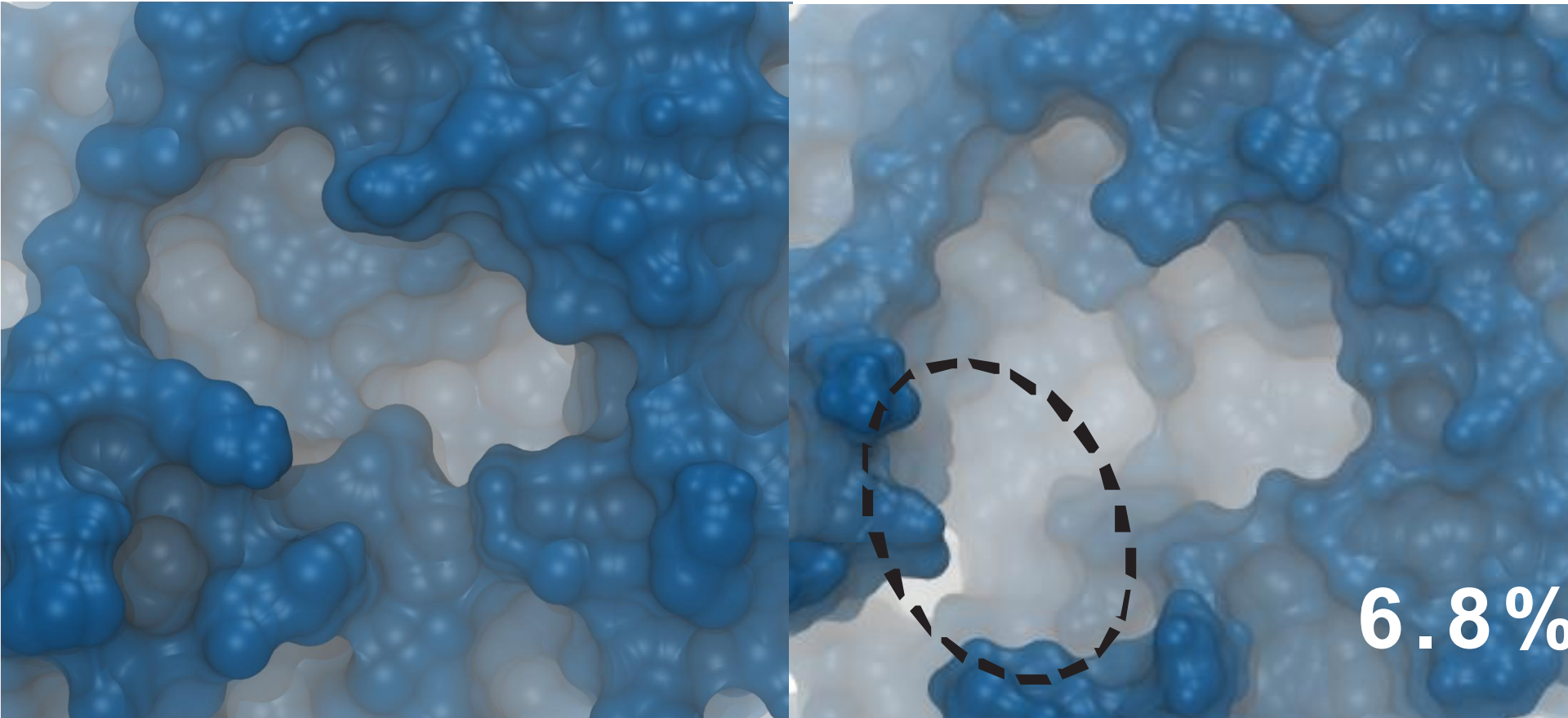
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most dominant MD structures



