

Optical Trapping and Manipulation of a Single Human Virus

Presented by:



Optical Trapping and Manipulation
in Molecular and Cellular Biology
Technical Group

Optical Trapping and Manipulation in Molecular and Cellular Biology (BT)

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- [Therapeutic Laser Applications \(BA\)](#)
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Frequently Asked Questions

Optical Trapping and Manipulation in Molecular and Cellular Biology (BT)



Optical trapping has been widely used to uncover fundamental aspects of molecular and cellular biology, including the understanding of the movement mechanisms of molecular motors and the forces involved in cell adhesion. This group focuses on the development and application of novel optical trapping and manipulation techniques to biological problems. Focus areas include the use of evanescent fields and state of the art optical tweezers for molecular- and cellular-scale manipulation, integration of optical manipulation with microfluidics and lab-on-a-chip technologies, as well as optical sorting and optical methods for cell biology.

GROUP LEADERSHIP			UPCOMING MEETINGS	RECENTLY PUBLISHED
Name	Affiliation	Title		
Steven Leonard Neale	University of Glasgow	Chair		
Peter Pauzauskie	University of Washington	Vice Chair		
Peter John Reece	University of New South Wales	Director of Events		
Stephanie Jones	University of Victoria	Director of Social Media		
Daniel Richard Burnham	University of Washington	Secretary		

Announcements

Join the Optical Trapping and Manipulation in Molecular and Cellular Biology Technical Group for their inaugural webinar on Thursday, 16 June 2016, at 11:00 EDT.

Dr. Wei Cheng from the University of Michigan will present his work demonstrating that a single HIV-1 virion can be stably trapped, manipulated and measured in physiological media with high precision.

[Register for the Webinar Now>>](#)

View the feature issue of *Biomedical Optics Express* on [Optical Trapping Applications](#) online now. The issue presents studies that were the focus of the OTA Topical Meeting, which was held in April 2015 in Vancouver, Canada.

Join our Online Community

Stay connected with the Optical Trapping and Manipulation in Molecular and Cellular Biology Technical Group by following [#BTTechGroupOSA](#) on [Twitter](#).

#BTTechGroupOSA

 **Stephanie Jones** @DrSHJones
Don't forget to register for: Optical Trapping and Manipulation of a Single Human Virus shar.es/1Jmtrnw [#BTTechGroupOSA](#)

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Stephanie Jones @DrSHJones · Jun 3
Don't forget to register for: Optical Trapping and Manipulation of a Single Human Virus shar.es/1Jmtmw #BTTechGroupOSA

Lynn Paterson and 3 others follow

Peter Reece @peterjreece · May 25
OSA Webinar: Optical Trapping and Manipulation of a Single Human Virus shar.es/1dAEdA via @sharethis #BTTechGroupOSA

Steven Neale @sneale22 · Apr 13
Optical manipulation to power interstellar travel bbc.co.uk/news/video_and... #BTTechGroupOSA



BBC News - Star system project backed by Stephen Hawking
A project to send tiny spacecraft to another star system within a generation has been backed by Stephen Hawking.
bbc.co.uk

Steven Neale @sneale22 · Mar 15
Congratulations to Kishan for being awarded the R.W. Wood prize for contributions to optical manipulation research #BTTechGroupOSA



Optical Trapping and Manipulation
in Molecular and Cellular Biology
Technical Group

Webinars (today is our first!)

*Previous webinars will be available for
viewing at the OSA Technical Group
website*

Panel discussions, discussion forums,
and social gatherings at conferences

*Look for us at the Optical Trapping
Applications (OTA) and other conferences*

Facebook page

*Optical Cooling and Trapping (OT)
Technical Group;*

<https://www.facebook.com/groups/187451984746395/>

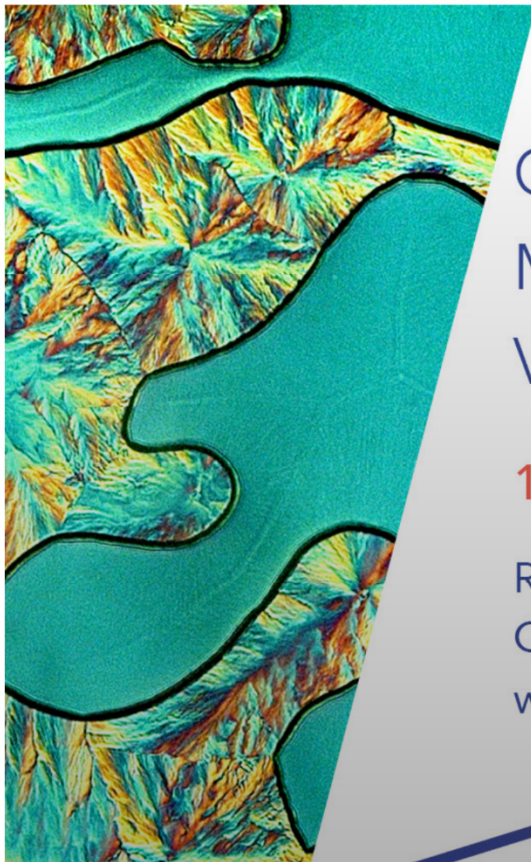
A screenshot of the Facebook page for the 'Optical Cooling and Trapping OSA TG' group. The page header features a banner image with the text 'OPTICAL COOLING AND TRAPPING TECHNICAL GROUP' and 'Optical Cooling & Trapping OSA TG Public Group'. Below the banner are navigation tabs for 'Discussion', 'Members', 'Events', 'Photos', and 'Files', along with a search bar. The main content area shows a 'Write Post' section with a text input field and options for 'Add Photo / Video', 'Create Poll', and 'More'. Below this is a 'RECENT ACTIVITY' section featuring a post by 'Onofrio Maragò' from June 11 at 10:16am, with a link to a paper on ACS Photonics. The post includes a thumbnail image with the text 'Arrested dimer's diffusion by self-induced back-action optical forces - ACS Photonics (ACS...)'. To the right of the main content is a sidebar with 'ADD MEMBERS' (168 Members), 'DESCRIPTION' (This group is concerned with the physics of laser cooling, elect...), 'GROUP TYPE' (Study Group), and 'TAGS' (Optics - Photonics - Optical Society of America). At the bottom of the sidebar is a 'CREATE NEW GROUPS' section with a 'Create Group' button. The page also shows 'RECENT GROUP PHOTOS' at the bottom right.



Optical Trapping and Manipulation
in Molecular and Cellular Biology
Technical Group

Welcome to Today's webinar!

Dr Wei Cheng – University of Michigan



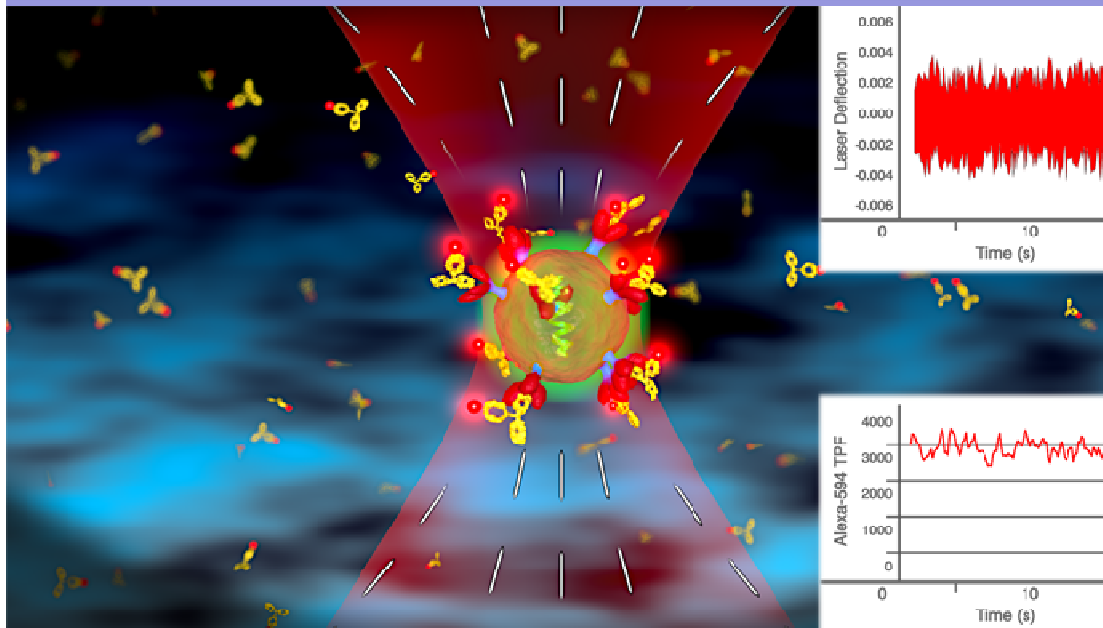
OPTICAL TRAPPING AND MANIPULATION OF A SINGLE HUMAN VIRUS WEBINAR

16 June 2016 • 11:00 EDT

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OSA Technical Group
webinar >>

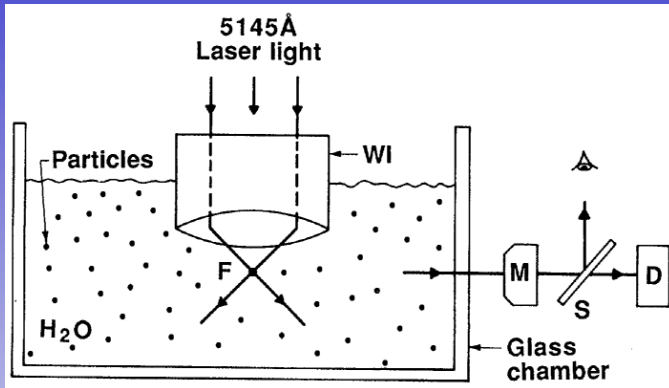
OSA Optical Trapping and Manipulation
in Molecular and Cellular Biology
Technical Group

