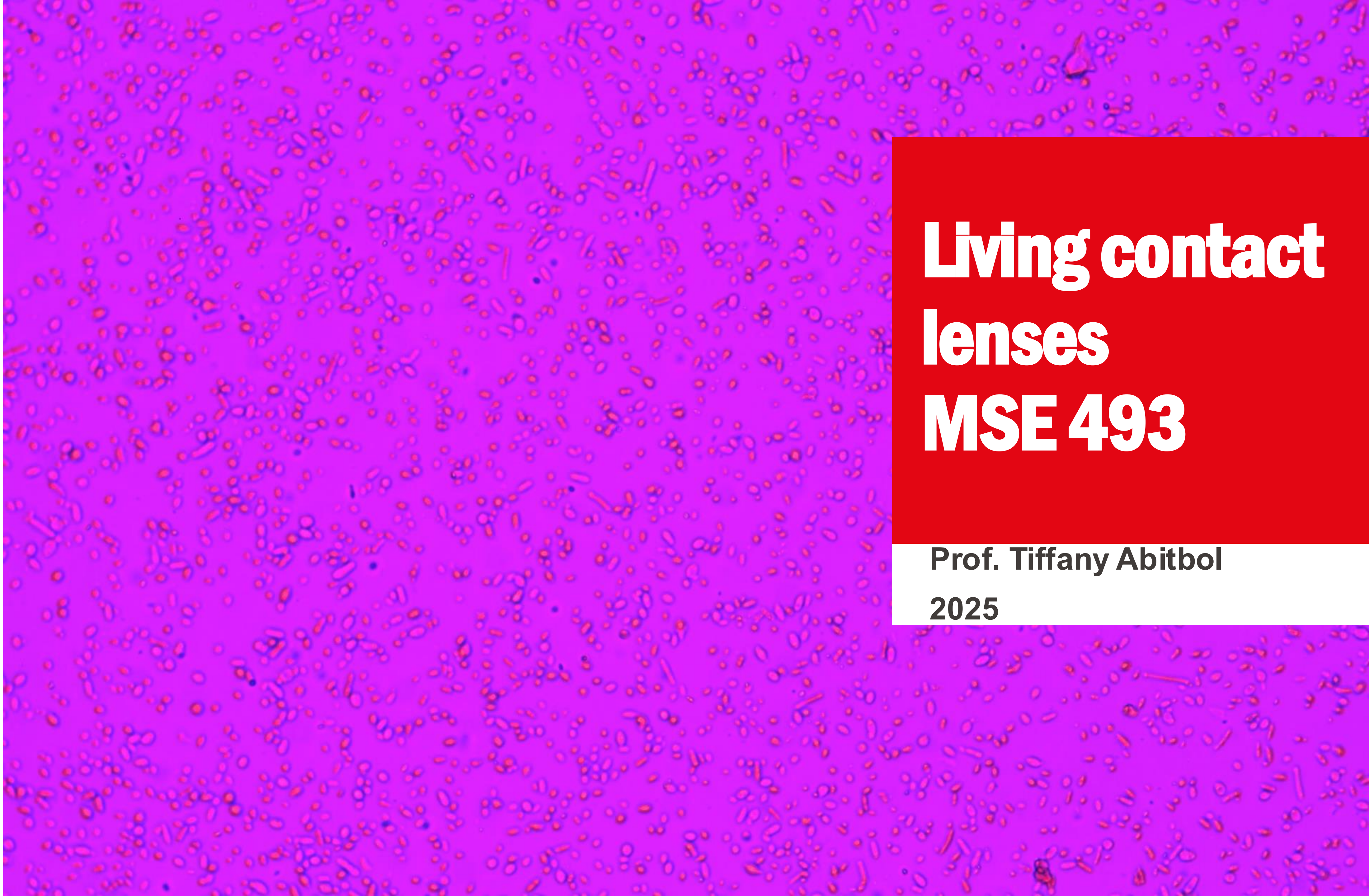
