# Virtual micro-reality

## Immersive manipulation of live microscopic systems

SAPIENZA
UNIVERSITÀ DI ROMA

DiLeonardoLab

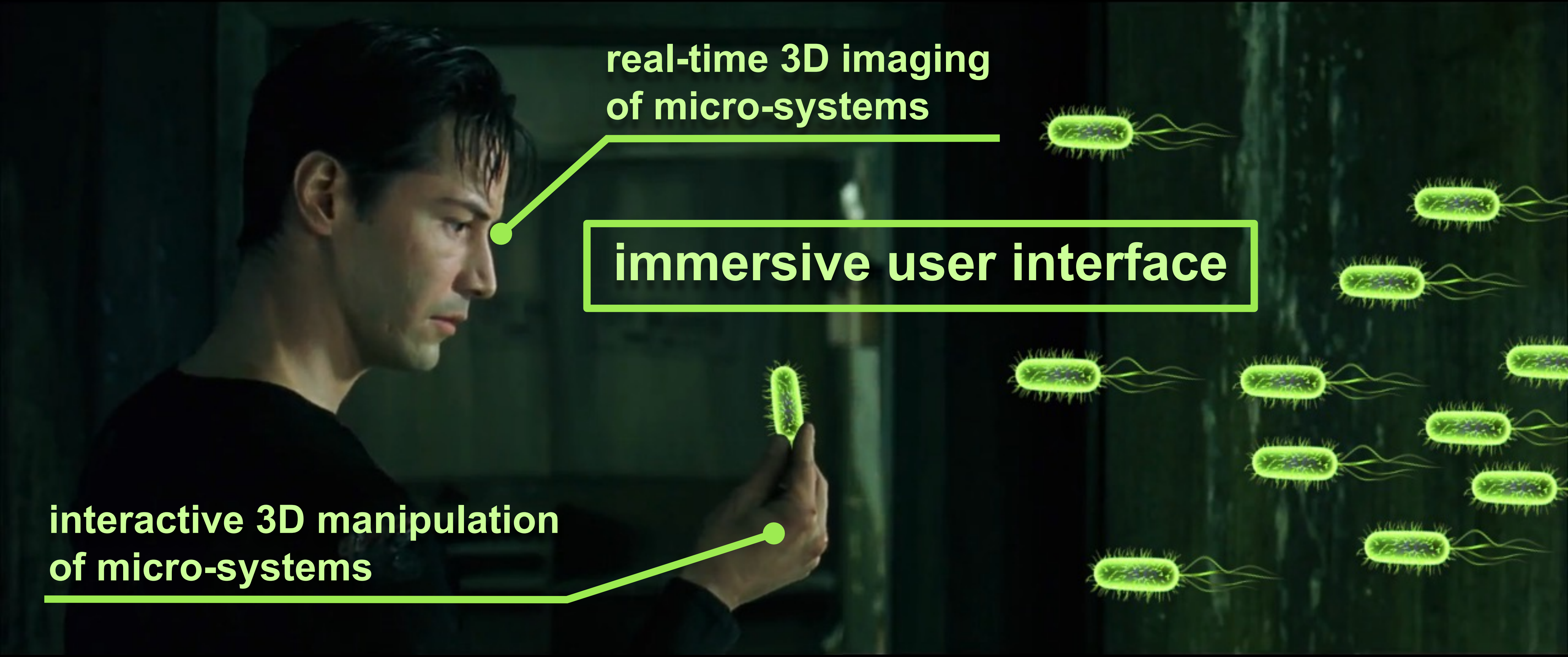
Stefano Ferretti

Scuola Dottorale ‘‘Vito Volterra’’
PhD in Physics
Cycle XXXIII

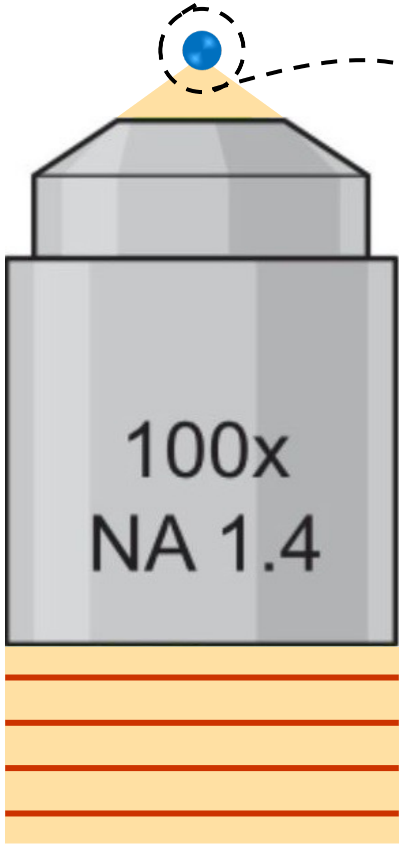
*PhD seminar series*

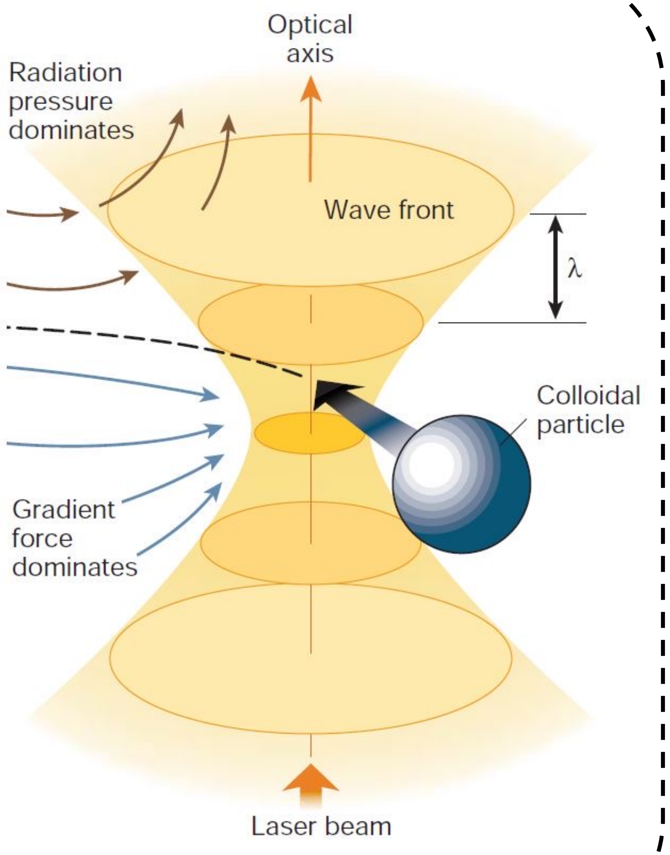
23 / 06 / 2021

# Interactive exploration and manipulation of microscopic systems: what do we need?

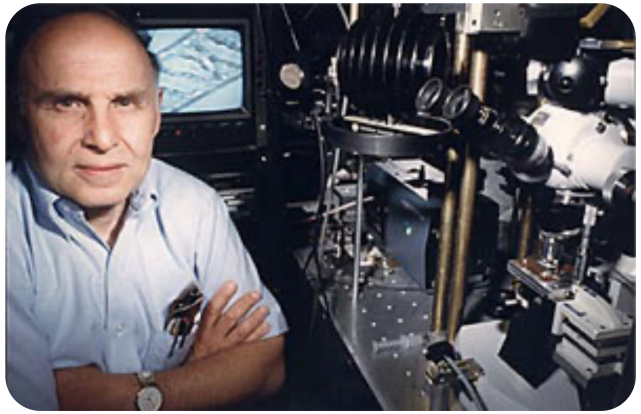


# Optical tweezers for micromanipulation




Grier, Nature (2003)



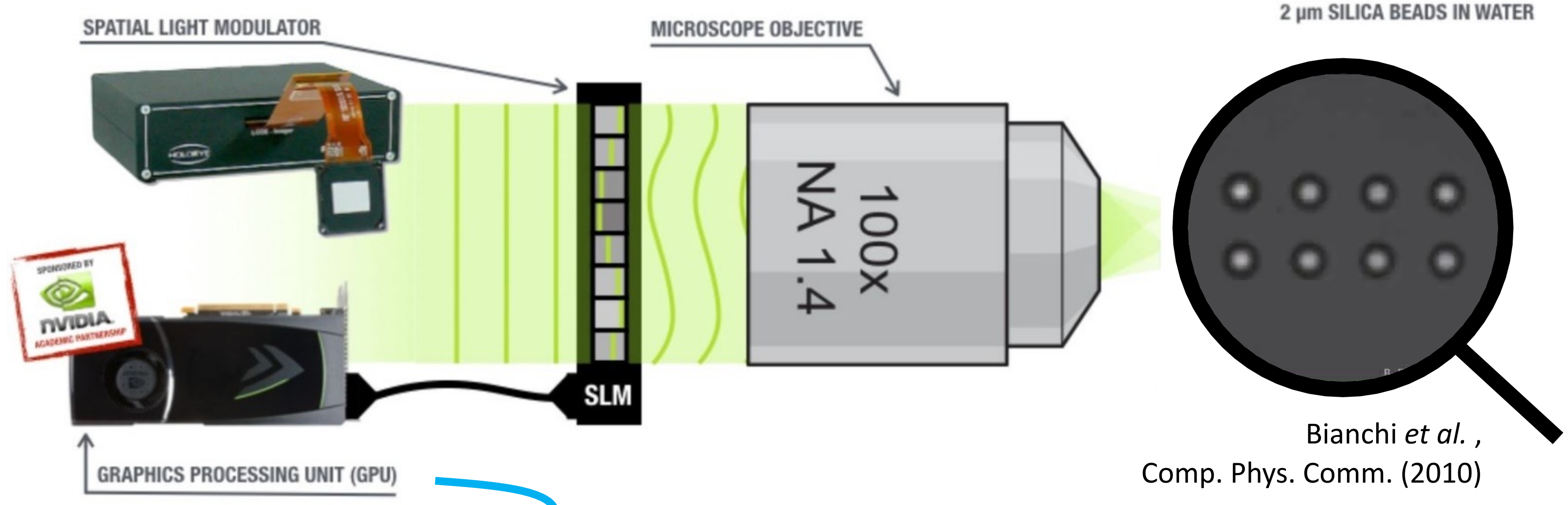
**Arthur Ashkin**

1986: single-beam optical tweezers

2018: Nobel prize

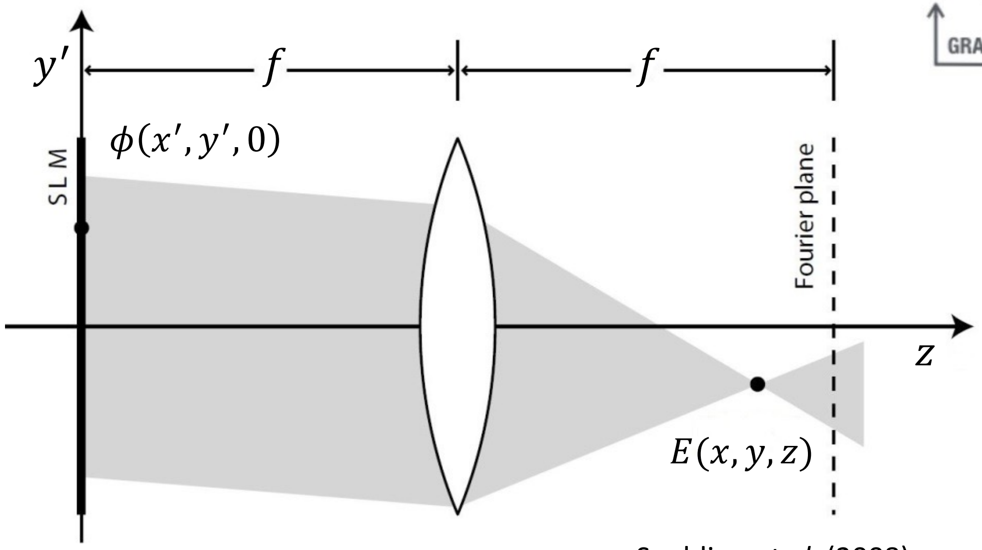
# Holographic tweezers for dynamic 3D micromanipulation