Optical Trapping and Manipulation of a Single Human Virus



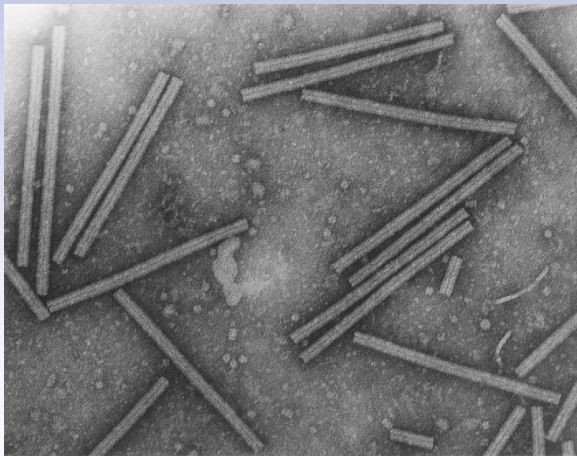
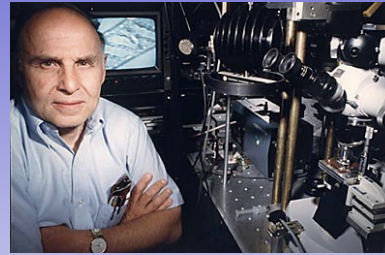
Wei Cheng
Associate Professor
Pharmaceutical Sciences
Biophysics
Biological Chemistry
University of Michigan, Ann Arbor

Trapping of Single Tobacco Mosaic Virus

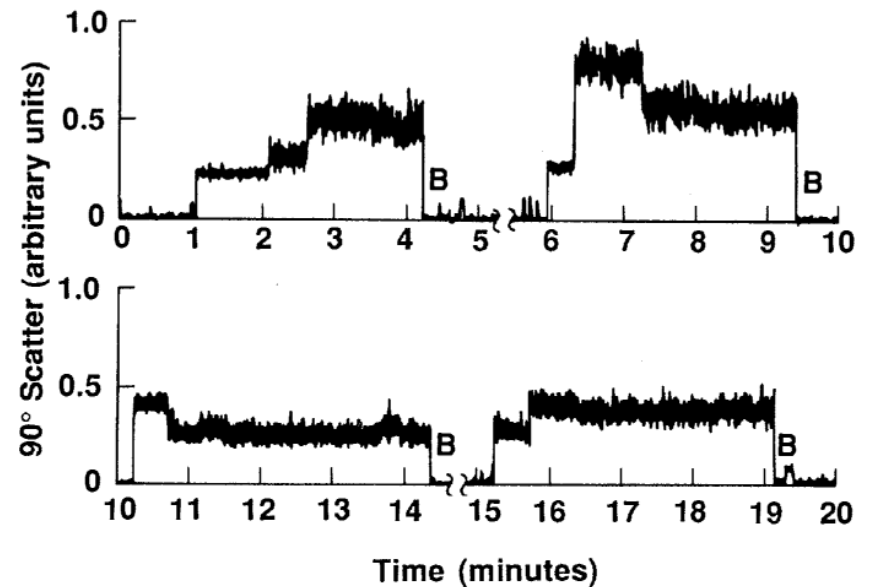


Optical Trapping and Manipulation of Viruses and Bacteria

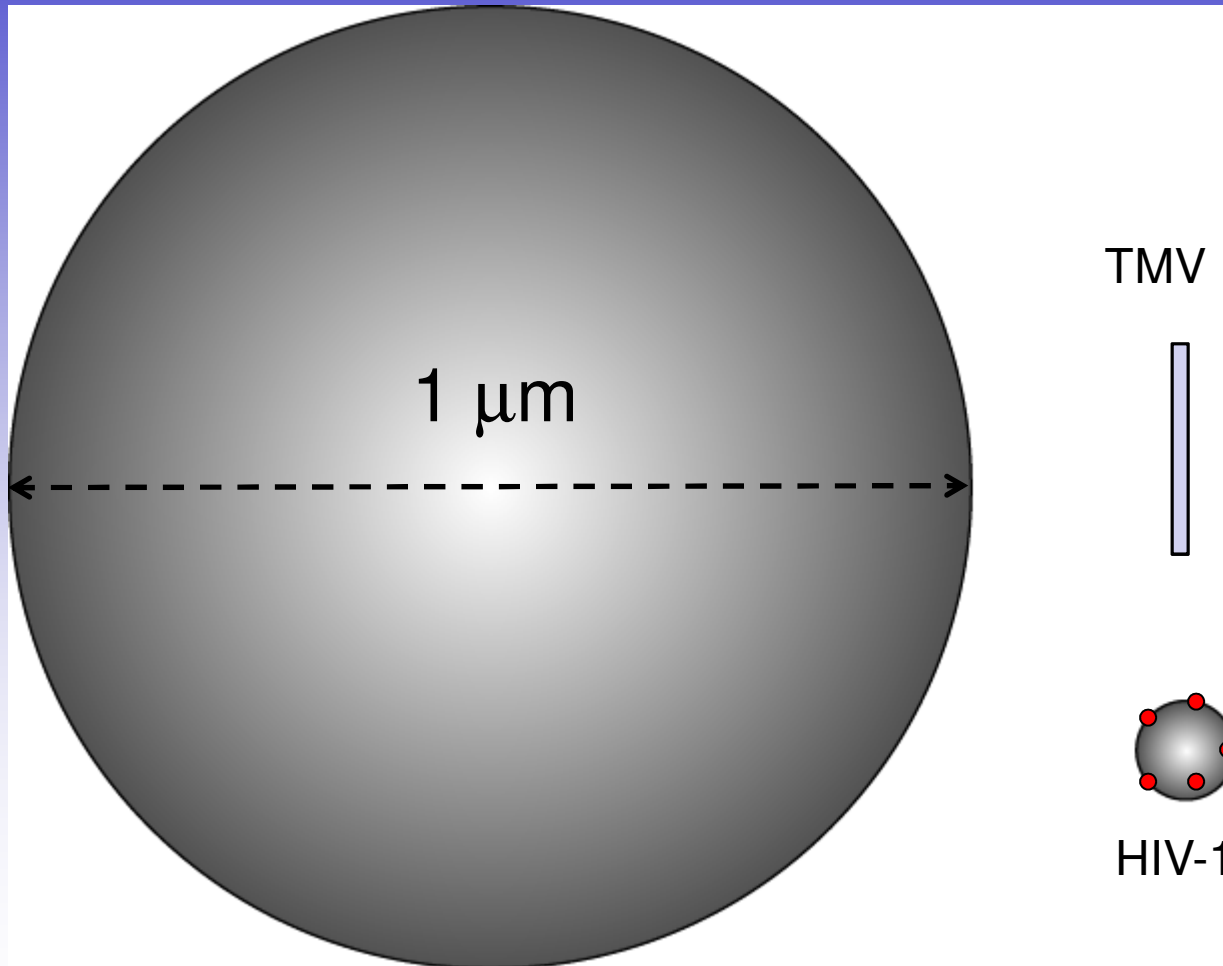
Ashkin & Dziedzic, *Science* 1987



TMV, 300 nm long, 18 nm diameter



Challenges for Trapping Animal Viruses



glass bead

(1) **Small size**
small dipole moment

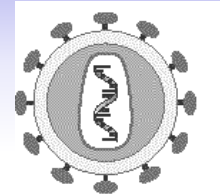
$$\left| \vec{P} \right| \propto d^3 \quad \text{RI}$$

TMV has permanent dipole Moment,
Biopolymers (1976) 15: 301

(2) **Index of refraction unknown**

Technical Elements to Prepare for Trapping of a Single Virus

(1) The choice of trapping laser wavelength: **830** nm instead of 1064 nm
Less heating, free of oxygen-mediated photo damage



DNA or RNA genome

(2) Back-focal-plane interferometry with high accuracy:
Diffusion coefficient, corner frequency, particle diameter, trap stiffness

(3) Simultaneous **two-photon** fluorescence excitation by the 830 nm trapping laser with **single-fluorophore** sensitivity

830 nm CW laser can excite **GFP**

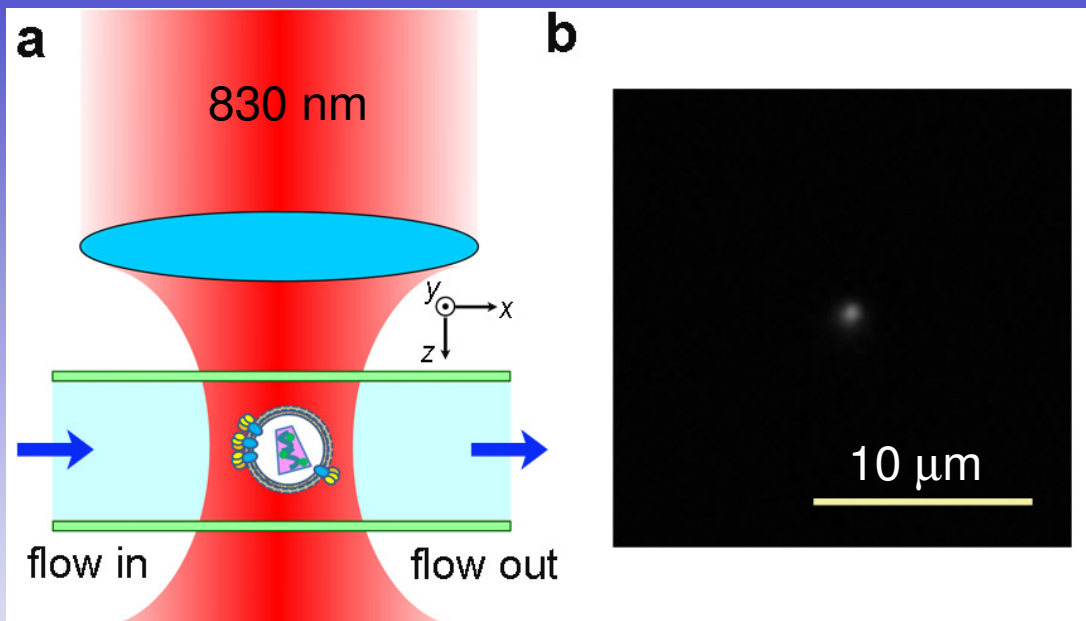
Cheng, Hou & Ye, *Opt. Lett* (2010) 35: 2988

