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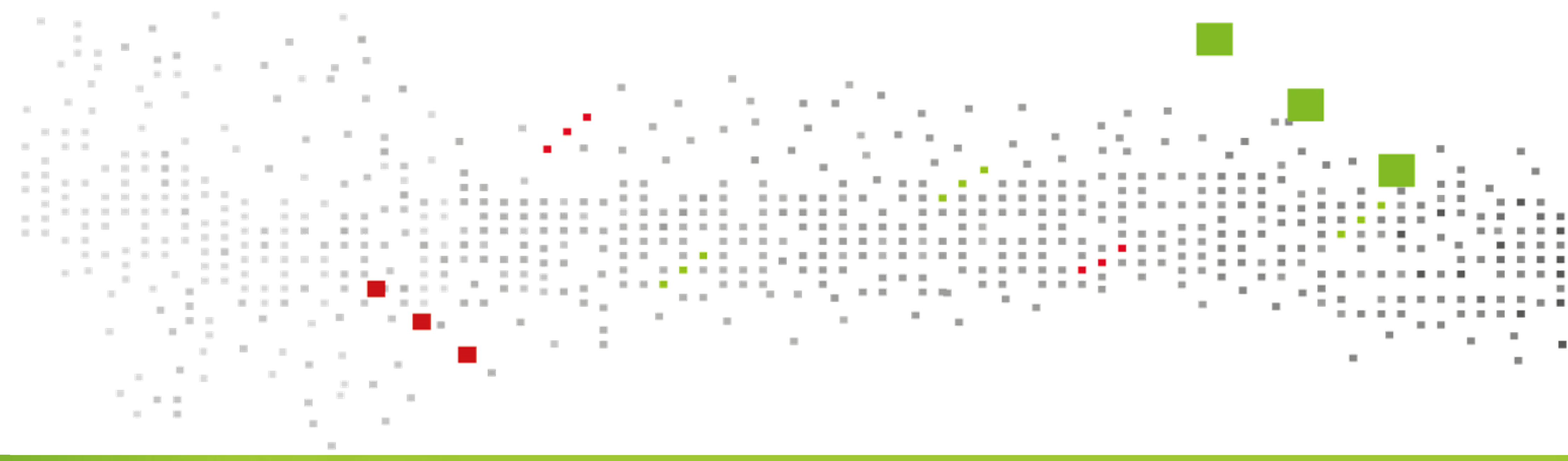
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LENSFREE DIFFRACTIVE TOMOGRAPHY FOR THE IMAGING OF 3D CELL CULTURES

