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Background

Cell-generated forces

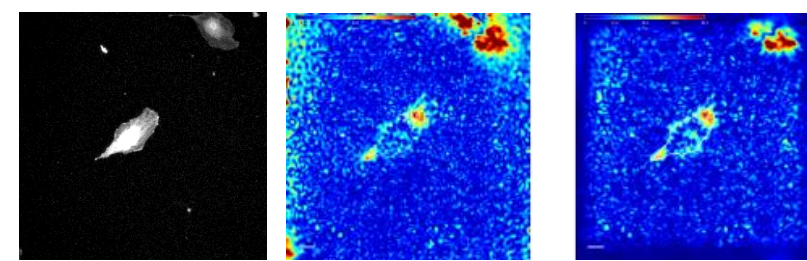
- Regulate cell processes: migration & embryonic development
- Exuberant forces linked to pathological conditions e.g. cancer & CCM

Development of a multi-system generalized 2.5D TFM

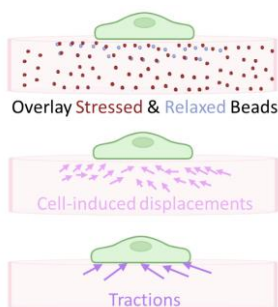
- Assumption-free
- Physics based regularization (PBIM)
- Compatible with complex geometries

Assumption violations

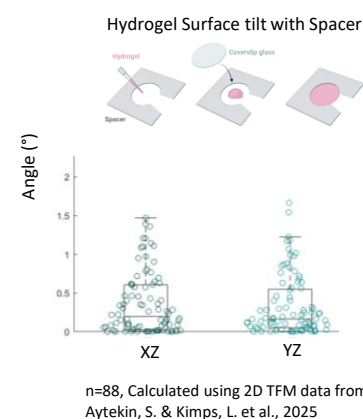
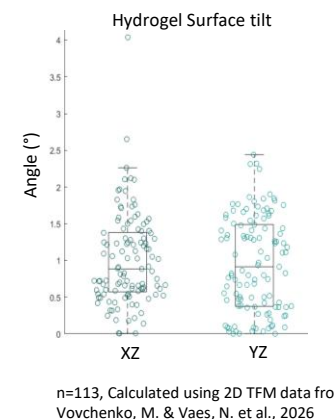
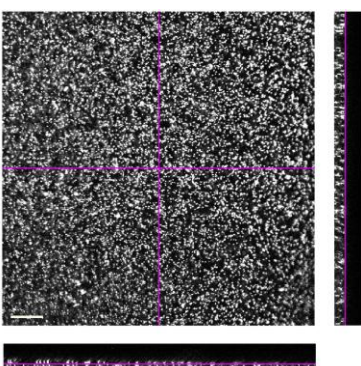
- High cell seeding density
→ Other cells present in FOV
- Hydrogel tilt
→ 0-2,5 degrees tilt
→ spacer reduces tilt
- Complex hydrogel geometries



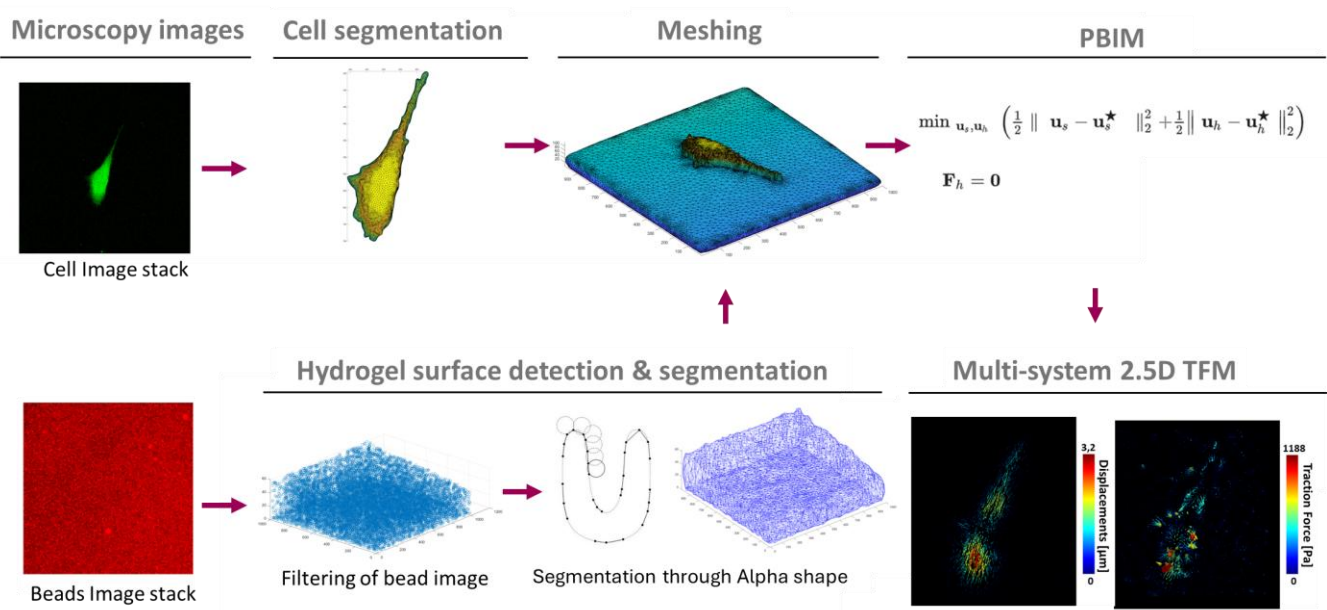
Traction Force Microscopy (TFM)