Hou & Cheng, *Opt. Lett* (2011) 36: 3185

Hou & Cheng, *Biomed. Opt. Express* (2012) 3: 340

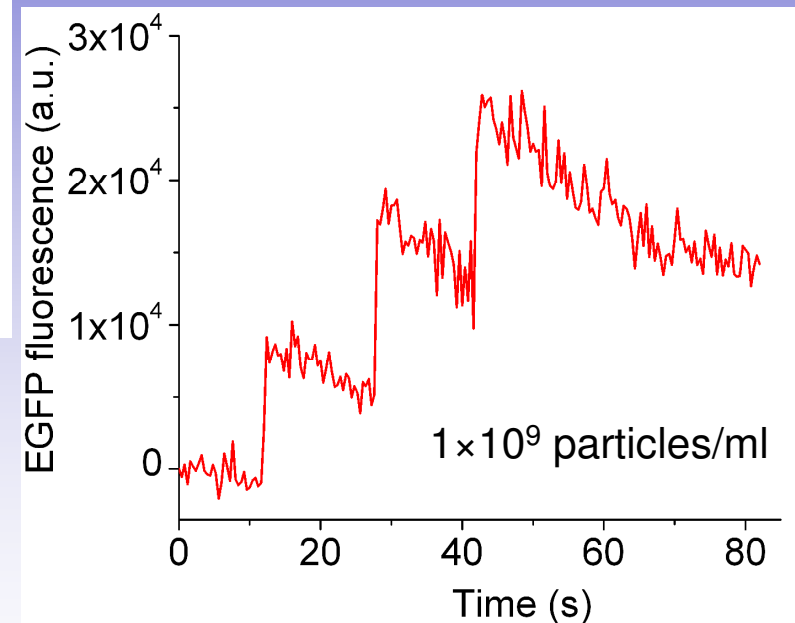
Optical Trapping of HIV-1 Virions in Culture Media

Pang...Cheng, *Nature Nanotech* (2014) 9: 624



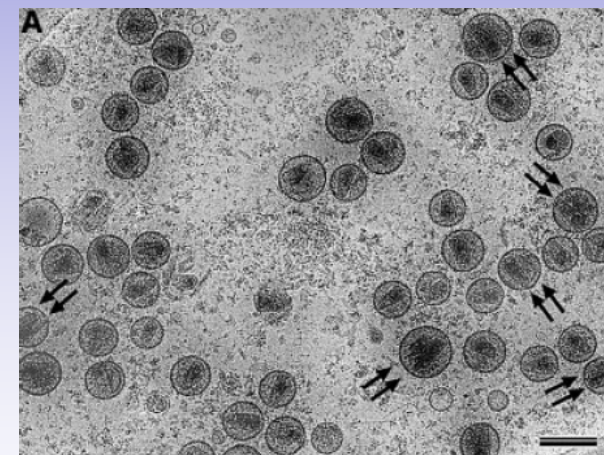
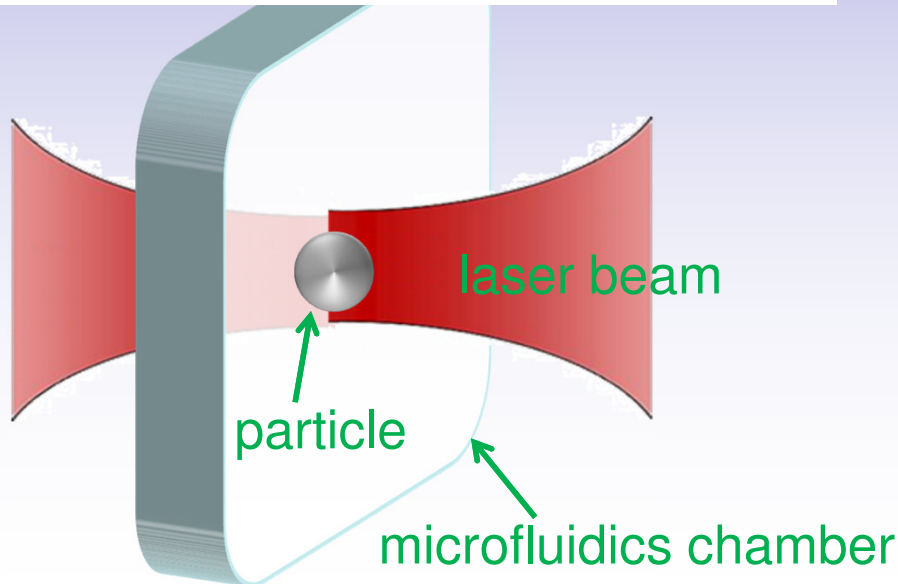
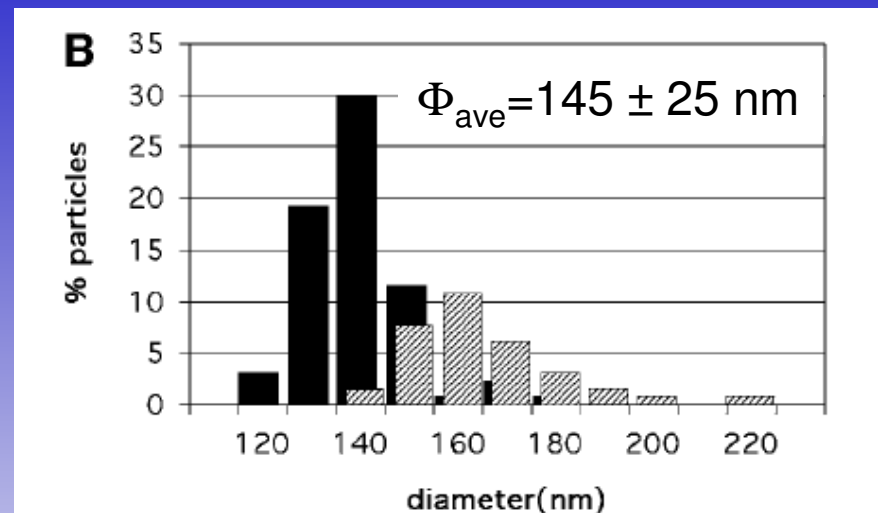
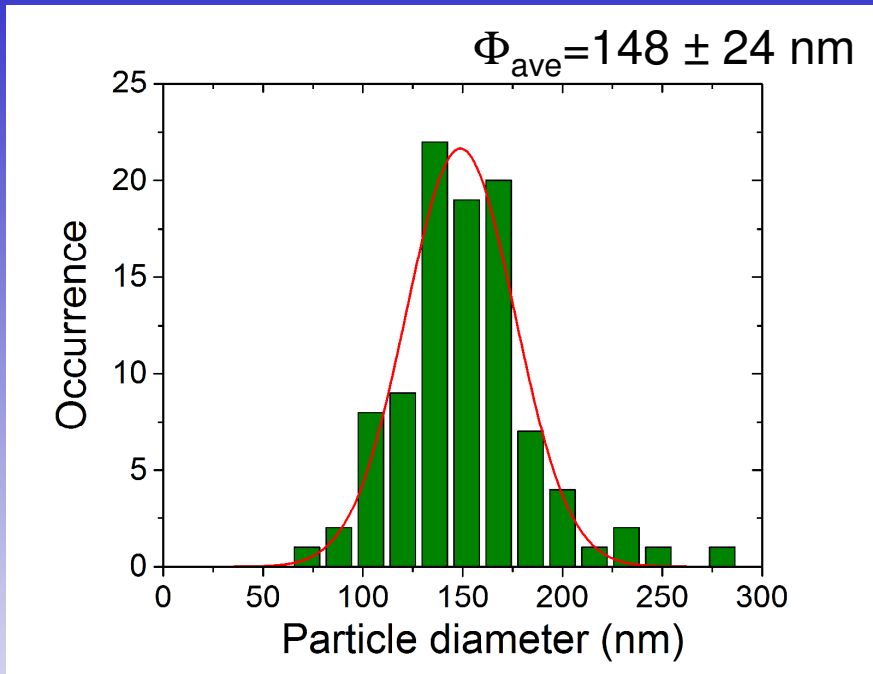
EGFP labeled HIV-1

Kim...Cheng, *PLOS One* (2013) 8: e67170.