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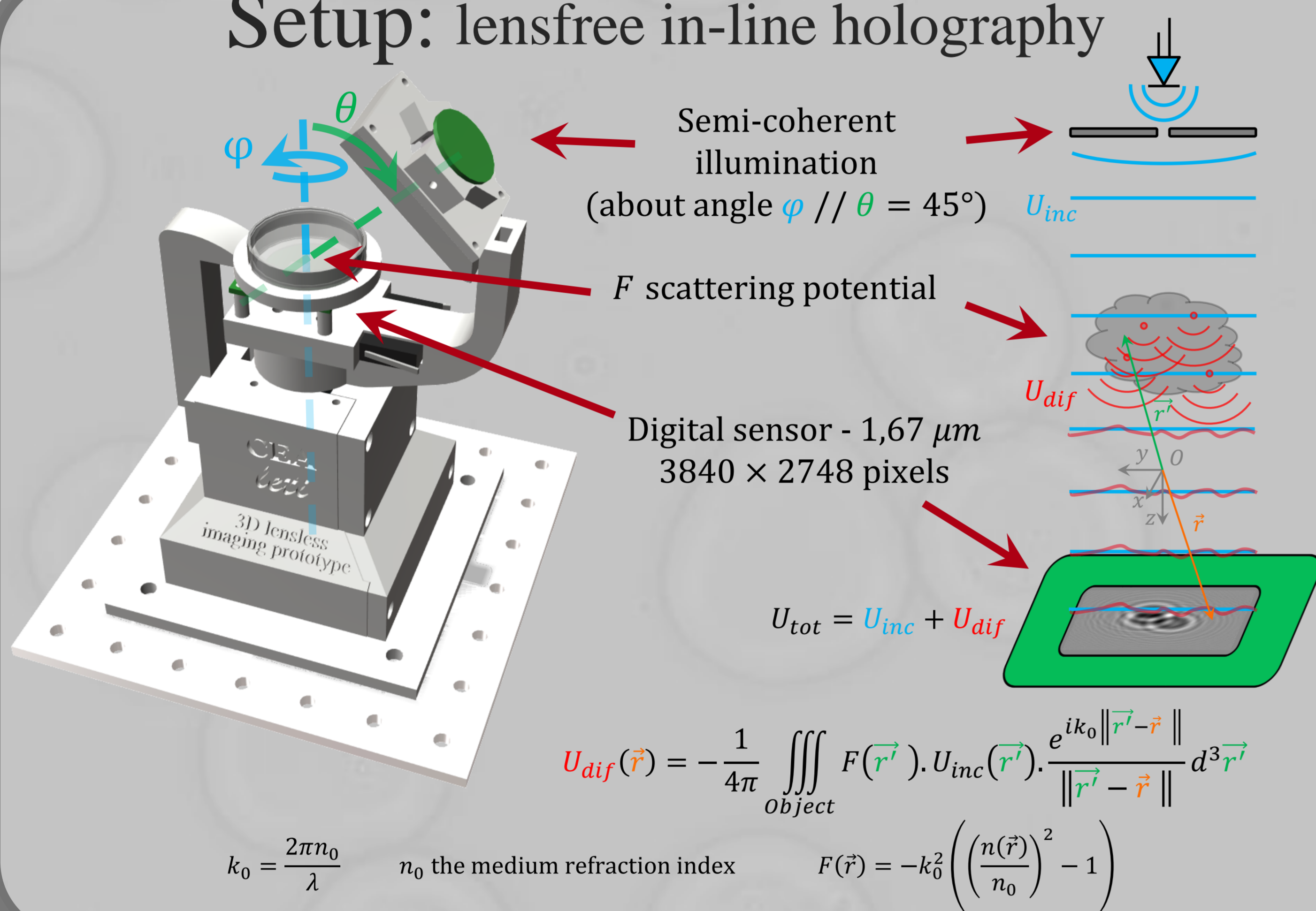
Context

- ✓ Growth of **3D cell culture** in organic gel
 - ✓ Lack of non-invasive imaging
 - ✓ Difficult to get acquisitions of large volumes
- ✓ Rise of **lensfree imaging** for 2D cell cultures
 - ✓ Cheap, robust and easy to implement
 - ✓ Label free and time lapse microscopy