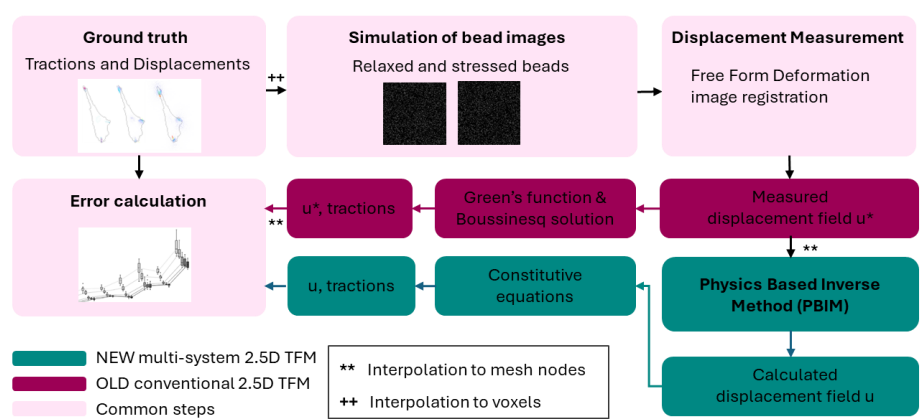
- Cell-induced displacements: fiducial marker tracking
- Traction recovery: Green's function & Boussinesq solution
→ Assumption semi-finite half space
⚡ Assumption often not valid experimentally
→ Tikhonov regularization
⚡ Manual process without clear guidelines



Methods



In Silico Validation



Error Calculation

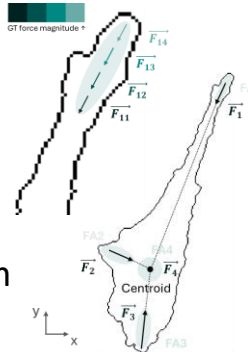
- Dice score
- Tilt angle difference
- Traction Correlation
- Total force error
- Max traction error
- Traction vector angle error

Ground Truth Beads

- Varying bead densities 0.005, 0.01, 0.03, 0.05, **0.07** beads/µm³
- Point spread function
→ Microscopy noise