(in complete culture media: 90% DMEM + 10% FBS)

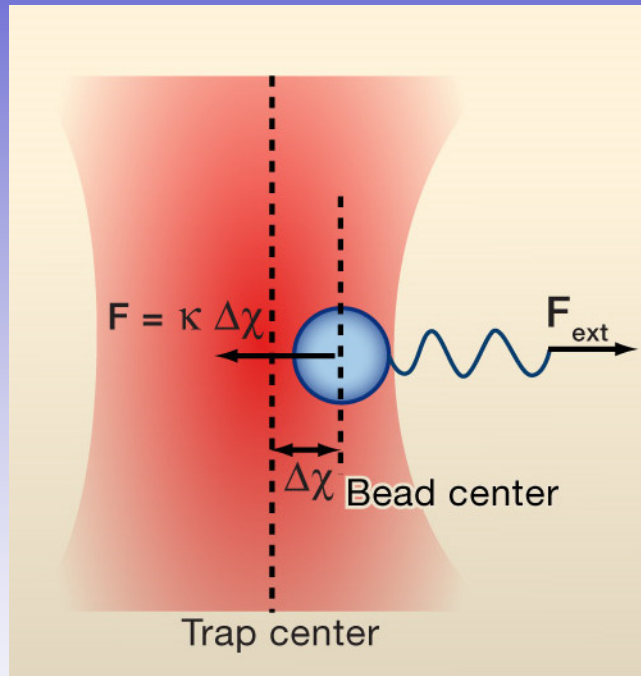
Polydispersity of HIV-1 Virions



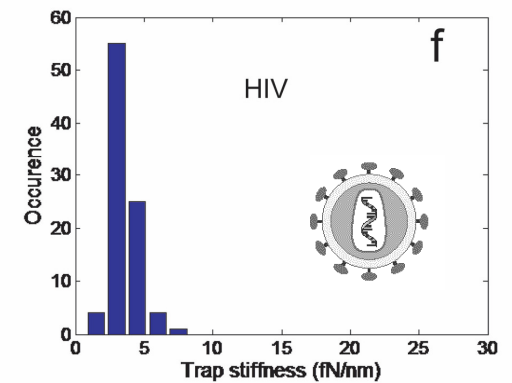
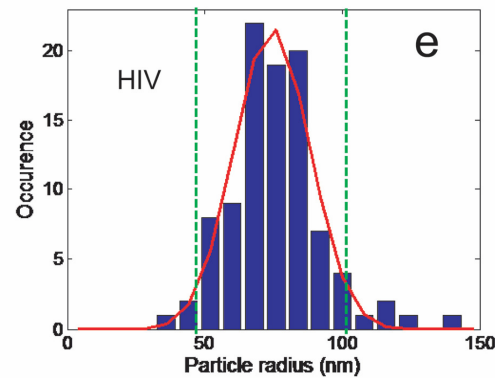
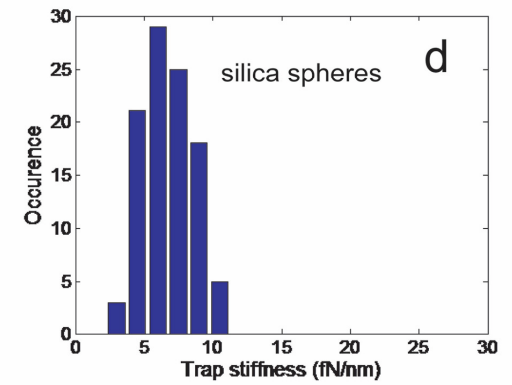
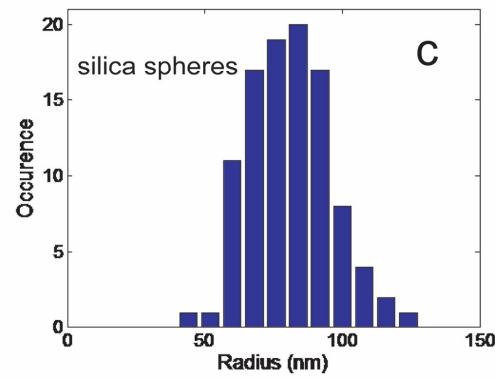
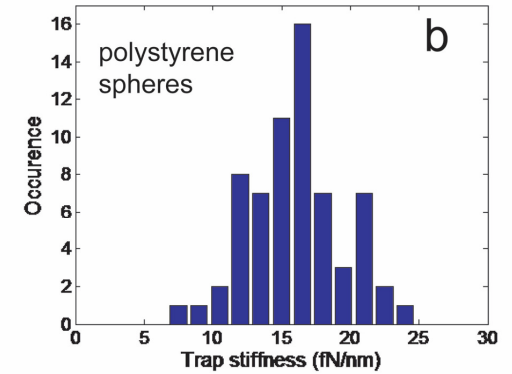
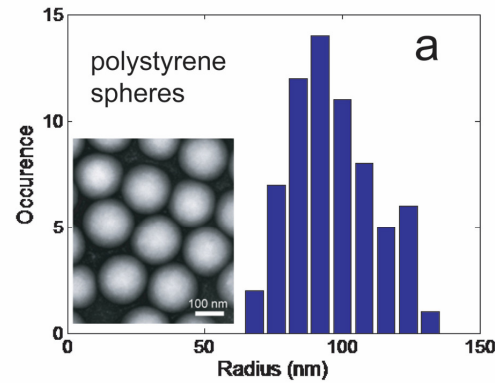
Briggs et al., *EMBO J* (2003) 22: 1707

Tolić-Nørrelykke...Flyvbjerg, *Rev. Sci. Instr.* (2006) 77: 103101

Optical Trap Stiffness and Materials

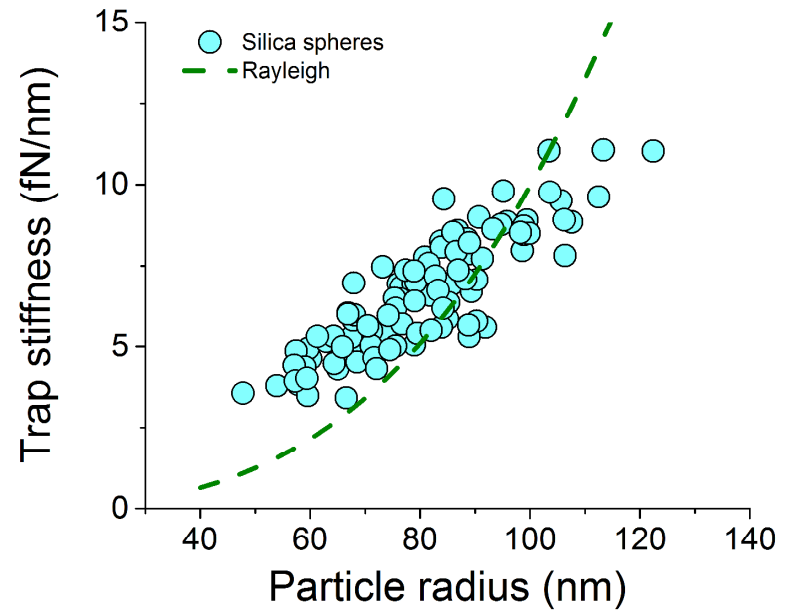
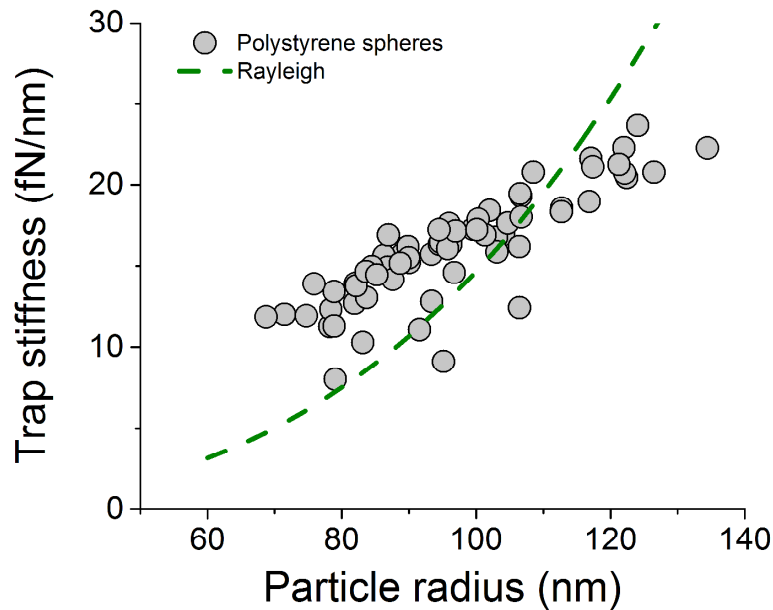


Bustamante, Cheng & Meija, *Cell* (2011) 144: 480



Relate Optical Trap Stiffness to Particle Size

Rayleigh particle, stiffness $\propto R^3$
 $4\pi n_0 R/\lambda \ll 1$, in reality > 1

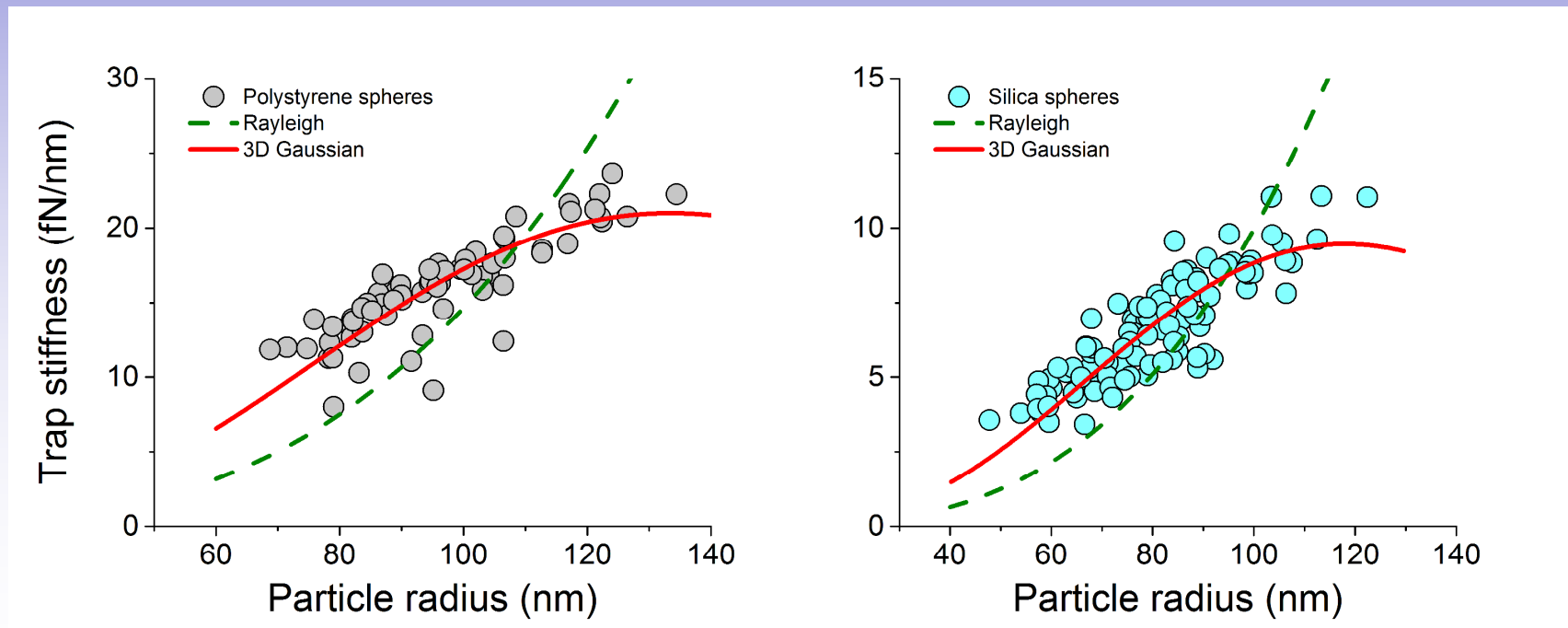


An Analytic Solution to Optical Trap Stiffness

$$\kappa = \alpha I_0 \omega_0 \frac{2\pi}{\xi^3} \left[\sqrt{2\pi} \left((\xi a)^2 + \frac{1}{4} \right) e^{-2a^2} \operatorname{erfi}(\sqrt{2} a \xi) - \xi a e^{-2a^2 / \epsilon^2} \right]$$