Objectives

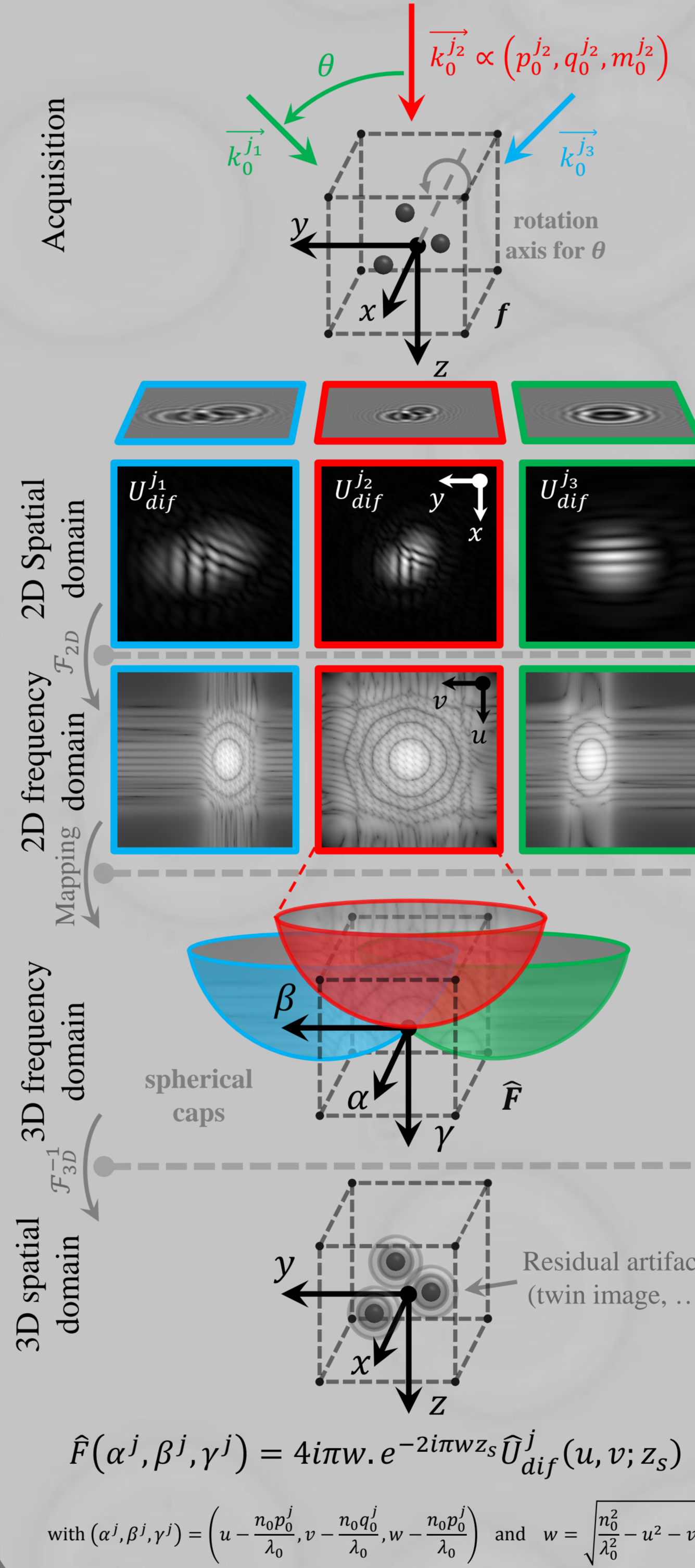
- Apply **lensfree microscopy** to 3D cell culture
 - Experimental prototype (first data on biological culture)
 - Proof of concept (first algorithms for 3D reconstruction)
- **Operational device**
 - Robust to incubator
 - Suited to living samples

Setup: lensfree in-line holography



Processing

3D Fourier mapping



Phase retrieval

Object modelled by a 2D transmission plane: $t_{2D} = 1 + \delta t$

$$U_{tot} = U_{inc} + U_{dif}$$

with $\begin{cases} U_{inc} = e^{i\vec{k}_0 \cdot \vec{r}} \\ U_{dif} = \delta t * h_{z, k_0} \end{cases}$ and $h_{z, k_0} = \frac{z}{i\lambda} \cdot \frac{e^{ik_0 \|\vec{r}'\|}}{\|\vec{r}'\|^2}$

$|U_{tot}|^2$ data $\xrightarrow{h_{-z, -k_0}}$ Simple back propagation

Lack of phase in the data:

- Introduction of a phase ramp to take into account the tilted wavefront
- Twin-image in the data inversion