**H**olographic
**O**ptical
**T**weezers




Bianchi *et al.* ,
Comp. Phys. Comm. (2010)

$$0.24\ \frac{\text{ms}}{\text{trap} \cdot \text{iteration}}$$




Spalding *et al*. (2008)

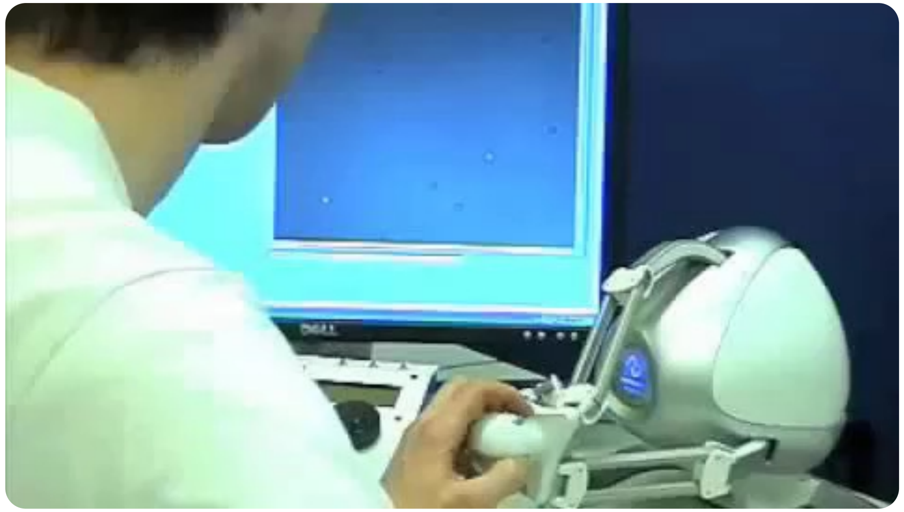
$$E(x,y,z) \propto \iint e^{i\phi(x',y',0)} e^{-i\frac{2\pi}{\lambda f}(xx'+yy')} e^{-i\frac{\pi z}{\lambda f^2}\left(x'^2+y'^2\right)} dx'dy'$$

# Advanced interfaces to holographic tweezers

**iTweezers**

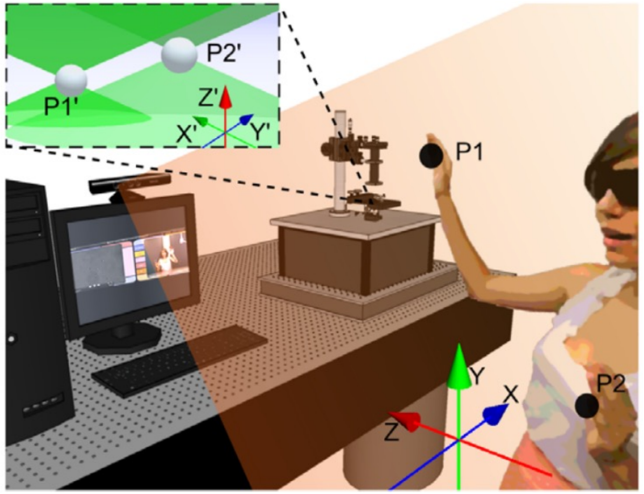
Bowman *et al.* , Journ. of Opt. (2011)

**Force-feedback optical tweezers**



Pacoret *et al.* , Opt. Express (2009)

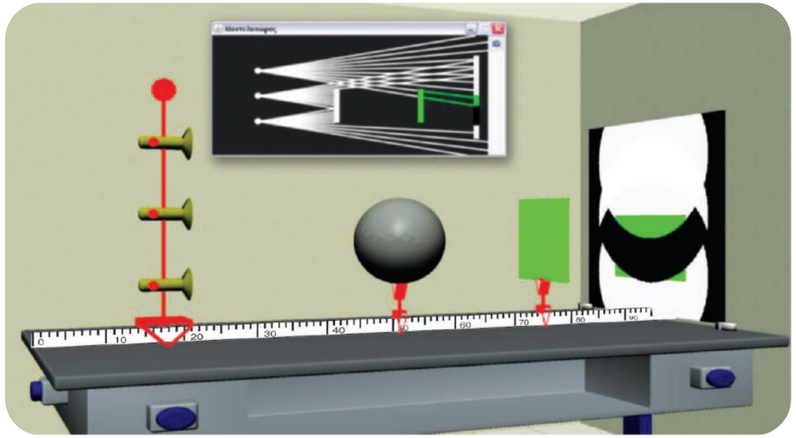
**Kinect – controlled optical tweezers**




Shaw *et al.* , Journ. of Opt. (2013)

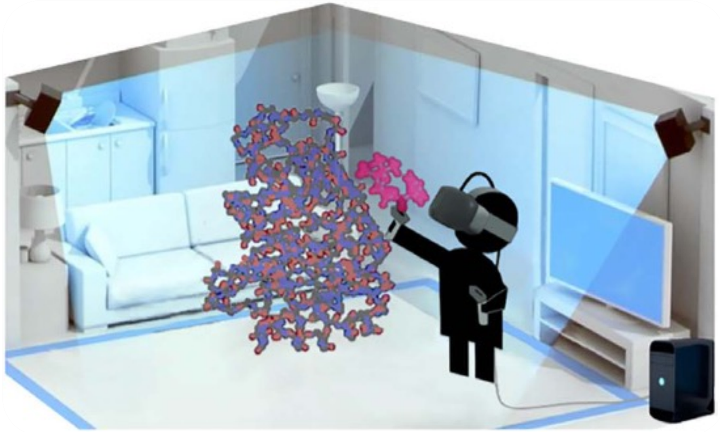
# Virtual reality

Virtual lab experiments



De Jong *et al.* , Science (2013)

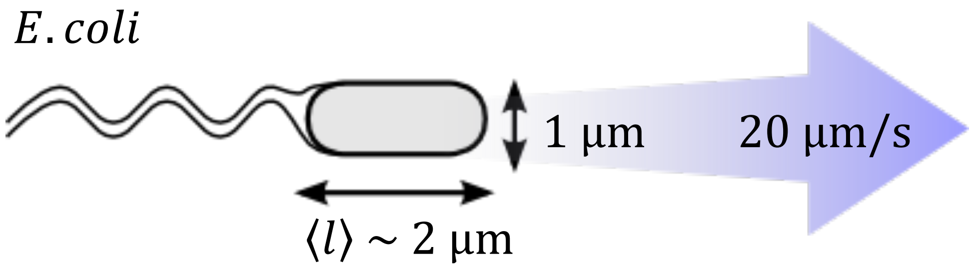
Molecular dynamics simulations



O'Connor *et al.* , Sci. Adv. (2018)

Flight simulations

# 3D imaging techniques




- Field of view: $50 \times 50 \times 20\ \mu m^3$
- Spatial resolution: $\Delta = 0.1\ \mu m$

$$\text{framerate} = \frac{v}{s_{xy}} = \frac{20\ \mu m/s}{l/10} = \frac{20\ \mu m/s}{0.2\ \mu m} = 100\ \text{fps}$$

$\Delta = 0.1\ \mu m$ $(\times 200)$

$$\text{framerate} = 20000\ \text{fps}$$

single frame dimension: $500 \times 500$ pixels

<u>Requirements:</u>

- high framerate
- good resolution ($< 1\ \mu m$)

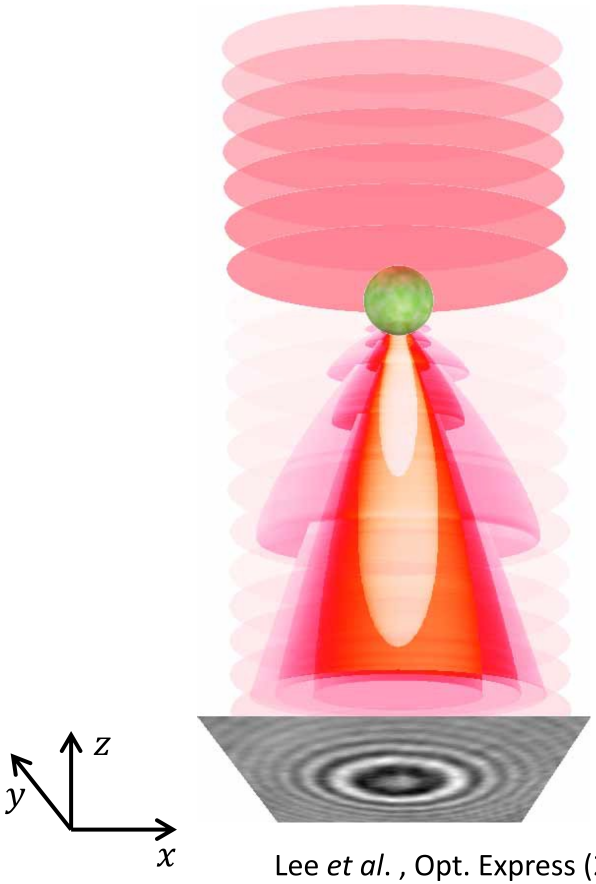
<u>State of the art:</u>

- ~~confocal microscopy~~
- ~~light-sheet microscopy~~
- ~~two-photon microscopy~~
- ~~diffraction tomography~~

Too time consuming!