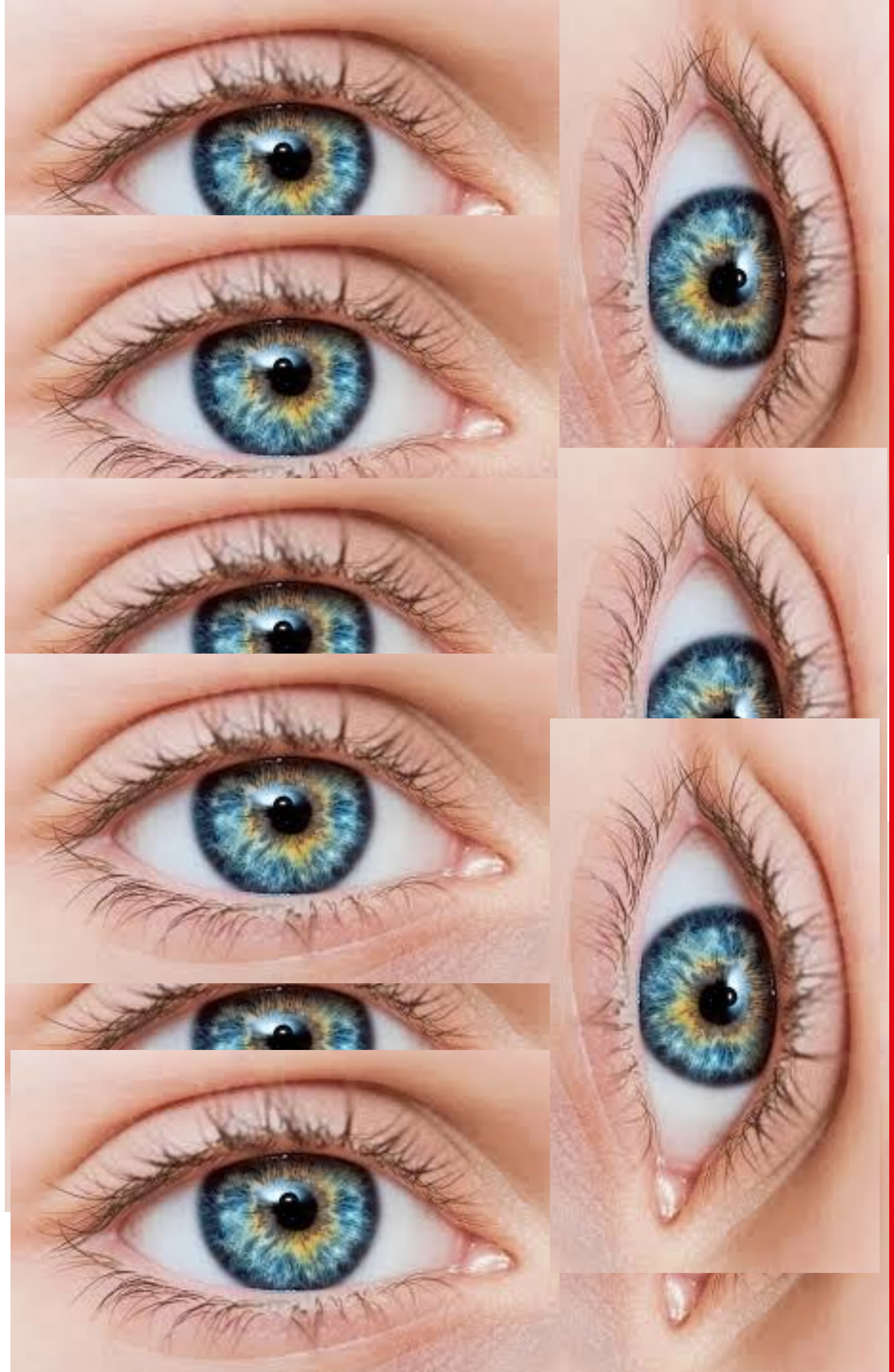