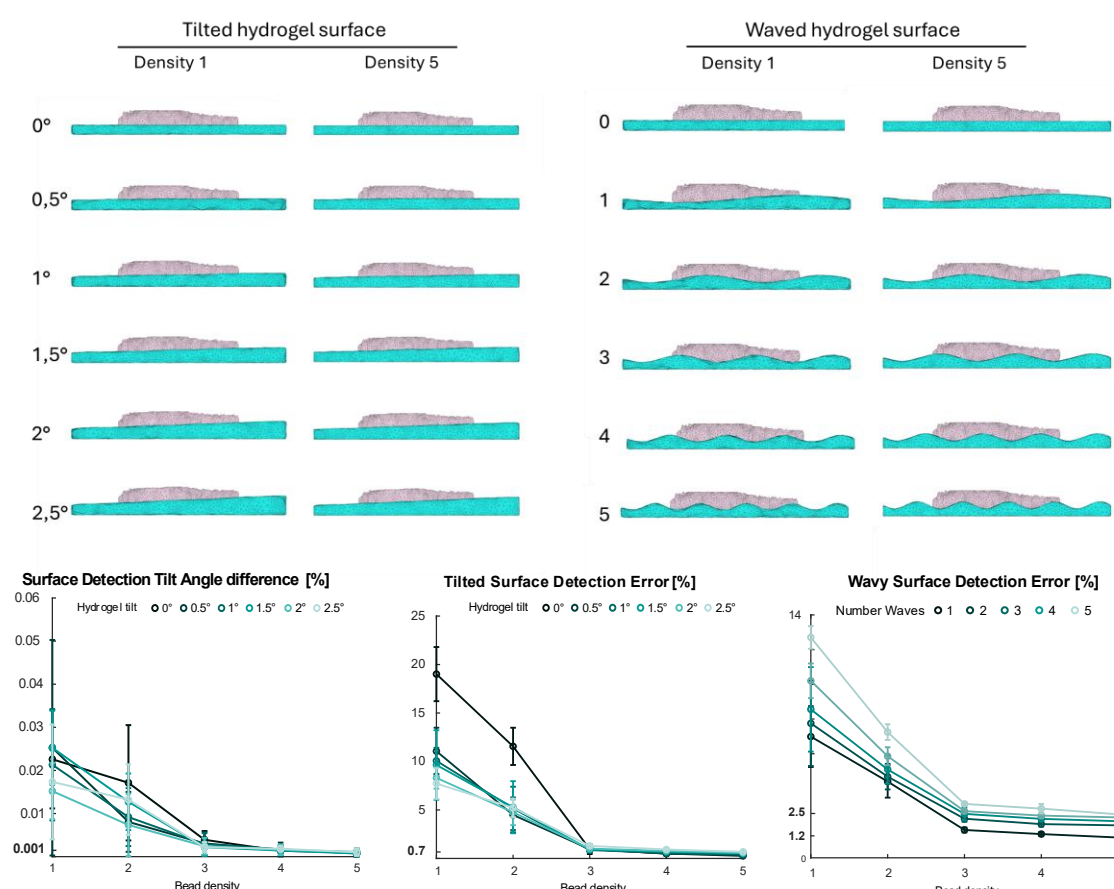
Ground Truth Force Simulation

- Ellipsoid FA
- Force gradient
- Balance of forces & momentum
- Total force of 250 nN