# Holographic microscopy for fast 3D reconstructions

On-axis **D**igital **H**olographic **M**icroscopy




Incident beam
$E_i$

Colloidal bead

Scattered beam
$E_s$

Hologram
$I = |E_i + E_s|^2 \approx |E_i|^2 + 2Re\{E_i^* E_s\}$

Lee *et al.* , Opt. Express (2007)

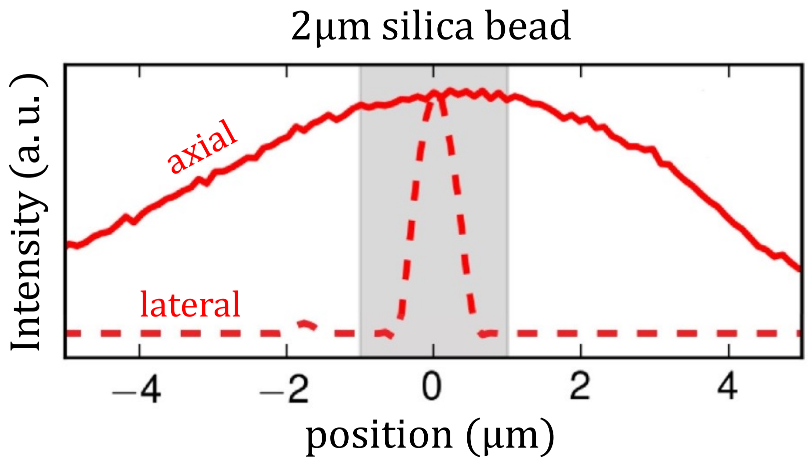
$$E_s \approx (I - |E_i|^2)/E_i^*$$

$$E_s(x,y,z) = G(x,y,z) * E_s(x,y,0) =$$

$$= FT^{-1}\left[\tilde{G}(k_x,k_y,z) \cdot FT[E_s(x,y,0)]\right]$$

$$G(x,y,z) = \frac{e^{jkr}}{2\pi}\frac{z}{r^2}\left(\frac{1}{r} - jk\right)$$

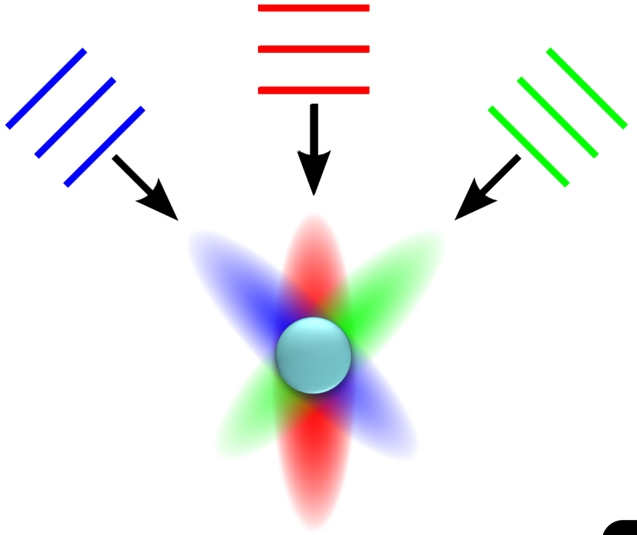
Shen & Wang, Appl. Opt. (2006)

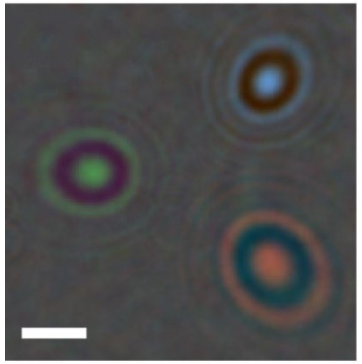


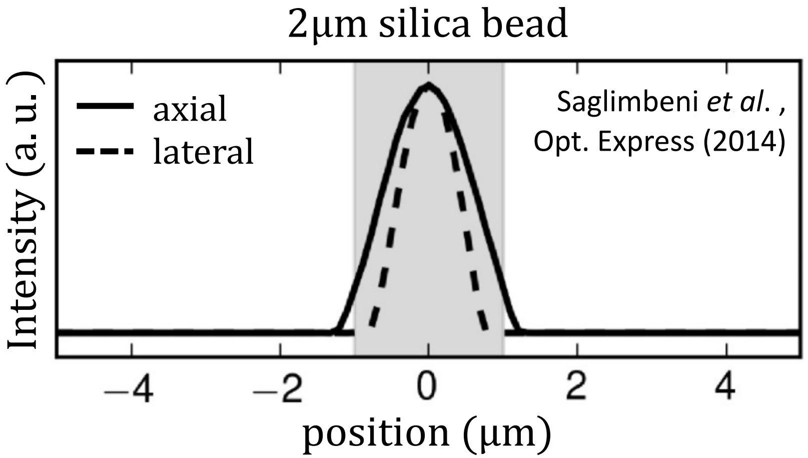

Saglimbeni *et al.* , Opt. Express (2014)

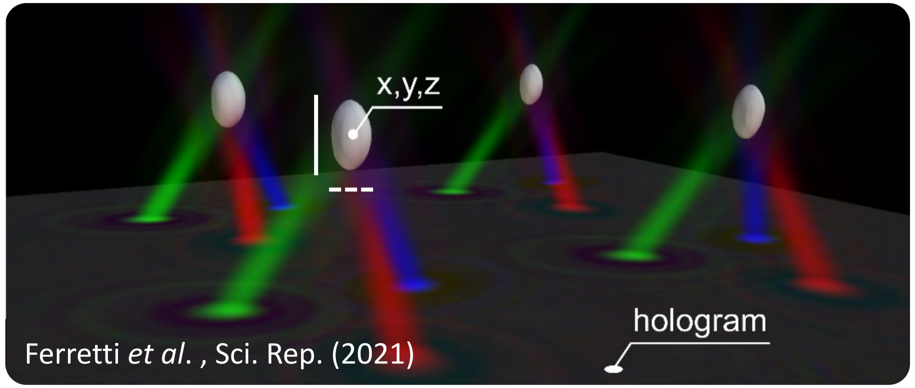
# Holographic microscopy for fast 3D reconstructions

3-axis **D**igital **H**olographic **M**icroscopy

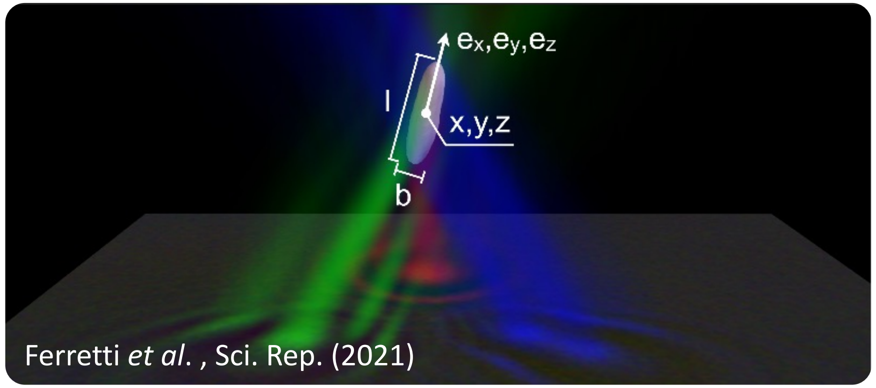






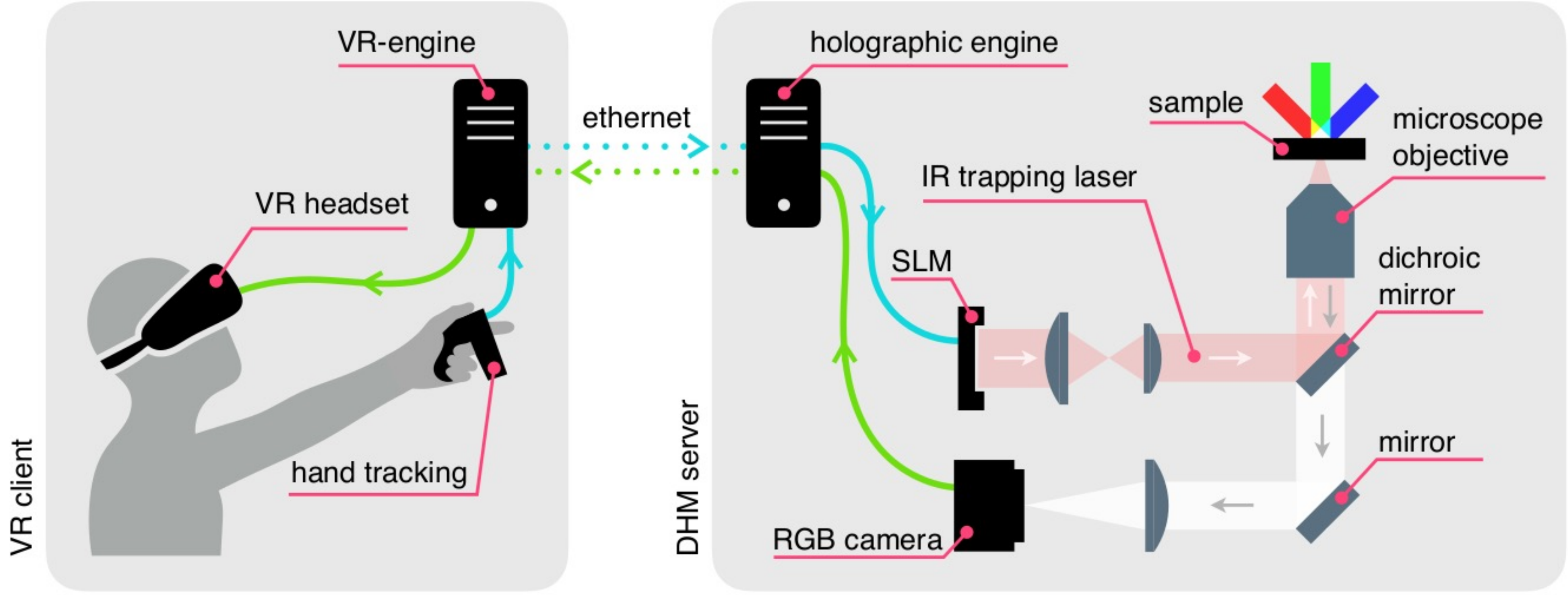



Ferretti *et al.* , Sci. Rep. (2021)

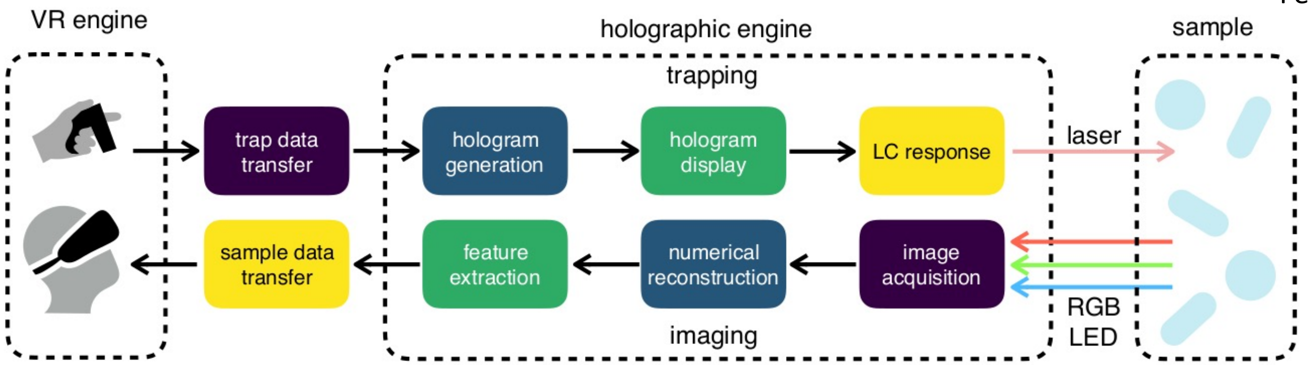


Ferretti *et al.* , Sci. Rep. (2021)