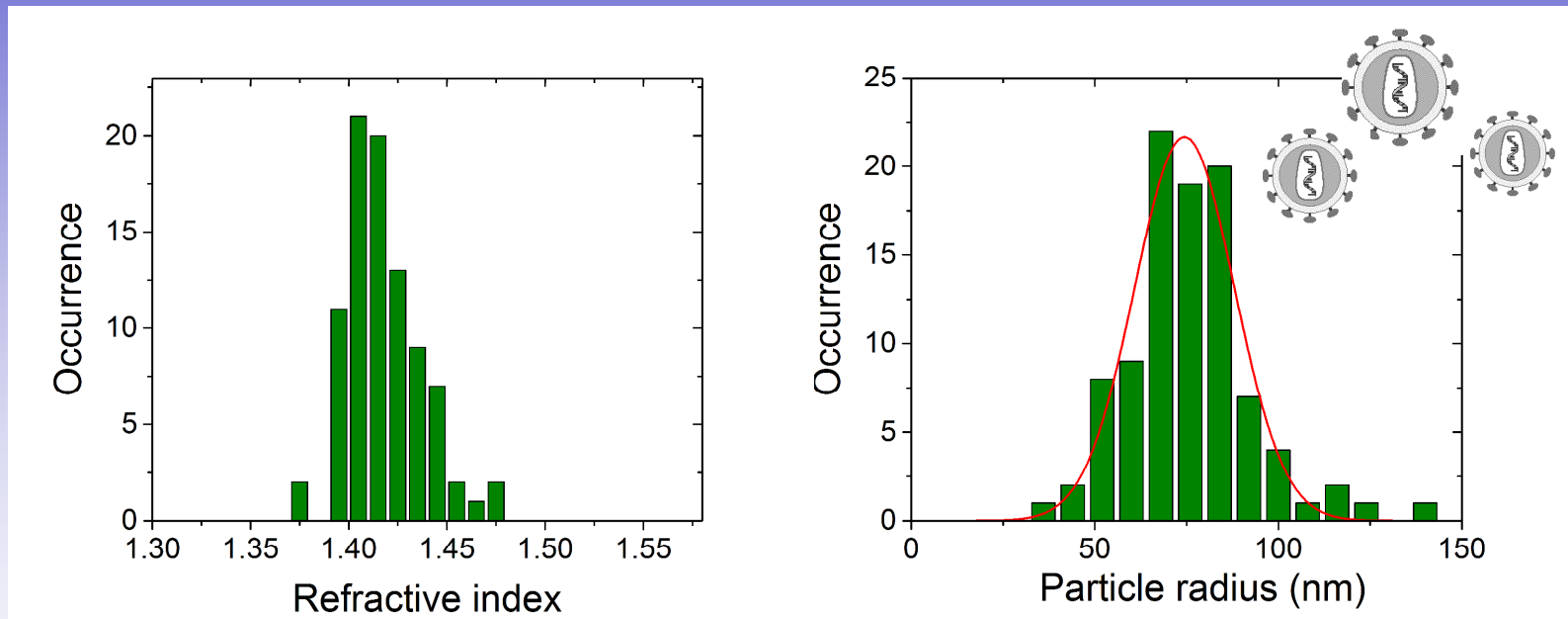
Applies to spherical particles < 160 nm radius

Stiffness = F(**particle radius**, **particle refractive index**, **beam parameters**)



Measure Refractive Index for Single HIV-1 with High Precision

Stiffness = F(**particle radius**, **particle refractive index**, **beam parameters**)



Mean \pm SD 1.42 \pm 0.02

CV 1.4%

74 \pm 12 (nm)

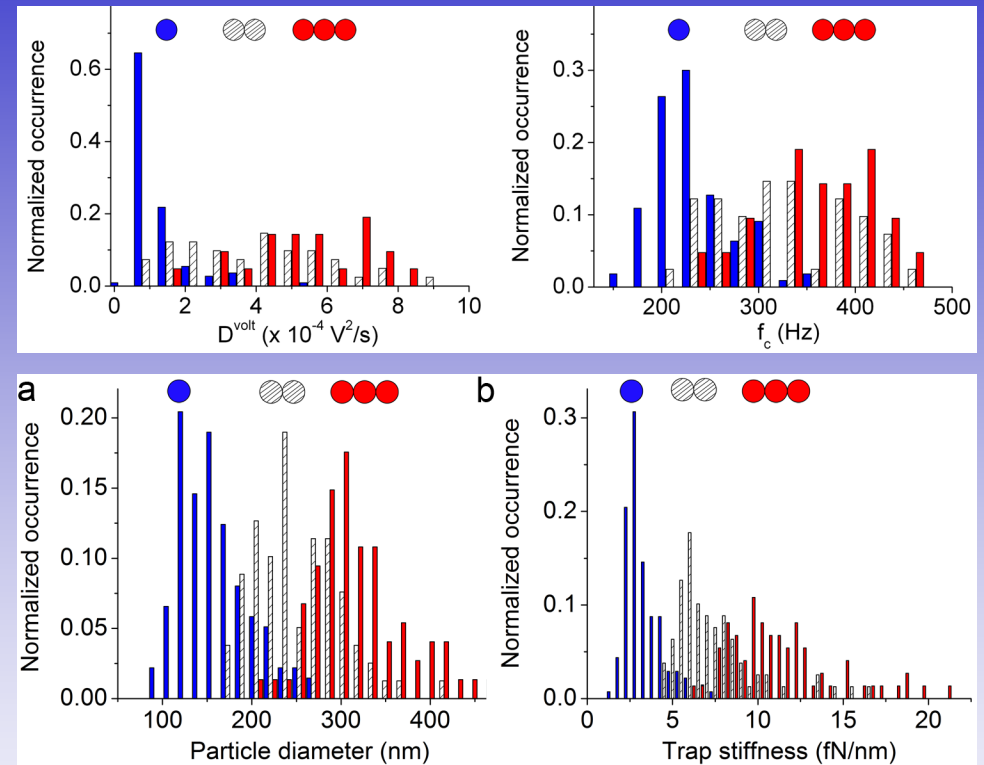
16%

Compared to 1.58 of polystyrene; close to 2M sucrose; first time that the RI of a single virus was ever measured.

Parameters from Optical Trap

- Diffusion coefficient
- Corner frequency
- Particle diameter
- Trap stiffness
- Index of refraction

Pang, Song & Cheng, *Biomed. Opt. Express* (2016) 7: 1672



Pang...Cheng, *Nature Nanotech* (2014) 9: 624

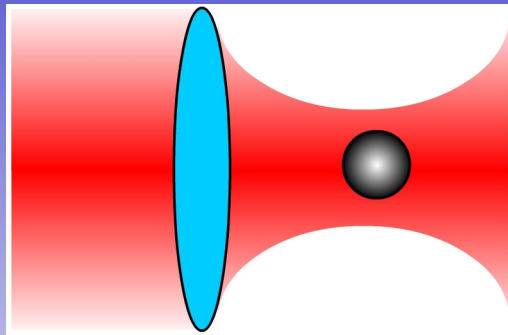
- Two-photon fluorescence
with single-molecule sensitivity

Multi-parameter **analysis** and potential **sorting** of biological nanoparticles

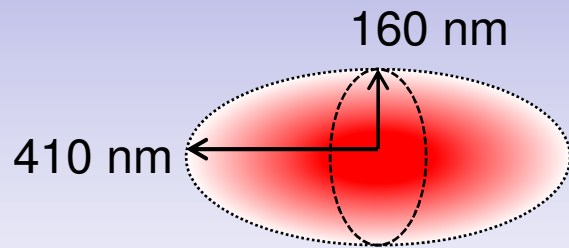
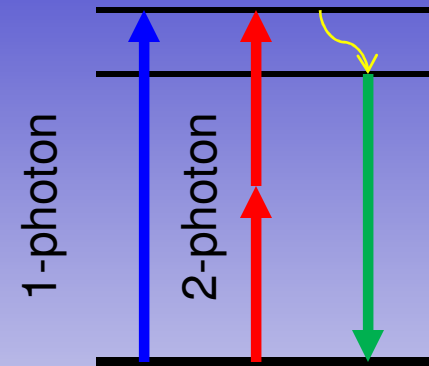
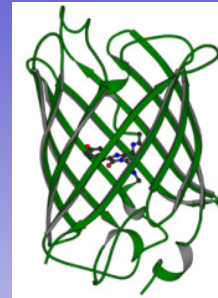
Current flow cytometry >300 nm

DeSantis & Cheng, *WIRES Nanomedicine and Nanobiotechnology* (2016)