Solution: inverse problem

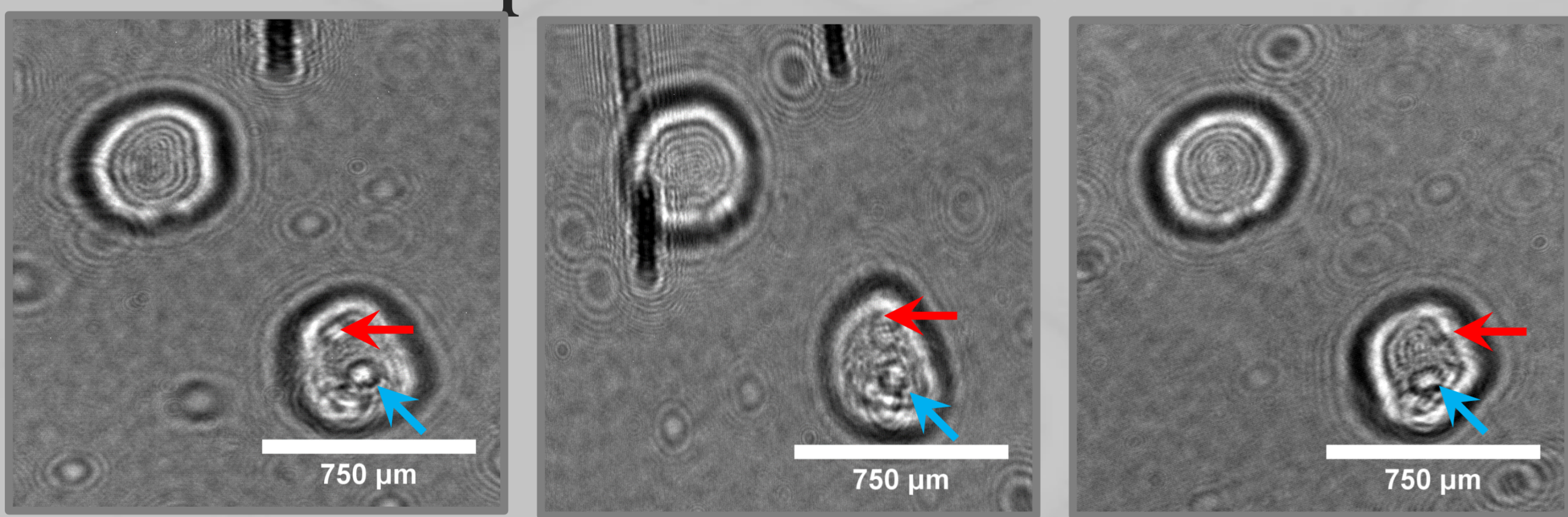
- l_1 -norm minimization: sparse objects
- TV minimization: sparse gradient
- $\Re(\delta t) < 0$: non-emissive objects

$$\delta t_0 = \min_{\Re(\delta t) < 0} \delta t \left(\| |data| - |U_{inc} + \delta t * h_{z, k_0}| \|^2 \dots + \mu_{l_1} \|\delta t\|_{L_1} + \mu_{TV} \|\nabla(\delta t)\|_{L_1} \right)$$