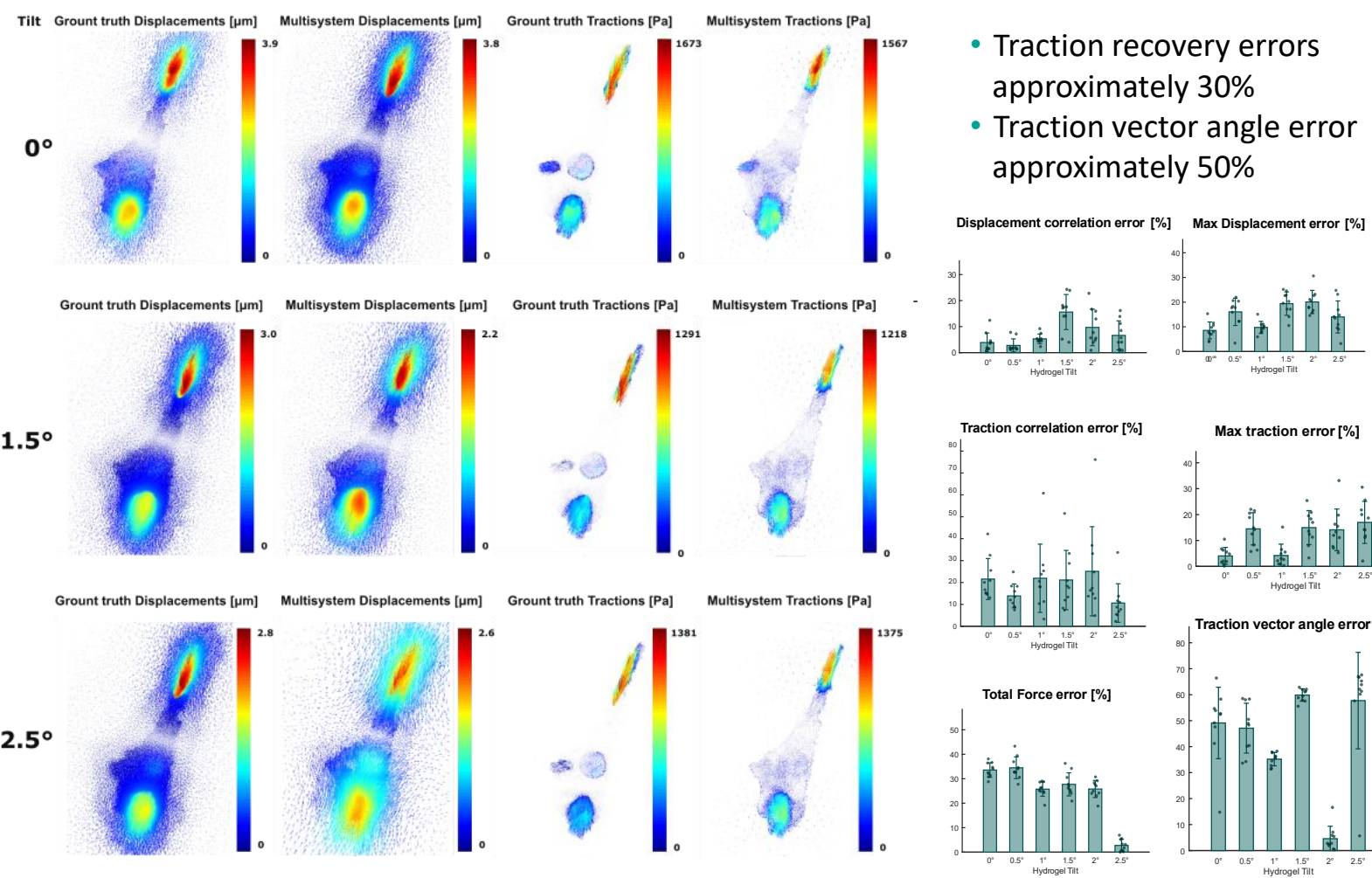
Results

In Silico Validation for Surface Detection

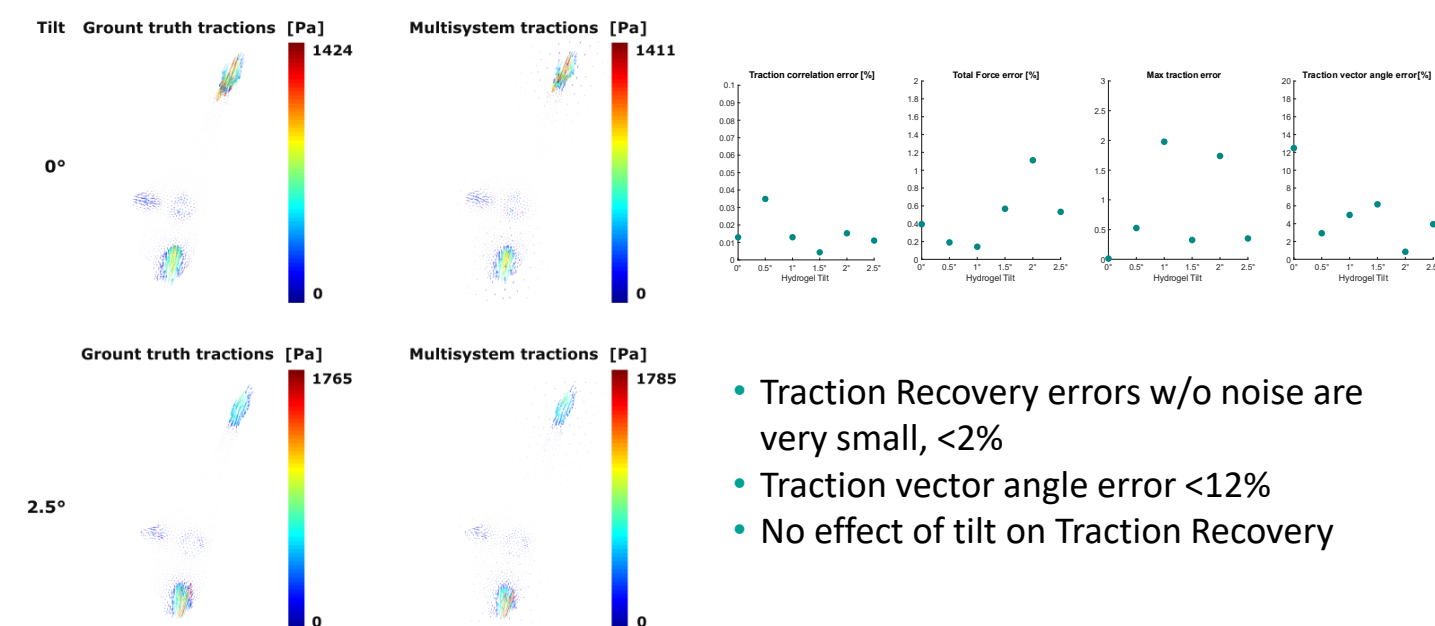


- Error tilted hydrogel <0,7% for in vitro-like bead density (0.07 beads/µm³)
- Error wavy hydrogels 1,2-2,5% for in vitro-like bead density

In Silico Validation for Traction recovery with noise - Tilted Hydrogels

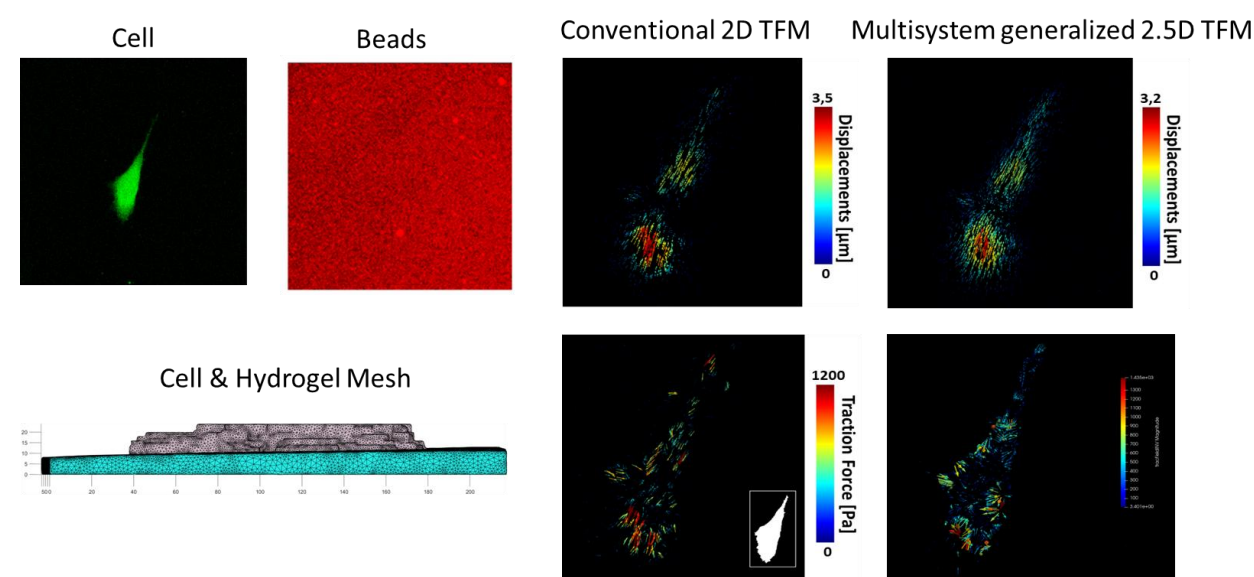


In Silico Validation for Traction recovery w/o noise - Tilted Hydrogels



- Traction Recovery errors w/o noise are very small, <2%
- Traction vector angle error <12%
- No effect of tilt on Traction Recovery

Multisystem generalized 2.5D TFM of real cells



CONCLUSION

- Development multisystem generalized 2.5D TFM
→ Allows for 2.5D TFM without constraints
- Setup of advanced in silico validation framework
- FUTURE: integration with TFMLAB
- Accurate surface detection
- Excellent performance in simulations w/o noise
- Good traction recovery for microscopy-like noise
- FUTURE: In silico comparison with Green's function method

ACKNOWLEDGEMENTS

The author would like to thank KU Leuven internal funding (iBOF/21/083) and FWO postdoc fellowship JBF (1259223N) for providing financial support to this project.

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