Two-photon Fluorescence with Single-Molecule Sensitivity

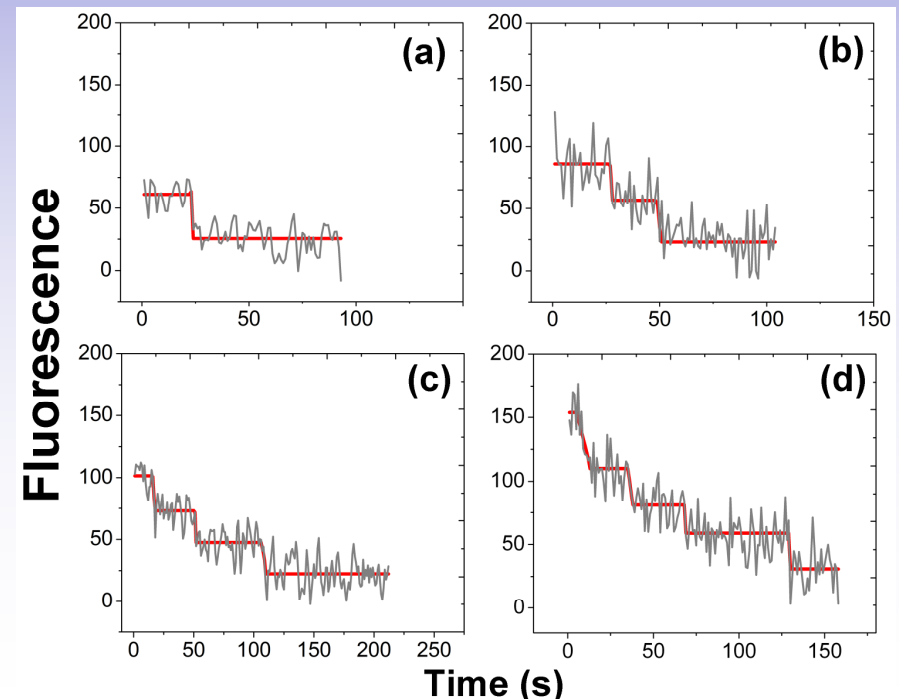


IR laser;
>100 mW



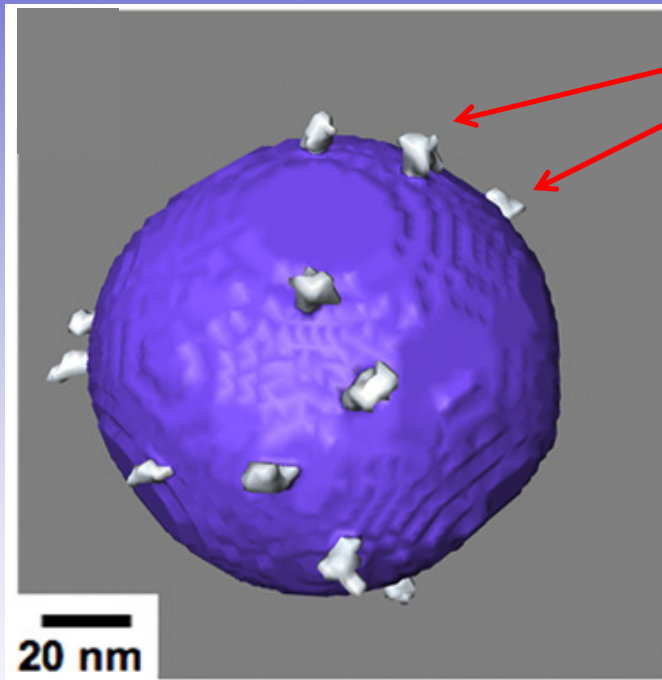
Excitation volume = 44 aL

1 molecule / 44 aL: 38 nM

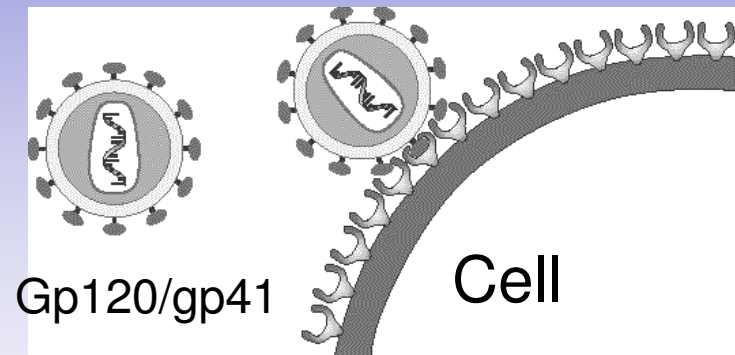


Heterogeneity Matters for Viruses

Model of HIV-1 virion

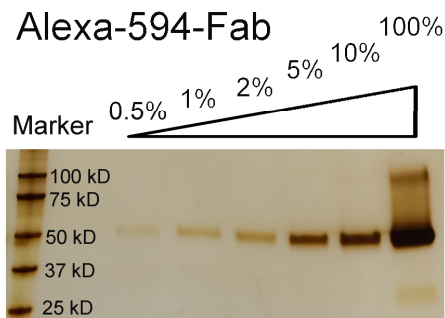
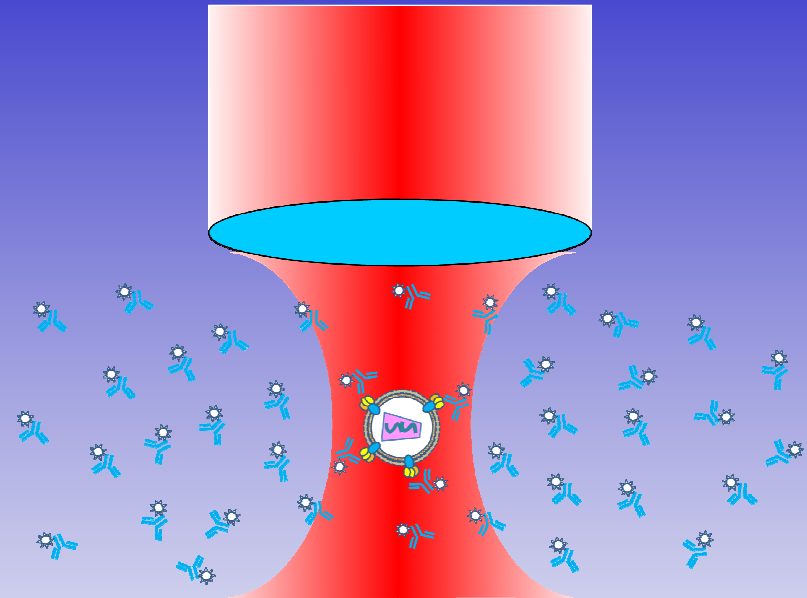
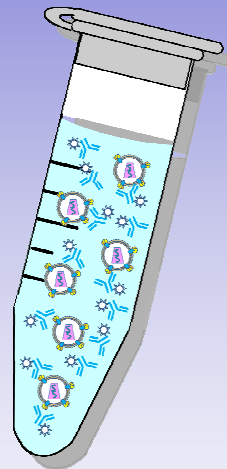
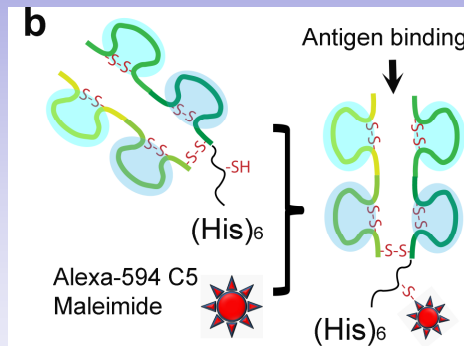
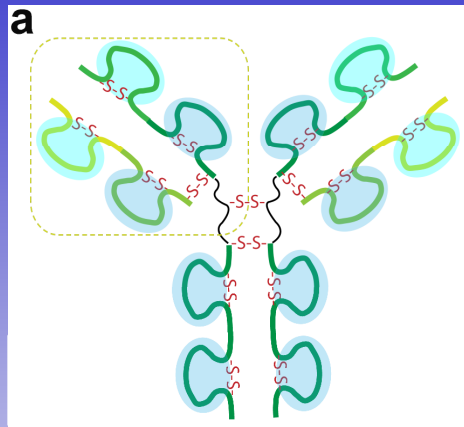


Presumed gp120/gp41

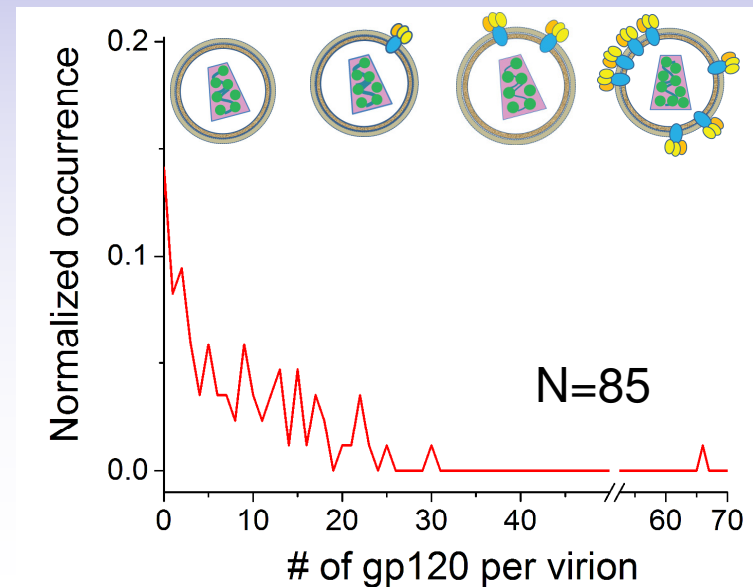


Zhu...Roux, *Nature* (2006) 441: 847

Optical Trapping 'Virometry'