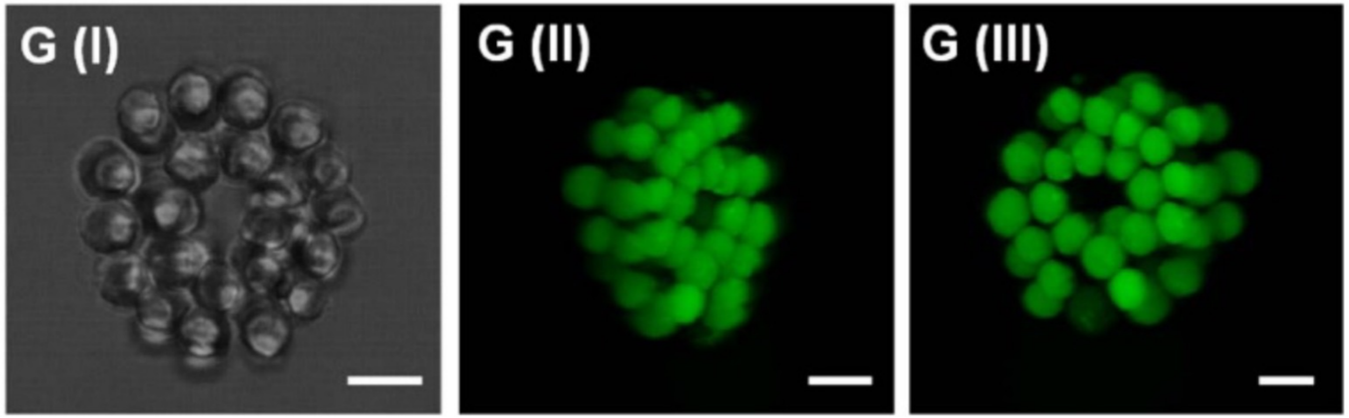
# Data and light flow diagram



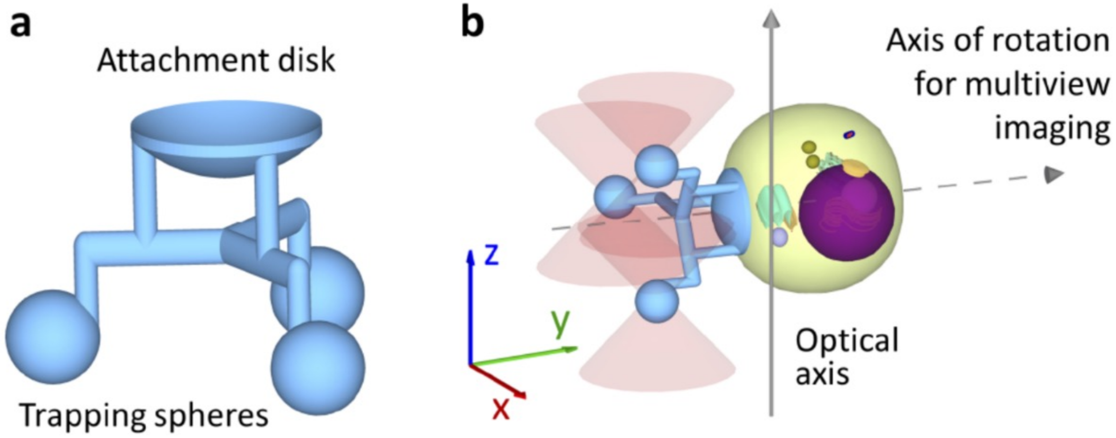

Ferretti *et al.* , Sci. Rep. (2021)



# The power of dynamic 3D micromanipulation

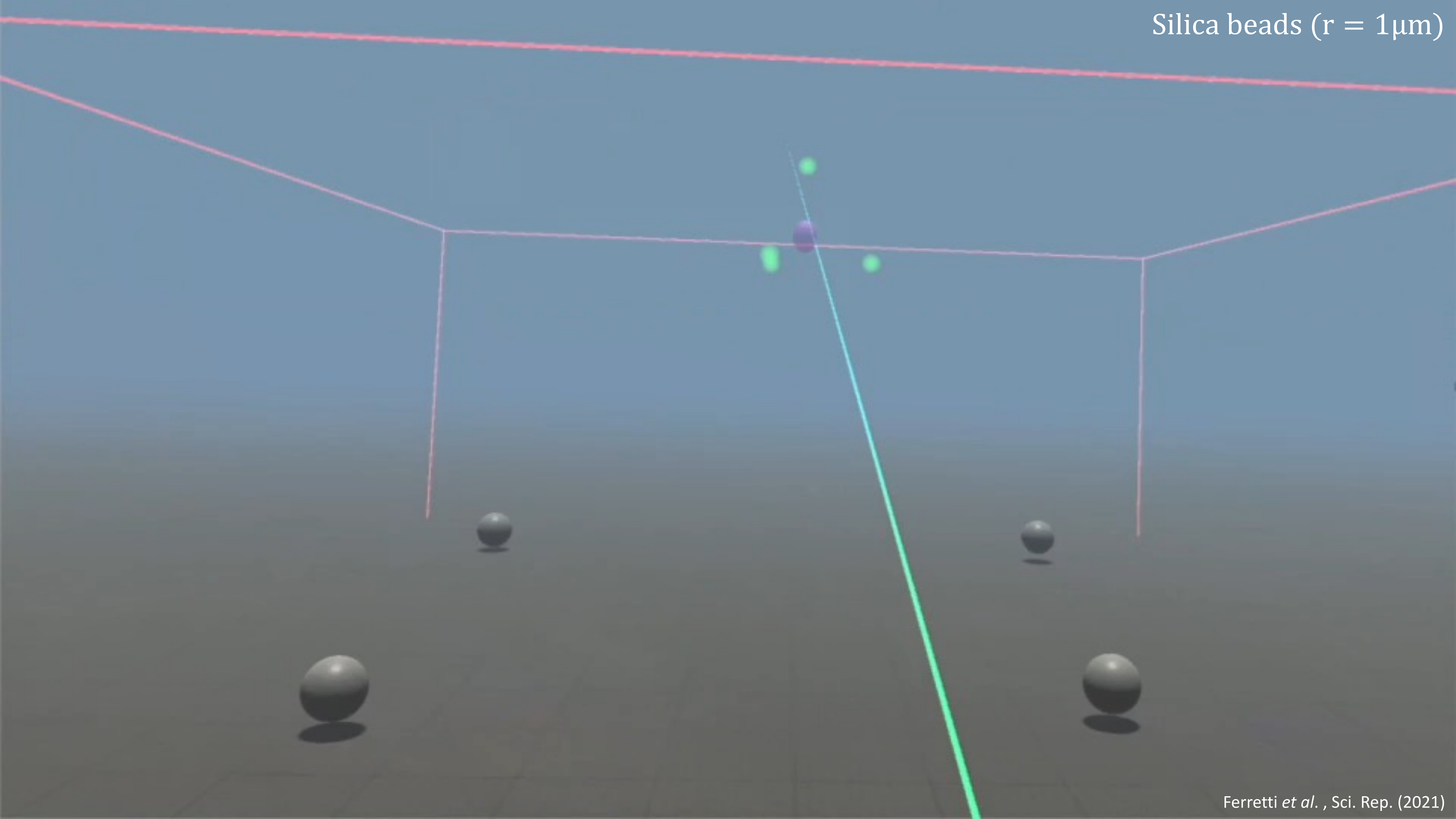



Kirkham *et al.* , Sci. Rep. (2015)

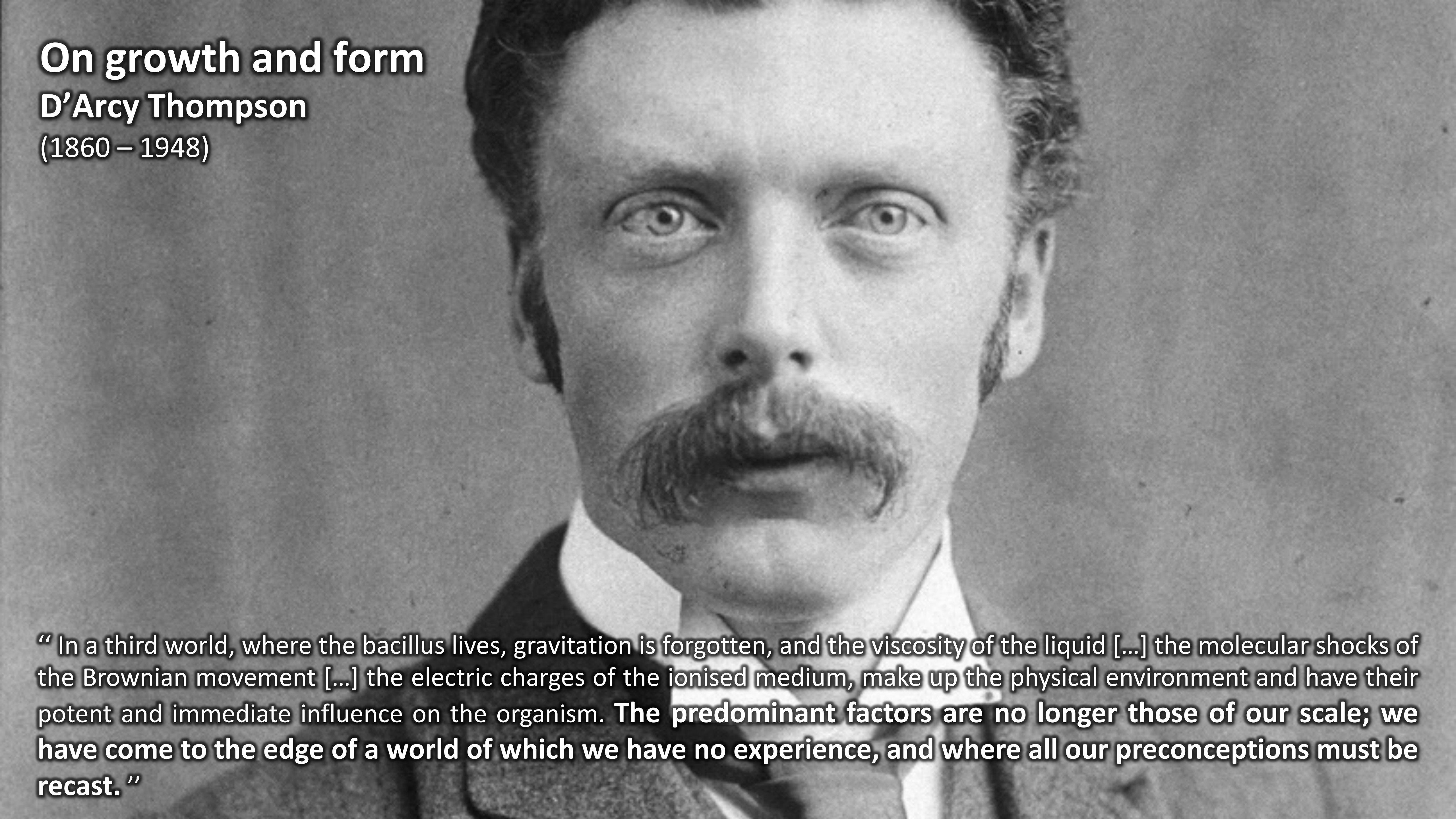



Vizsnyiczai *et al.* , Biomed. Opt. Express (2020)

Silica beads ($r = 1\mu m$)



Ferretti *et al.* , Sci. Rep. (2021)