N₂ also reveals an open cavity

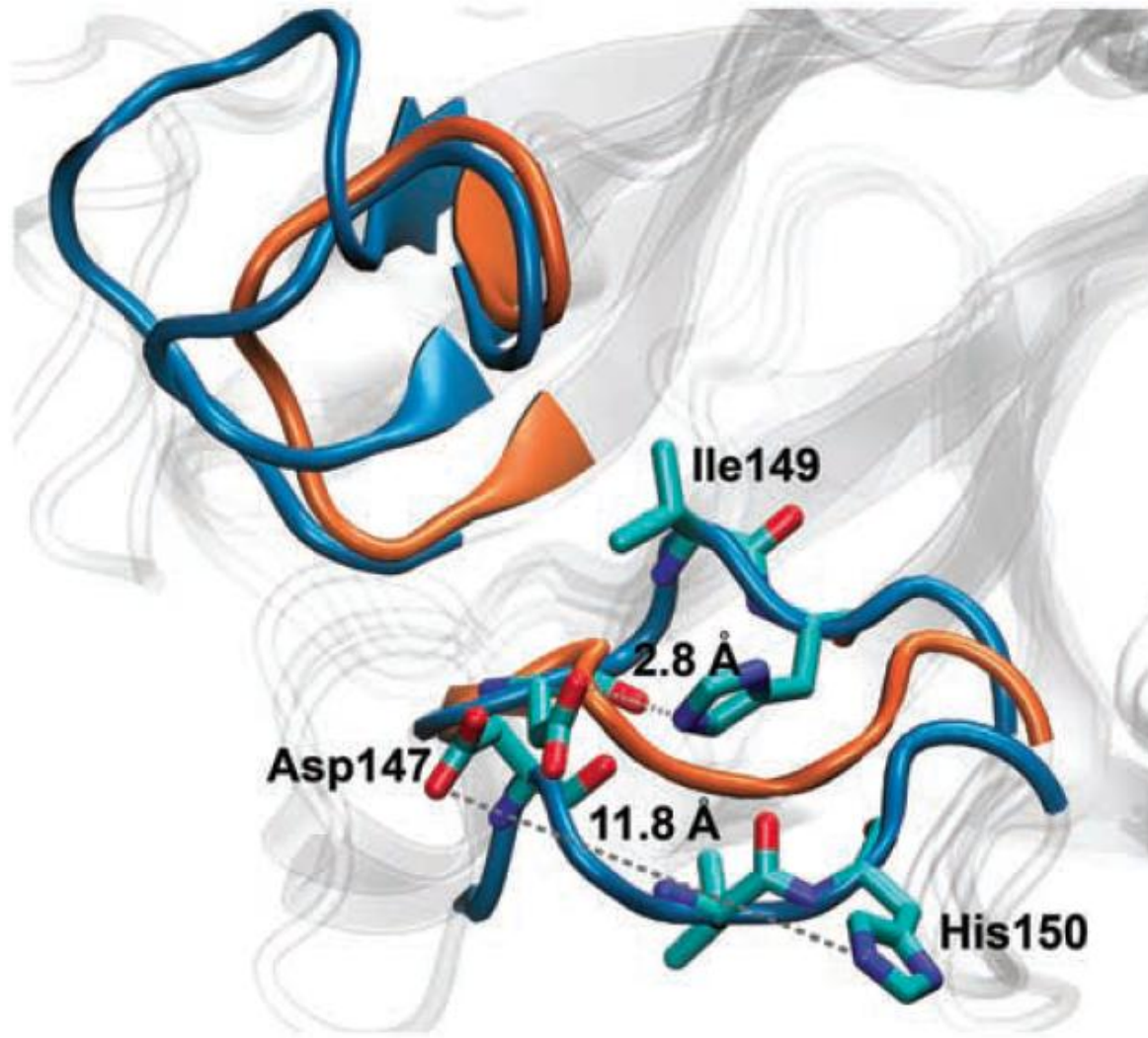


Surprising finding since N₂ always before believed to not have a 150-cavity ... how?

Amaro, Swift, Votapka, Li, Walker, Bush (2011), Nature Communications.