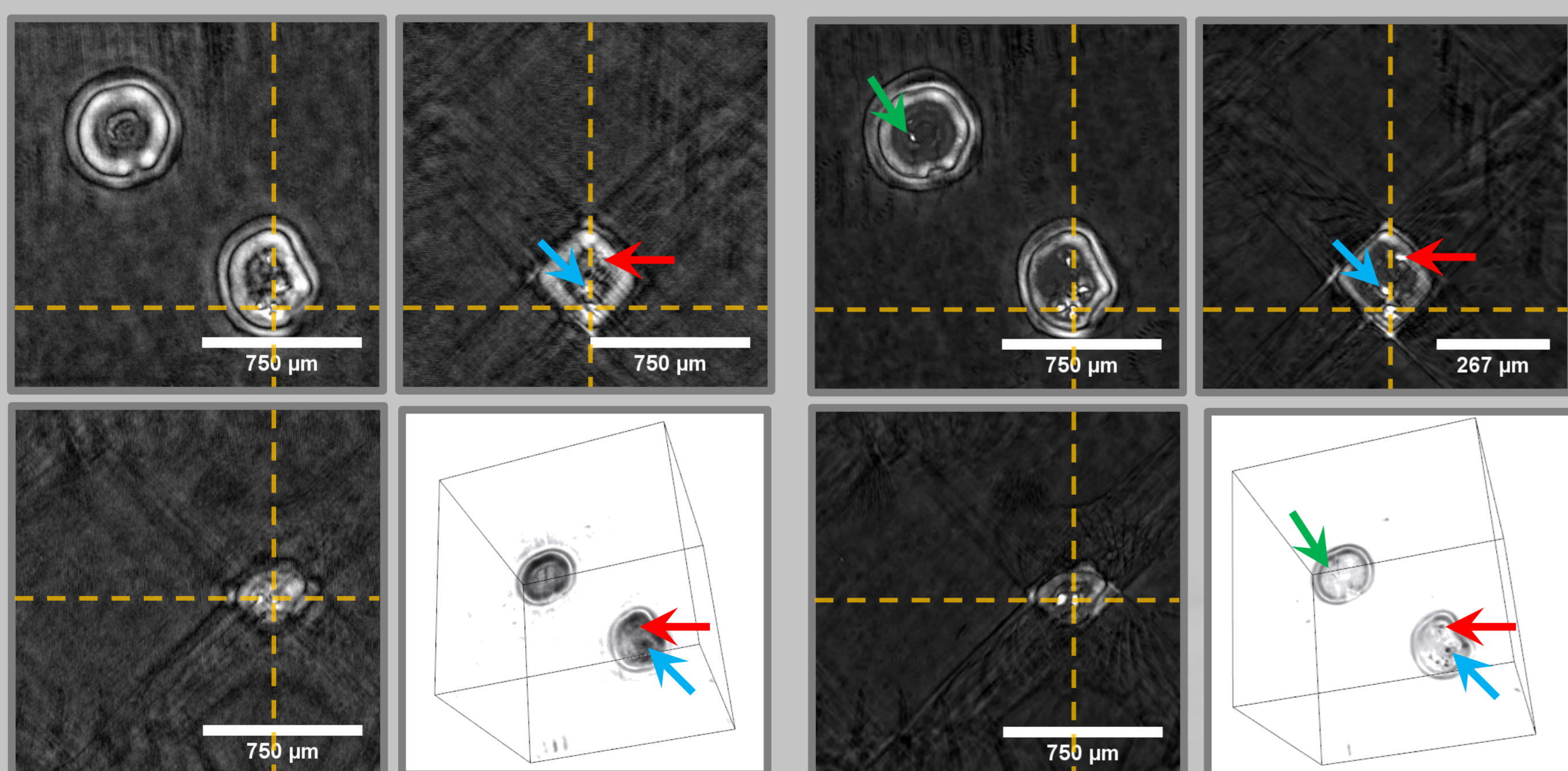
Retrieved phase

$t_{2D} = 1 + \delta t_0$

Acquisitions & results



Matrigel® capsules data $\begin{cases} \varphi = 0^\circ, 84.6^\circ, 169.2^\circ \\ \lambda = 630 \text{ nm} \end{cases}$ The arrows point on special features



Reconstruction of $512^3 \times 3.34^3 \mu\text{m}^3 = 5\text{mm}^3$ volumes without/with phase retrieval on the 2D dataset. 31 angles $\varphi = [0^\circ: 9.4^\circ: 282^\circ]$, $\theta = 45^\circ$. Cell-sized beads can be resolved both on xy -plane and z -axis.

Conclusions

- ✓ Working prototype with 3D biological samples acquisitions
 - ✓ 2D slantwise phase retrieval on real data acquisitions
 - ✓ First 3D reconstructions on several mm^3 volumes
-
- ## Perspectives
- Incubator-proof prototype for 3D + t acquisitions
 - Improve data alignment
 - Inverse problem algorithms on the 3D volume

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