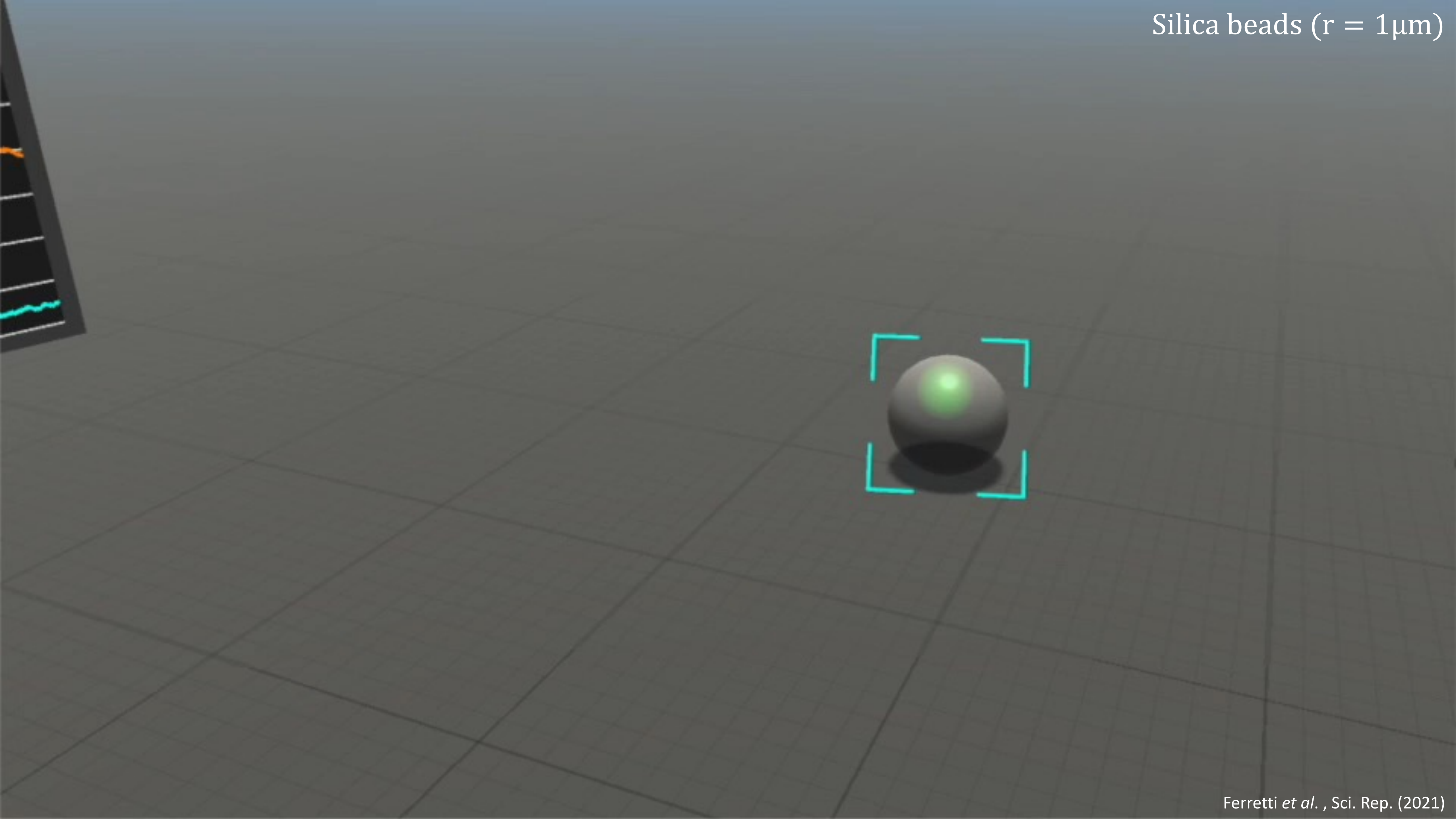
# On growth and form

## D’Arcy Thompson

(1860 – 1948)

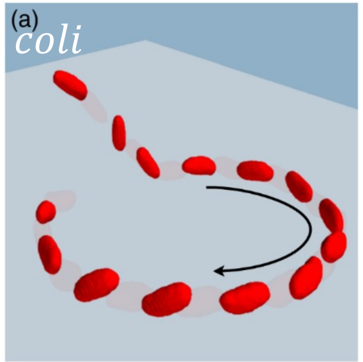
’’ In a third world, where the bacillus lives, gravitation is forgotten, and the viscosity of the liquid [...] the molecular shocks of the Brownian movement [...] the electric charges of the ionised medium, make up the physical environment and have their potent and immediate influence on the organism. **The predominant factors are no longer those of our scale; we have come to the edge of a world of which we have no experience, and where all our preconceptions must be recast.** ’’

Silica beads (r = 1μm)

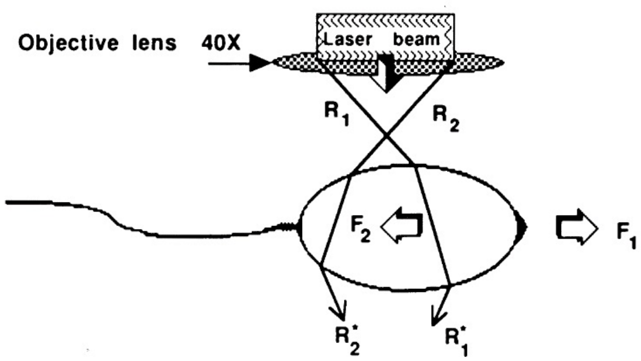


Ferretti *et al.* , Sci. Rep. (2021)

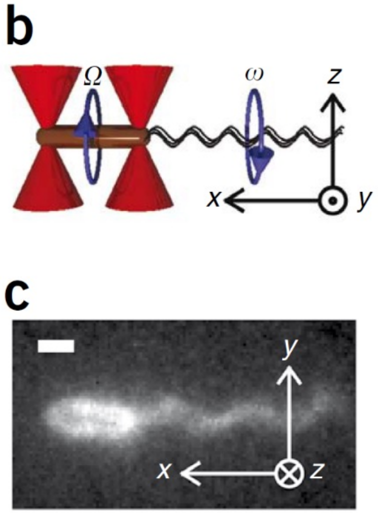
# Optical tweezers for cells sorting and analysis



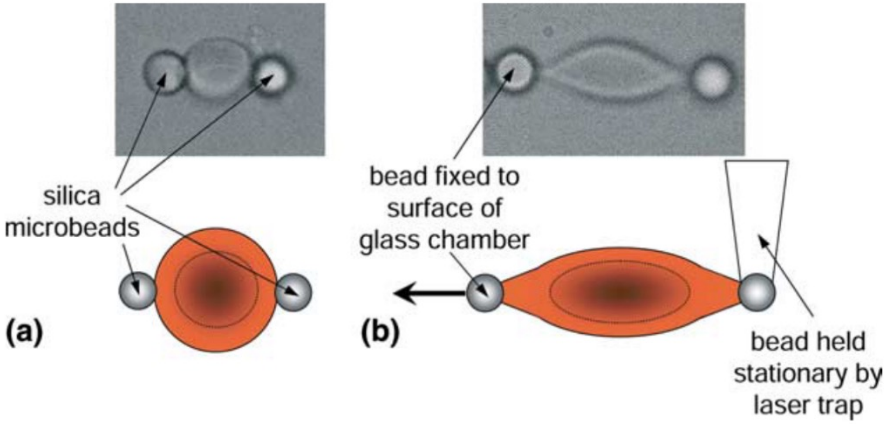

Bianchi *et al.* , Phys. Rev. X (2017)




Tadir *et al.* , Fertil. Steril. (1990)




Min *et al.* , Nat. Methods (2009)

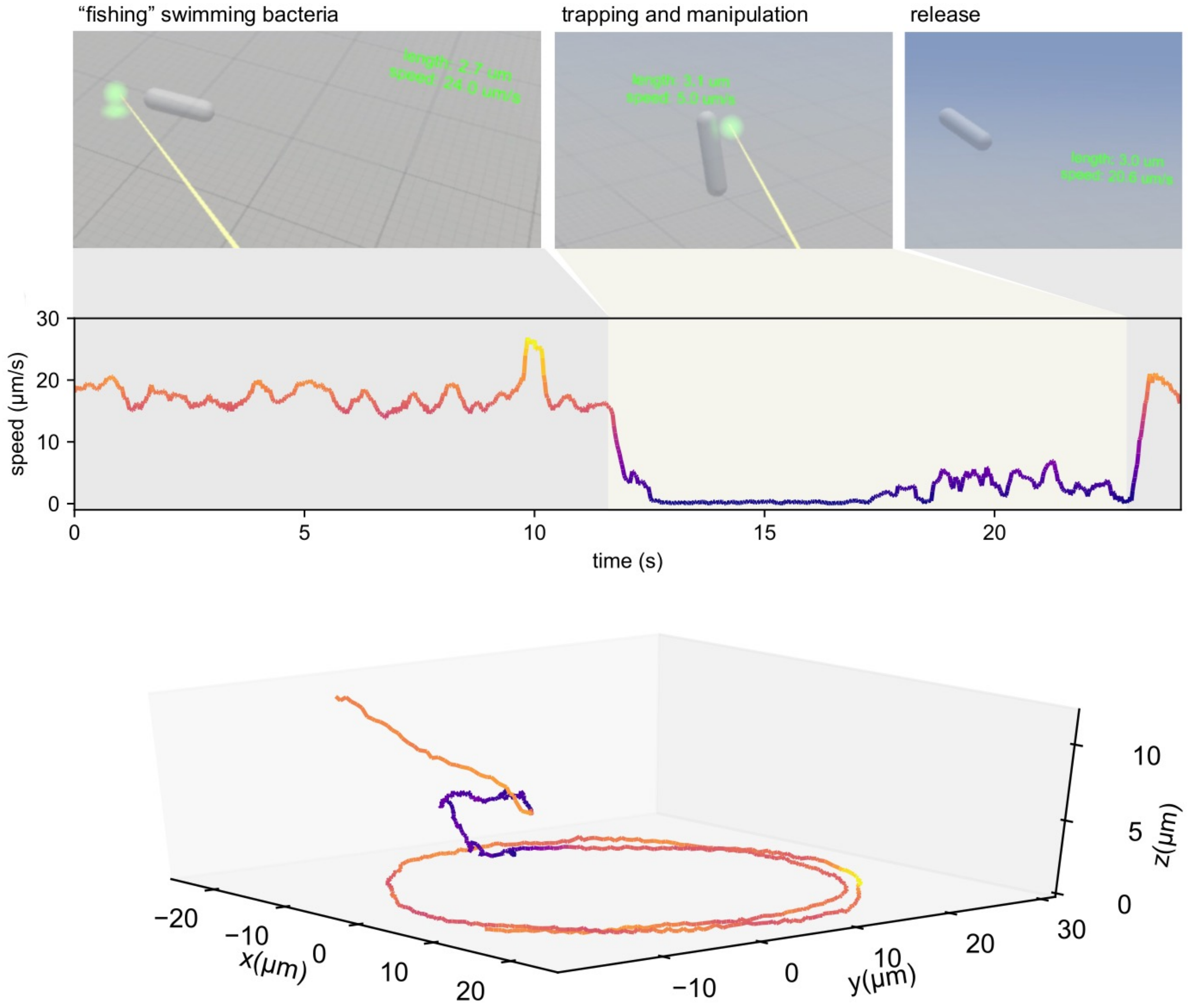



Lim *et al.* , Acta Mater. (2004)