DeSantis...Cheng, *J. Biol. Chem*
(2016) 291: 13088

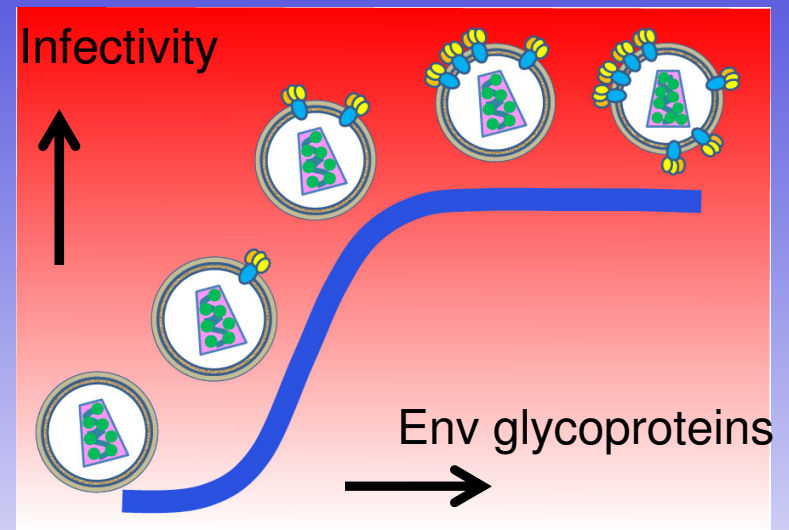
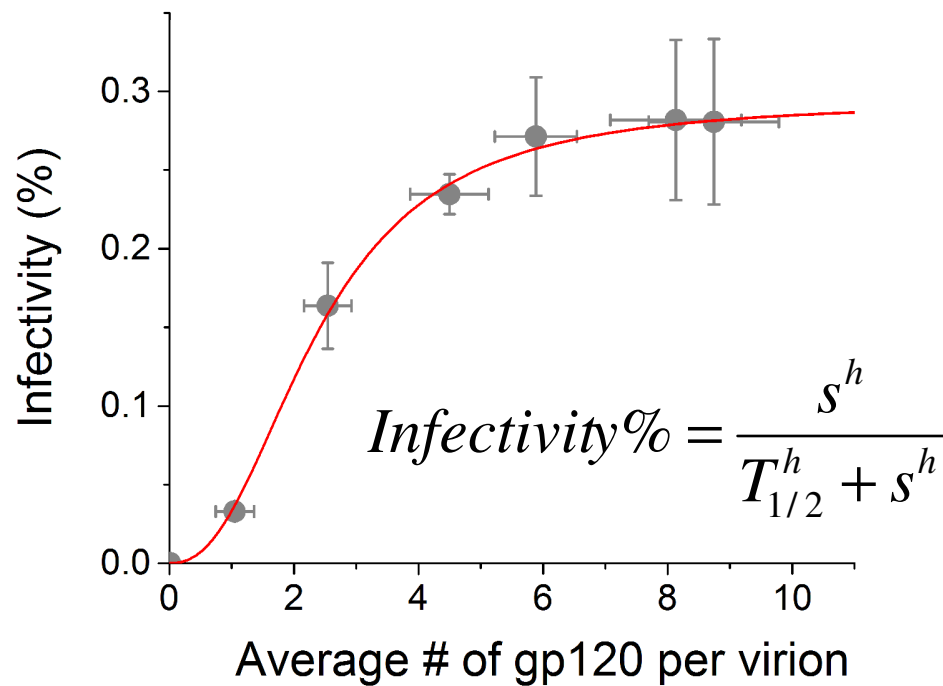


Cooperativity among Gp120 Molecules

Prepared seven populations of HIV-1, each population with on average different density of gp120 molecules

Virometry to measure # of gp120

Cell culture assay for infectivity

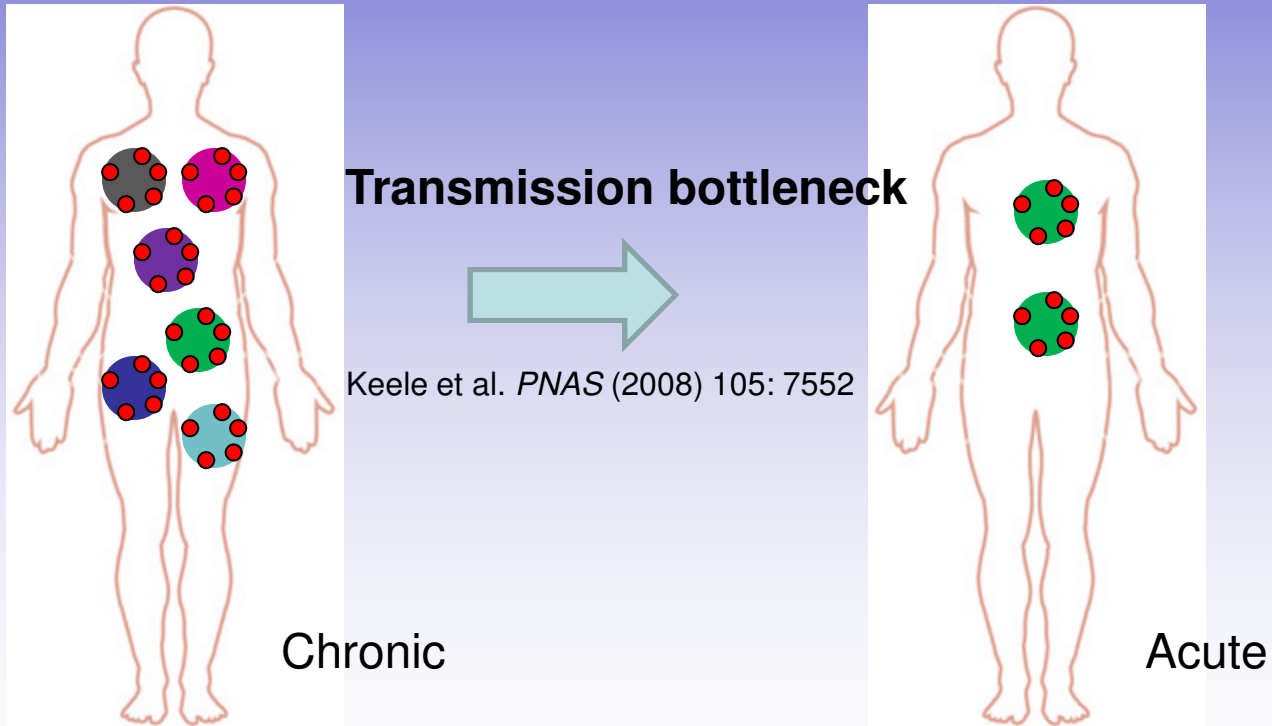


DeSantis...Cheng, *J. Biol. Chem* (2016) 291: 13088

Clinical Implications

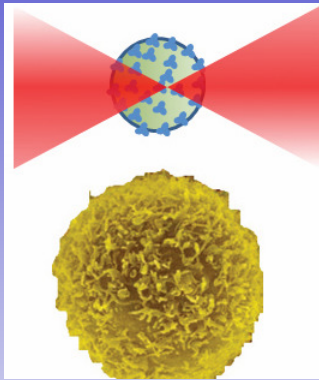
- Are they prone to transmission?
- Transmitted virus are enriched for higher gp120 content.

Parrish et al. *PNAS* (2013) 110: 6626

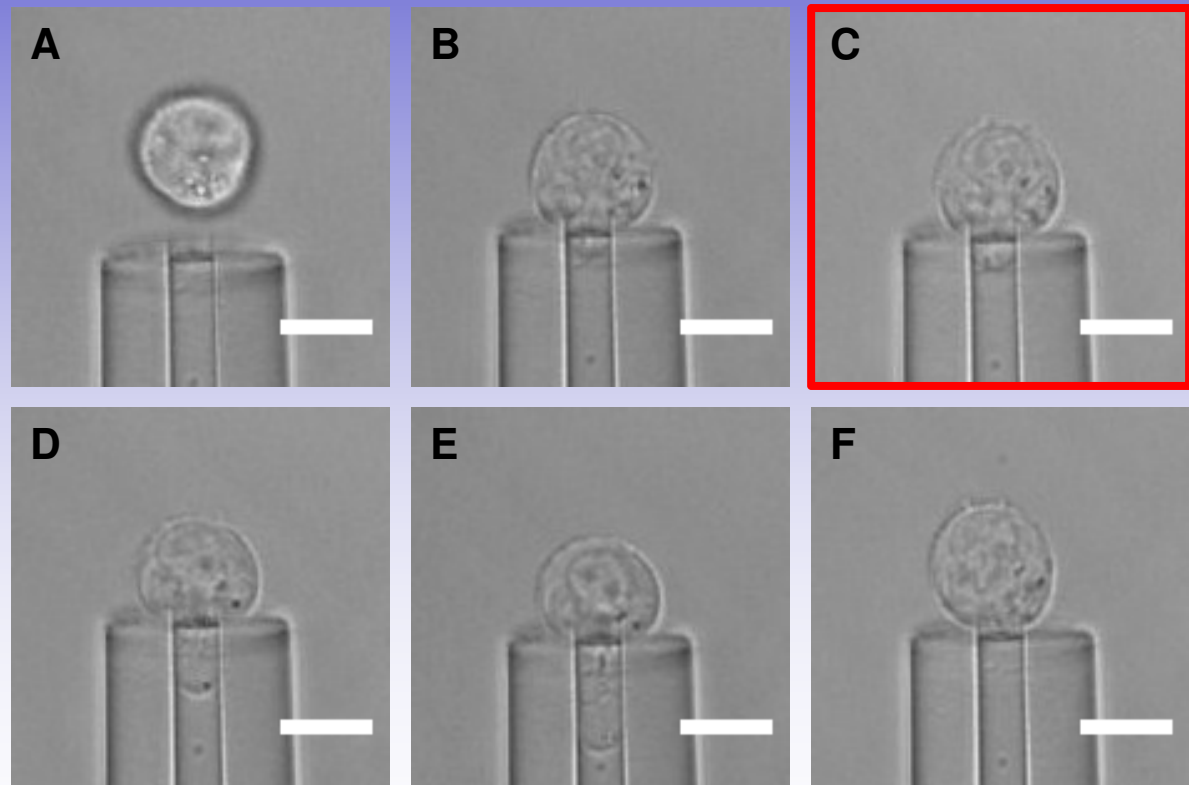
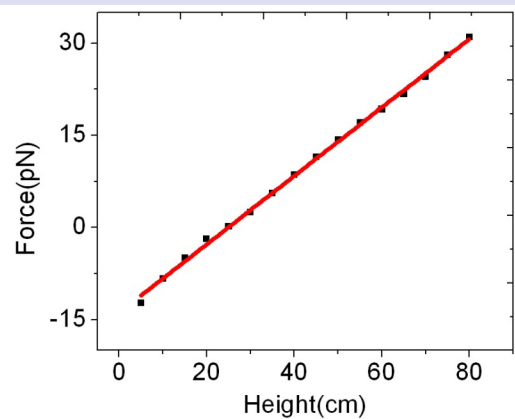


Not every HIV-1 virion is created equally!