Salt bridge controls 150-cavity



N2-MD
(initially closed
150-loop)

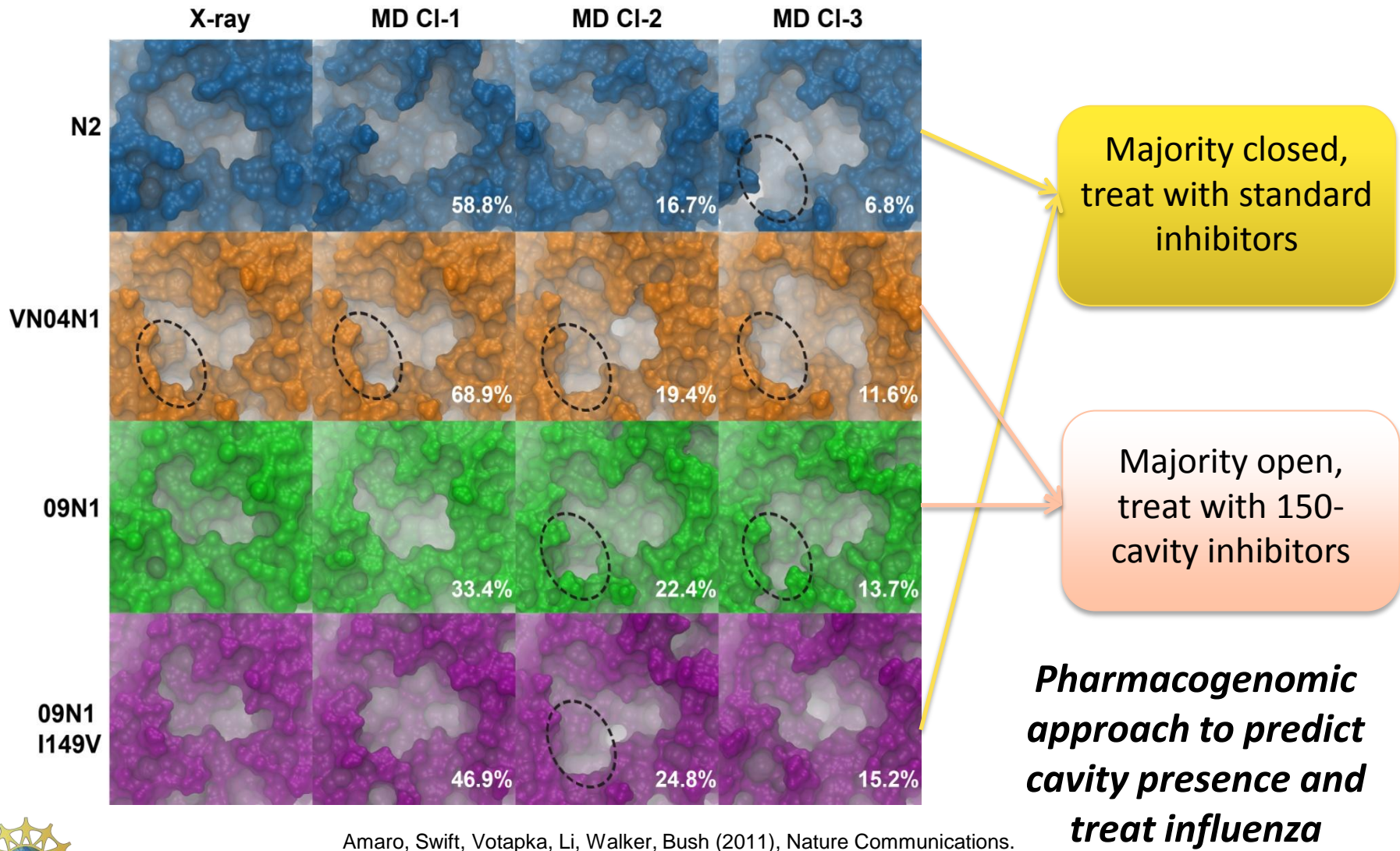
VN04N1-xtal
(open 150-loop)

Salt bridge
breaks in the
150-loop, cavity
opens

Amaro, Swift, Votapka, Li, Walker, Bush (2011), Nature Communications.



New structural understanding suggests new approaches to treat different infections



Amaro, Swift, Votapka, Li, Walker, Bush (2011), Nature Communications.





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Impact of calcium on N1 influenza
neuraminidase dynamics and binding
free energy

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