$E.coli$ bacteria

Ferretti *et al.* , Sci. Rep. (2021)

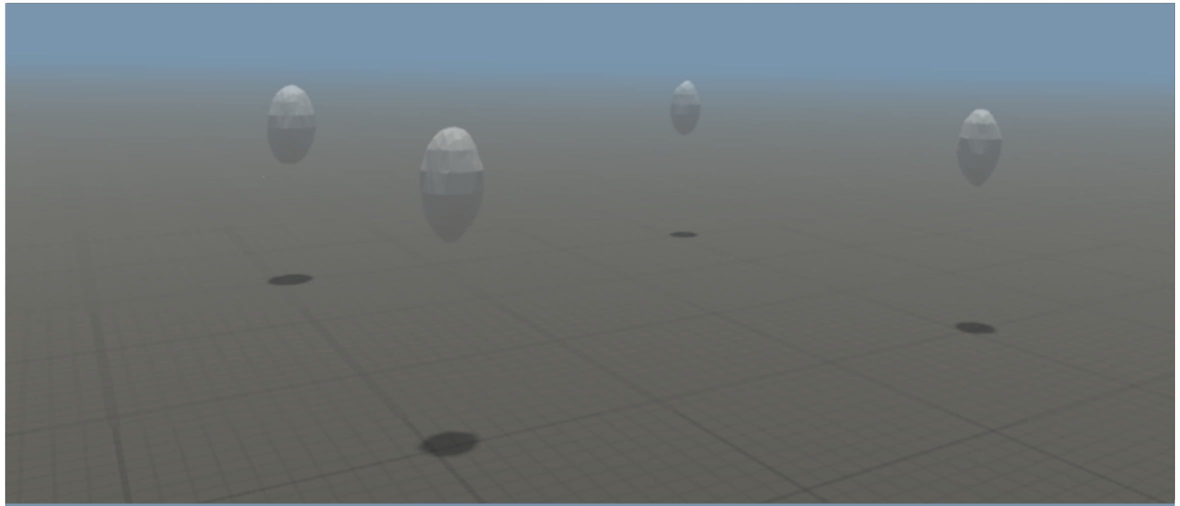
# Post processing data

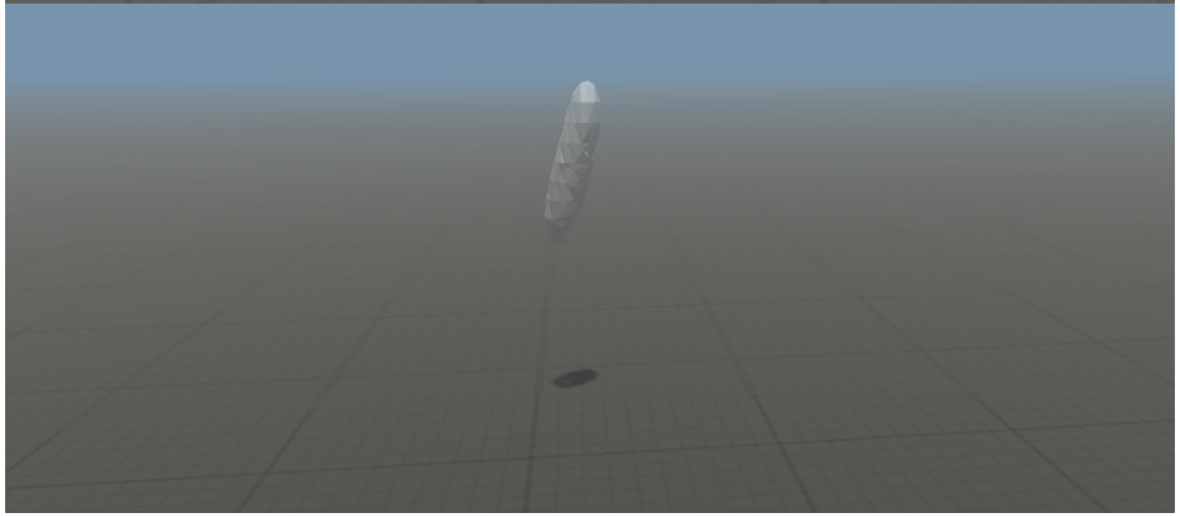


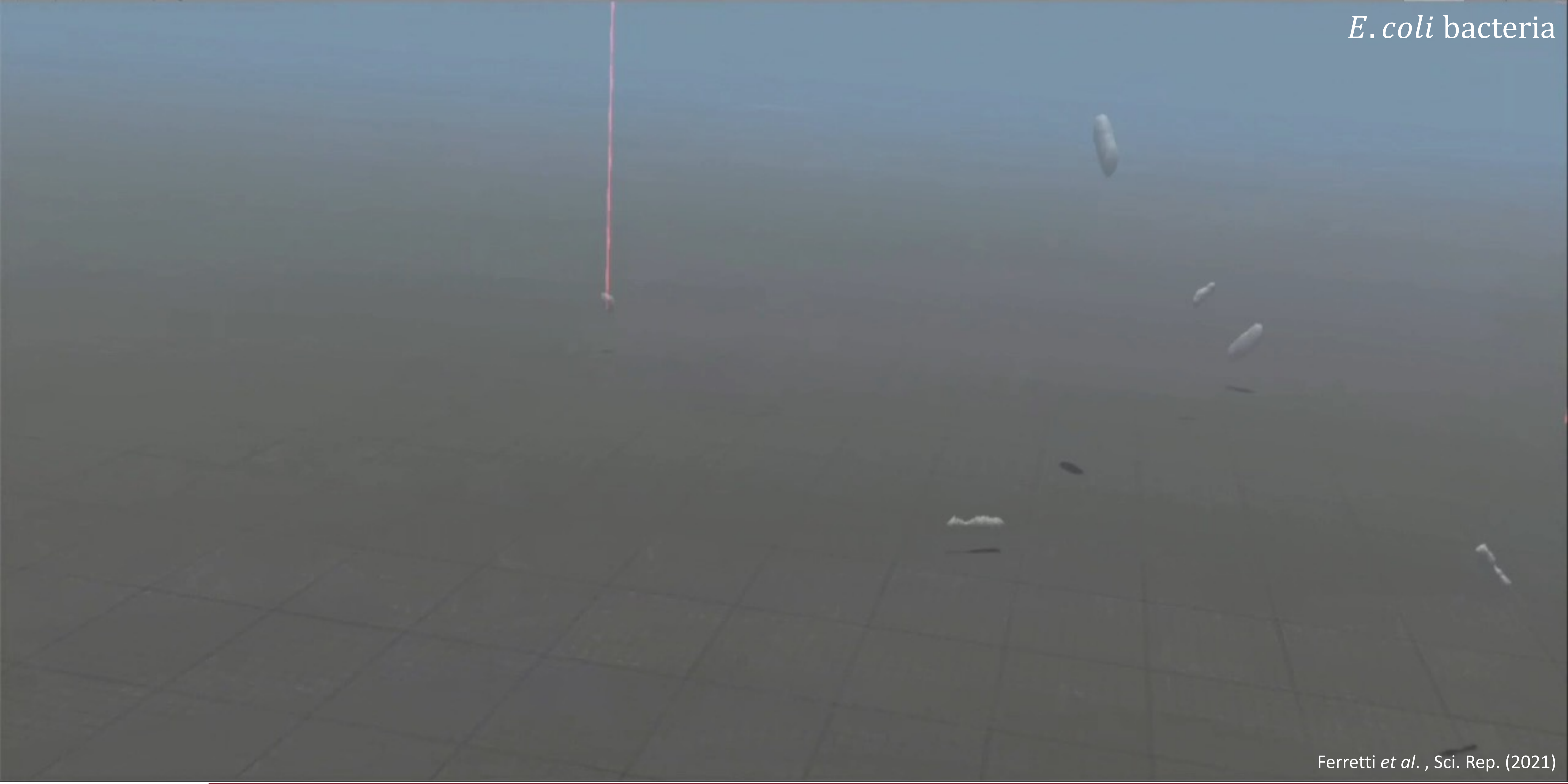

Ferretti *et al.* , Sci. Rep. (2021)

# Generic objects rendering

New strategy for the virtual rendering of generic objects with unknown morphology.





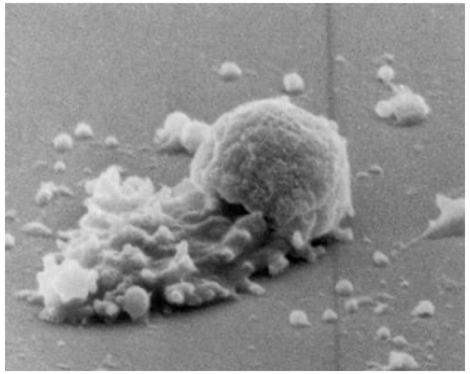


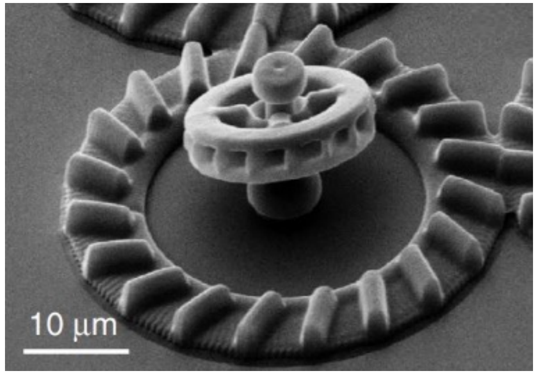
Ferretti *et al.* , Sci. Rep. (2021)

# $E. coli$ bacteria

# Next steps

- New advanced tomography algorithms to reconstruct simple objects like bacteria, aiming to extend this tool to more complex objects (other motile cells like sperm cells for motility studies, or crawling cells).
- Live analysis of bacteria dynamics in specific conditions (interaction of parallel swimming bacteria, interactive study of motility, speed and dimension, …).
- Real-time fabrication and manipulation of 3D micro-tools and interactive assembly of bio-hybrid micro-machines.