Single-Cell Manipulation for Single Virion Delivery



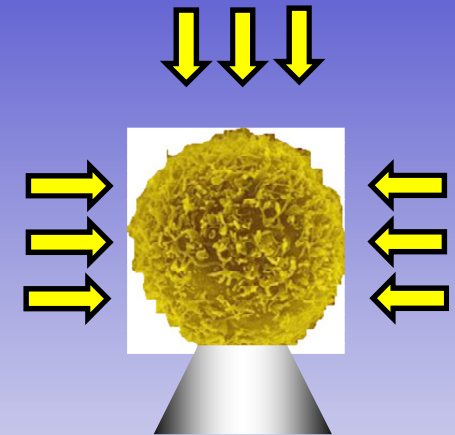
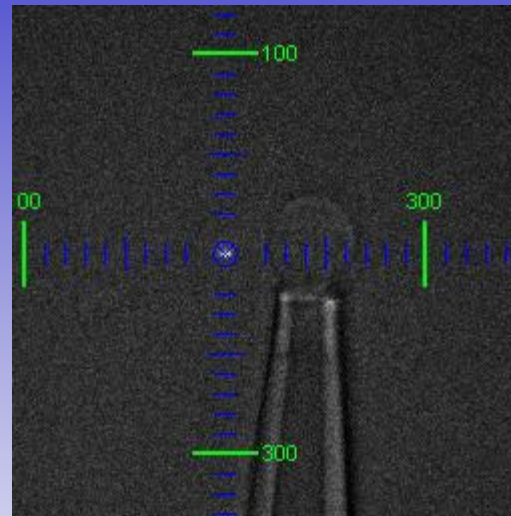
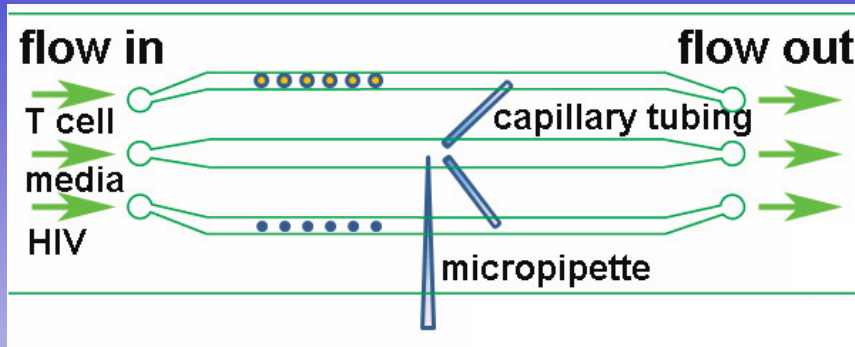
Suction force controlled by hydrostatic pressure



Scale bar: 10 μm

Hou & Cheng, unpublished

Specific Association upon a Single Collision is Rare



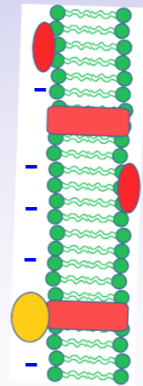
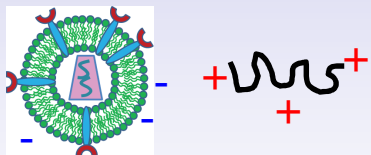
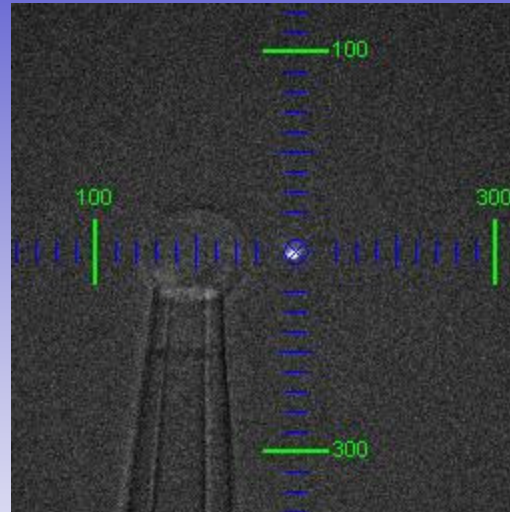
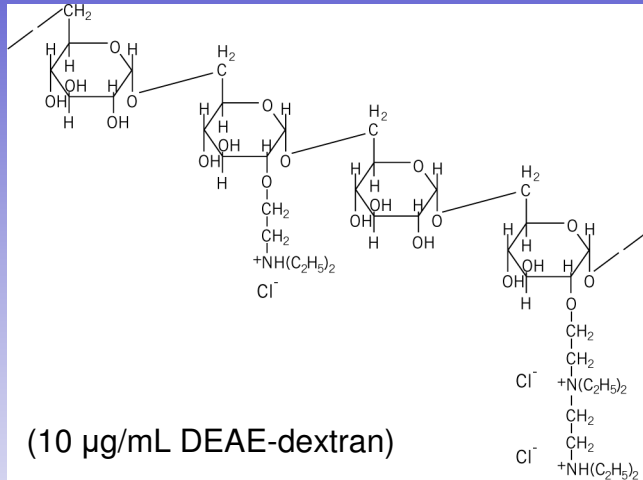
“**Forced**” delivery of HIV to CD4⁺ T cells

- An optically trapped virion is slowly brought into contact with a cell
- Attachment is easy to detect as an immobilized virion remains in focus
- The laser is turned off once the virion escapes

Trials	Attachments	Attachment Probability (%)
73	0	0

GFP labeled HIV-1, SUP-T1 cell, 20°C PBS

Frequent but Nonspecific Association Promoted by DEAE-dextran



Trials	Attachments	Attachment Probability (%)
77	59	>77

GFP labeled HIV-1, SUP-T1 cell, 20°C PBS

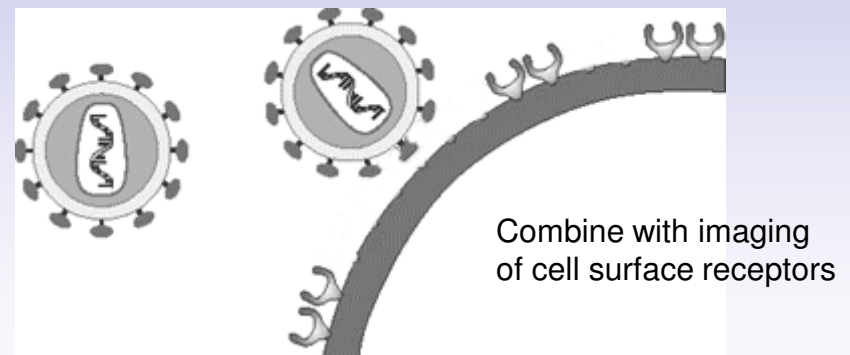
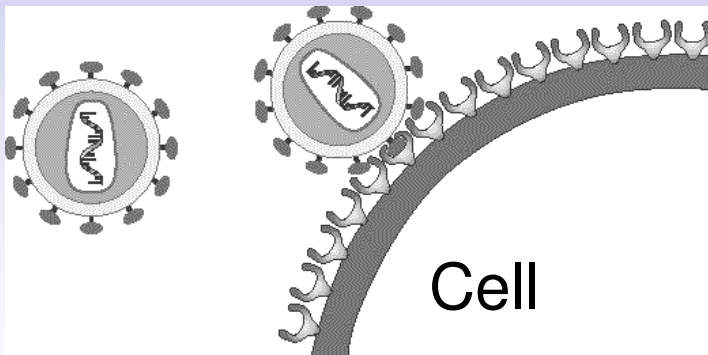
Polycation 'bridge'

Koh & Cheng, *Langmuir* (2014) 30: 10899

DeSantis & Cheng, unpublished

Possible Reasons for Lack of Attachment and Potential Future Development

- The virion may have low gp120; Combine with virometry
- Cell surface receptor may be low or distribution of receptors is heterogeneous



To form specific contact upon a single collision is a rare event!!

Conclusions

- ❑ For the first time, optical trapping of a single **human** virus
- ❑ For the first time, measurement of the **index of refraction** for a single virus particle
- ❑ Optical trapping virometry for **multi-parameter** analysis of biological particles.
- ❑ HIV-1 gp120 displays a positive **cooperativity** in mediating HIV-1 infection.
- ❑ The technique to **deliver** a single virus to a single cell.

Acknowledgments



Past lab members:

Yuanjie Pang, Ximiao Hou
Jin H. Kim, Hanna Song

Current lab members:

Mike DeSantis, Abhay Kotnala
Chunjuan Tian
Zhilin Chen, Tai-wei Li
Chu Chen, Amir Hobson

Current collaborators:

Per-Johan Klasse	Irina Grigorova
Mike Farzan	James Moon
John Moore	Jianping Fu
James Riddell IV	



National Science Foundation
WHERE DISCOVERIES BEGIN



Postdoc wanted!