# People

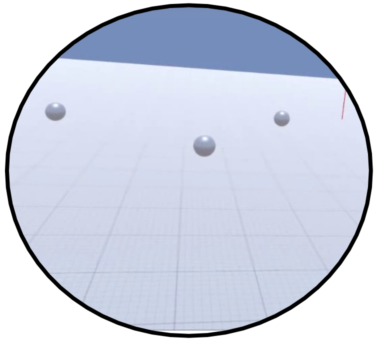
# Acknowledgements

European Research Council

European Commission

NVIDIA

REGIONE LAZIO

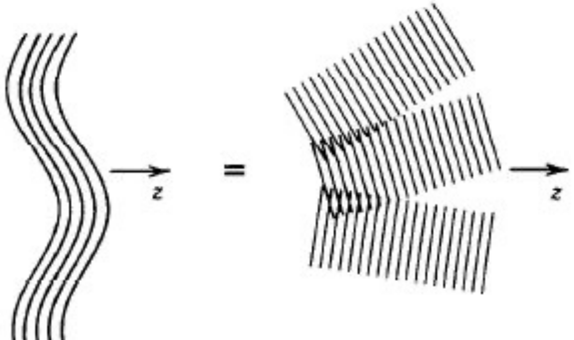


# Thanks for your attention!

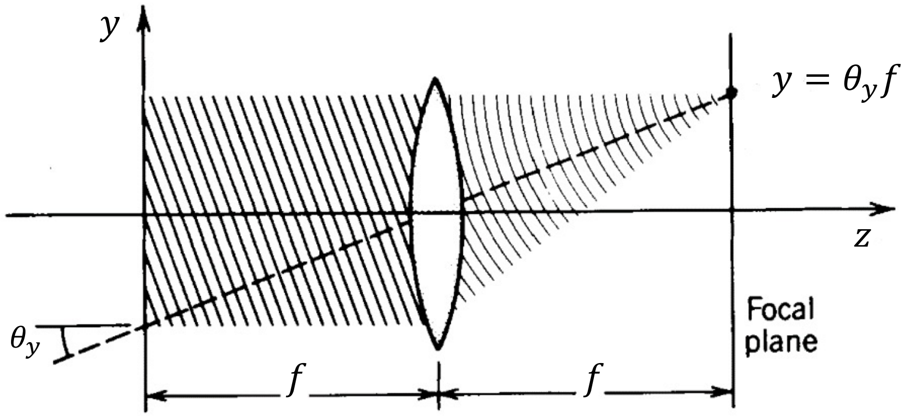


http://www.roma1.infn.it/~dileorob/
stefano.ferretti@uniroma1.it

# Fourier optics for wave propagation



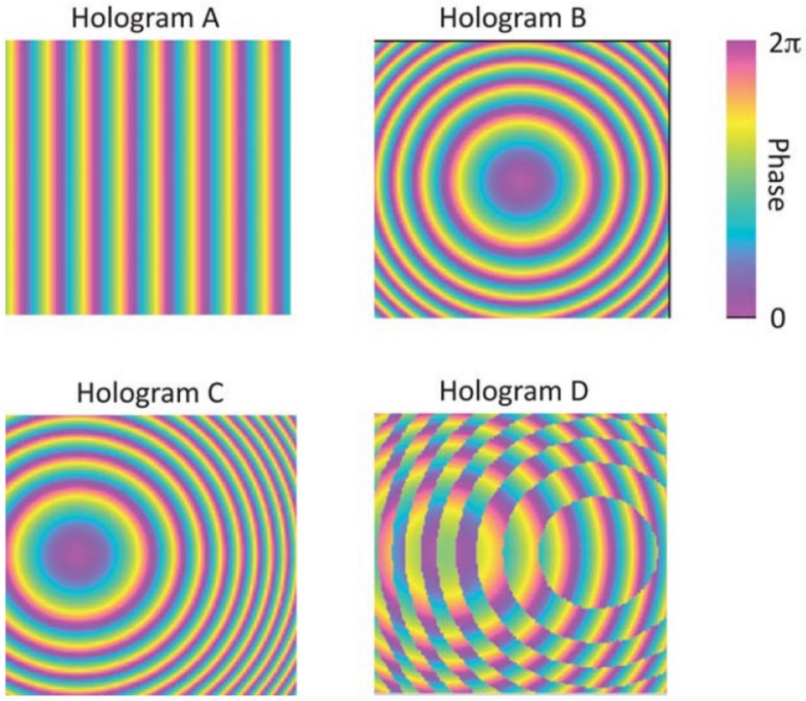

Saleh *et al.*, John Wiley & Sons (1991)



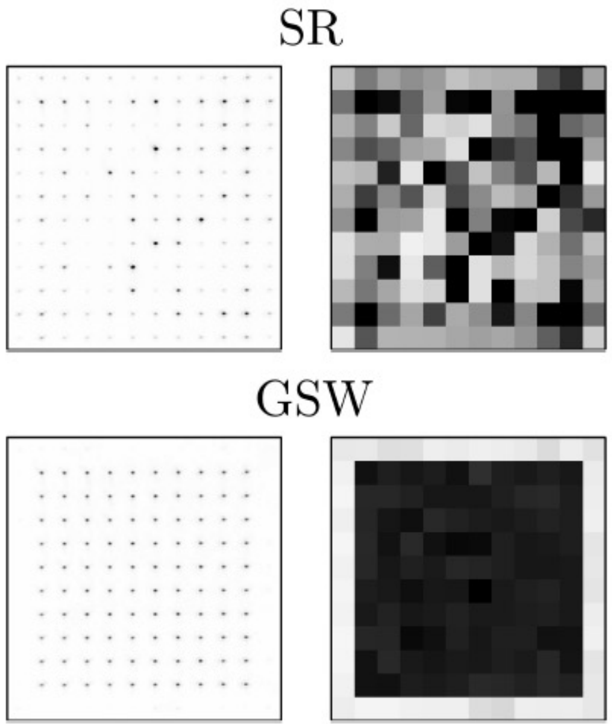

$$y = \theta_y f = \frac{\lambda f}{2\pi} k_y \quad \Longrightarrow \quad k_y = \frac{2\pi y}{\lambda f}$$

$$E(x, y, 0) = A \cdot e^{i(k_x x + k_y y)}$$

$$\theta_{x,y} \approx \frac{k_{x,y}}{k} = \frac{\lambda}{2\pi} k_{x,y}$$




Padgett *et al.*, Lab Chip (2011)

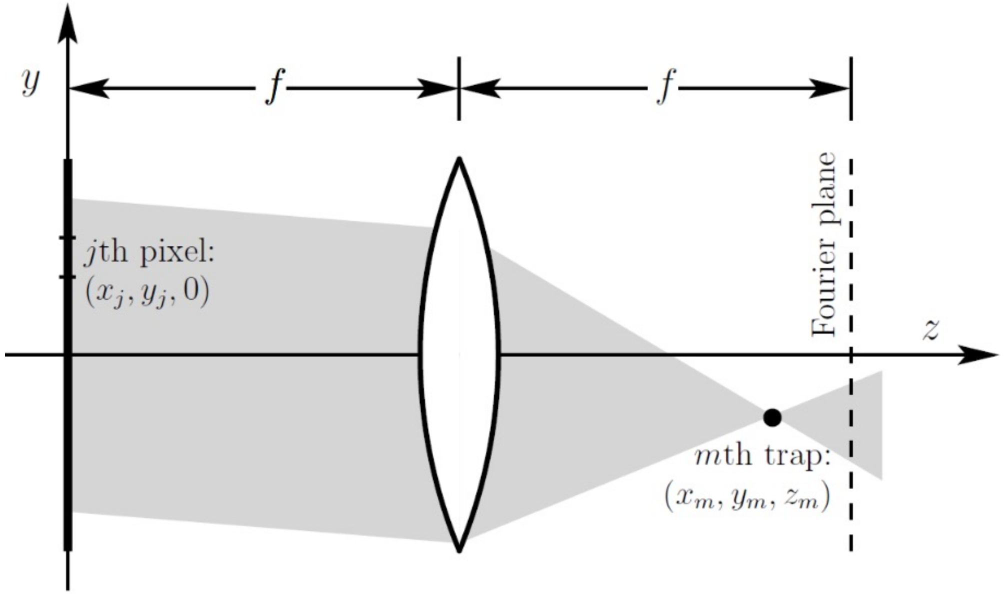



Di Leonardo *et al.*, Opt. Express (2007)

# Iterative algorithms: phase mask computation

$$j = 1, \dots, N \quad \text{pixels} \quad \rightarrow \quad U(x_j, y_j) = U_j = |U_j| \cdot e^{i\phi_j}$$
$$m = 1, \dots, M \quad \text{traps}$$

$$|U_j| = 1$$

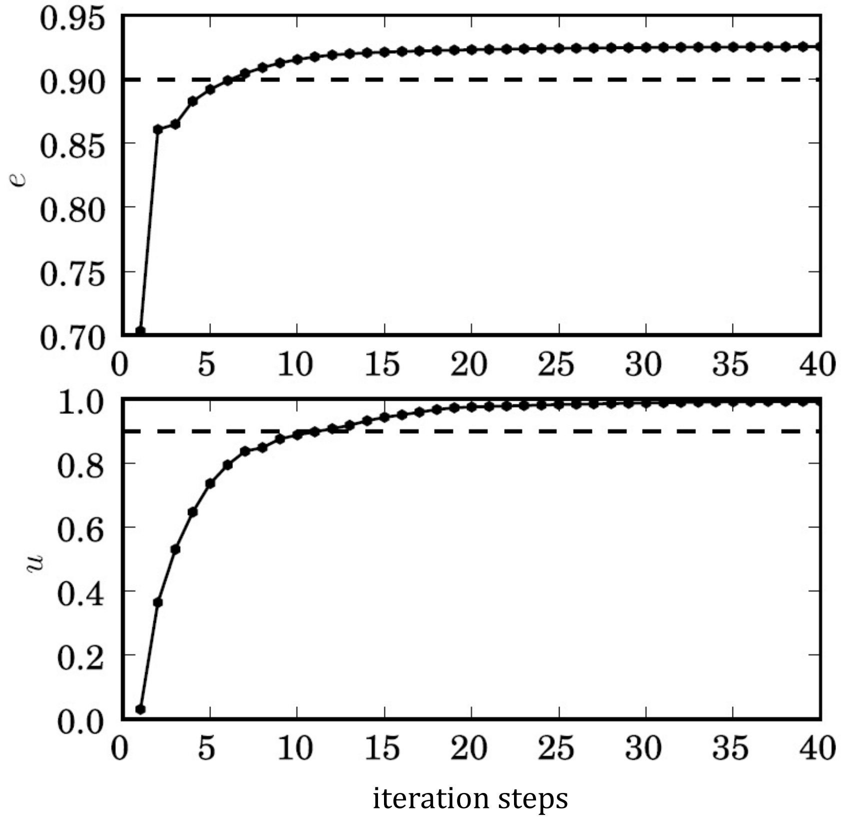



Bianchi *et al.* , Comput. Phys. Commun. (2010)

$$e = \sum_m |V_m|^2 = \sum_m I_m$$

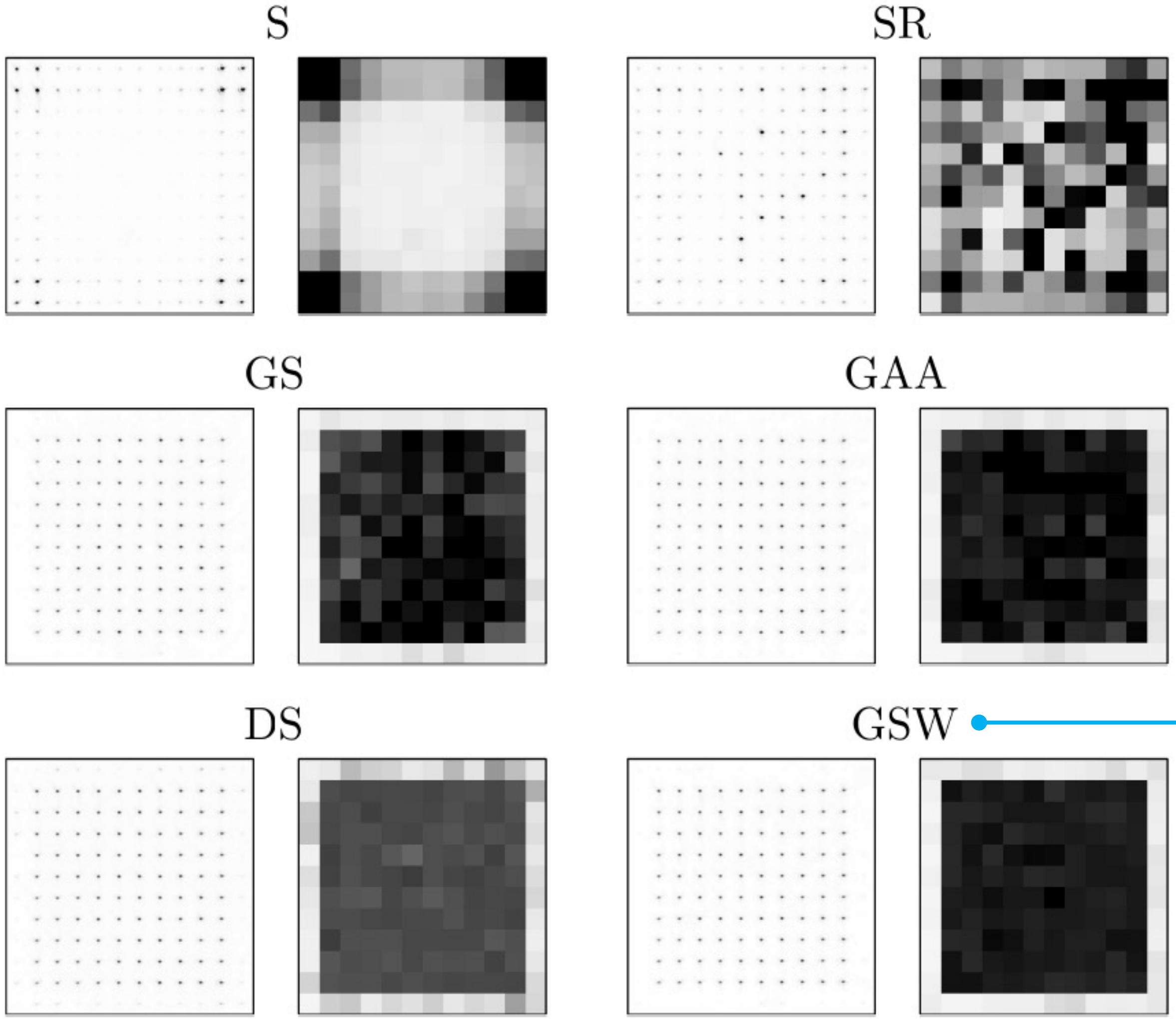
$$u = 1 - \frac{\max[I_m] - \min[I_m]}{\max[I_m] + \min[I_m]}$$

Di Leonardo *et al.*, Opt. Express (2007)



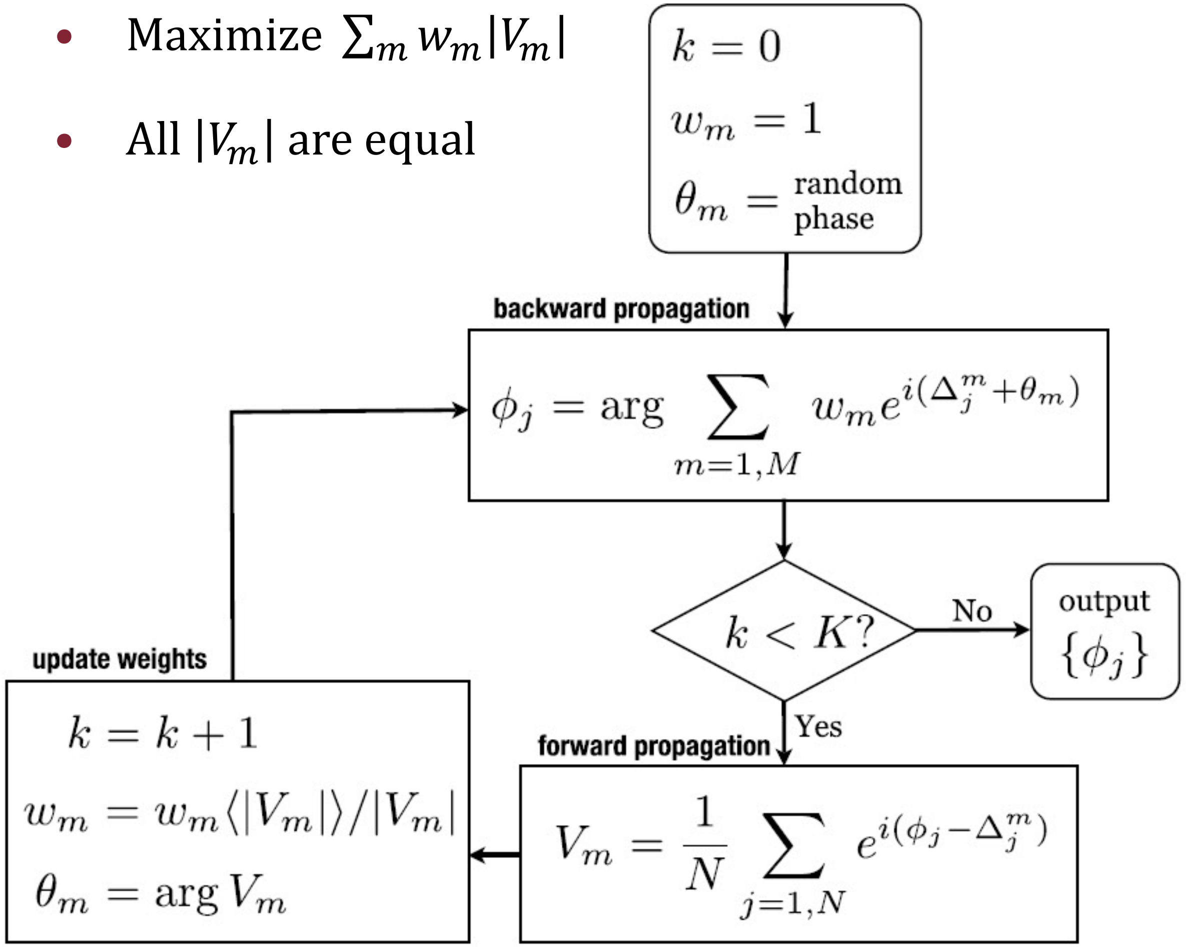

$$V_m = V(x_m, y_m, z_m) = \frac{1}{N} \sum_j e^{i\phi(x_j, y_j)} \underbrace{e^{-i\frac{2\pi}{\lambda f}(x_j x_m + y_j y_m)} e^{-i\frac{\pi z_m}{\lambda f^2}(x_j^2 + y_j^2)}}_{-i\Delta_j^m} = \frac{1}{N} \sum_j e^{i(\phi_j - \Delta_j^m)}$$

# Iterative algorithms: some results



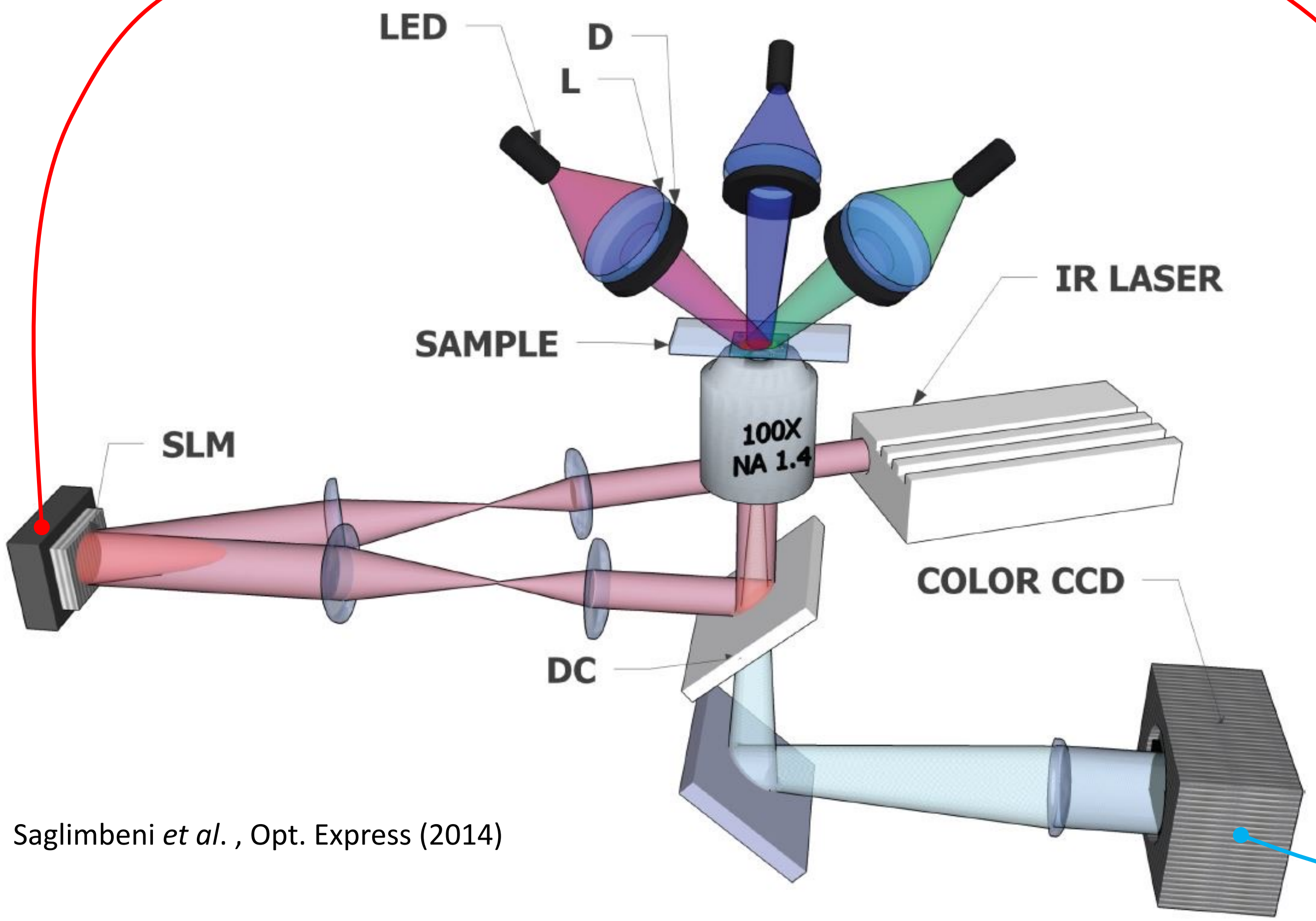

Di Leonardo *et al.*, Opt. Express (2007)

- Maximize $\sum_m w_m |V_m|$
- All $|V_m|$ are equal




Bianchi *et al.* , Comput. Phys. Commun. (2010)

# Real-time 3D exploration and manipulation




Saglimbeni *et al.* , Opt. Express (2014)

- Framerate: 20 f. p. s.
- Field of view: $56 \times 56 \times 20\ \mu m^3$
- Spatial resolution: $< 1\ \mu m$