Living contact lenses
MSE 493

Prof. Tiffany Abitbol

2025

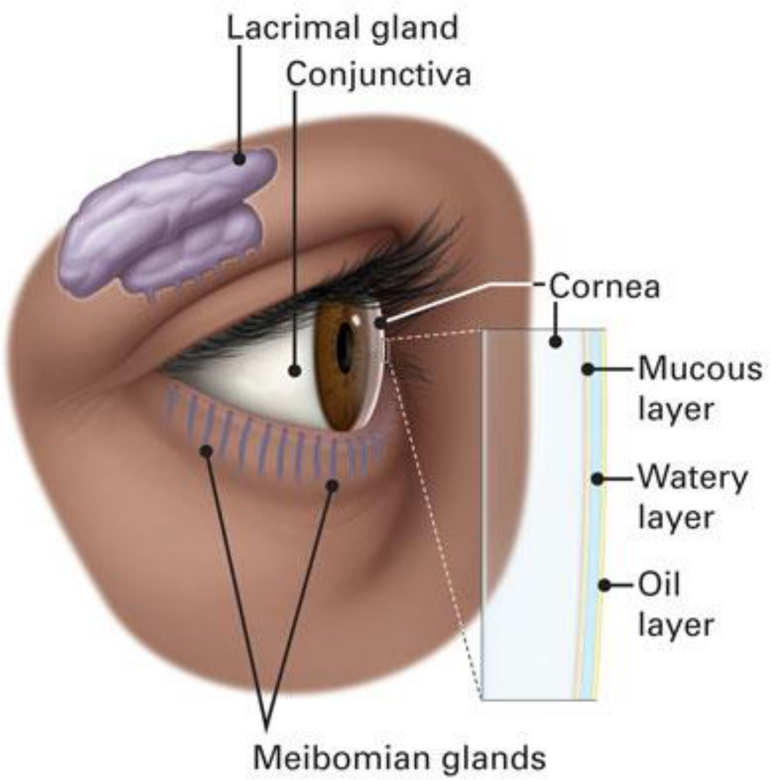
EPFL



Background

The eye, corrective lenses, dry eye

Anatomy of the eye



- Cornea is a transparent, dome shaped surface that the front of the eye, protein the iris and pupil, made of collagen and water mostly, no blood vessels to stay clear!

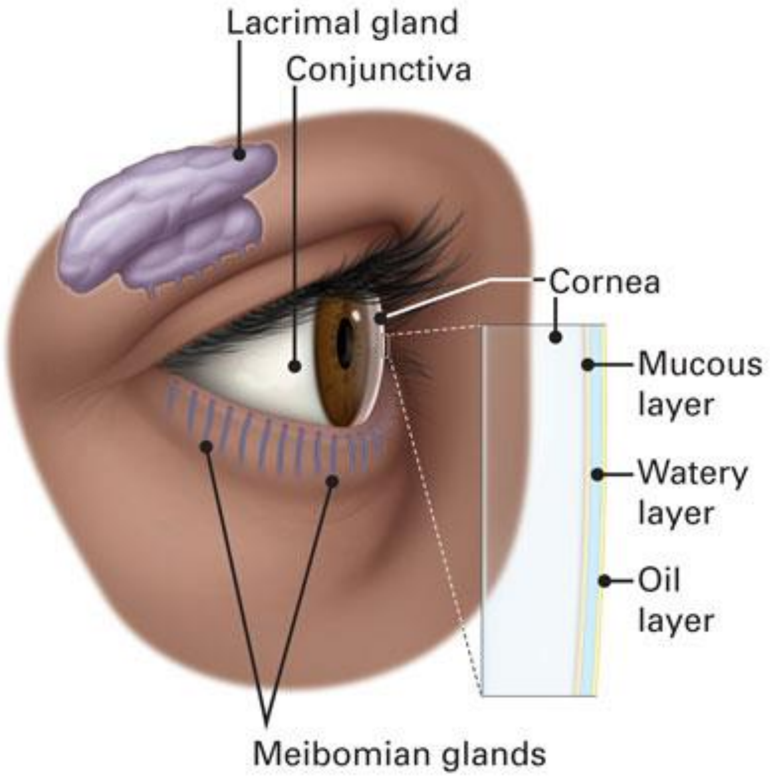
- Whites of eye and inner eyelid are covered by a clear membrane called a **conjunctiva**

- Tear film covers cornea and conjunctiva and consists of 3 layers
  - Mucous layer (inner layer) – produced by goblet cells
  - Watery layer (middle layer) – secreted by lacrimal glands
  - Lipid layer – produced by meibomian

- Tears drain from eyes from the tear duct

Anatomy of the eye

Function of tear films



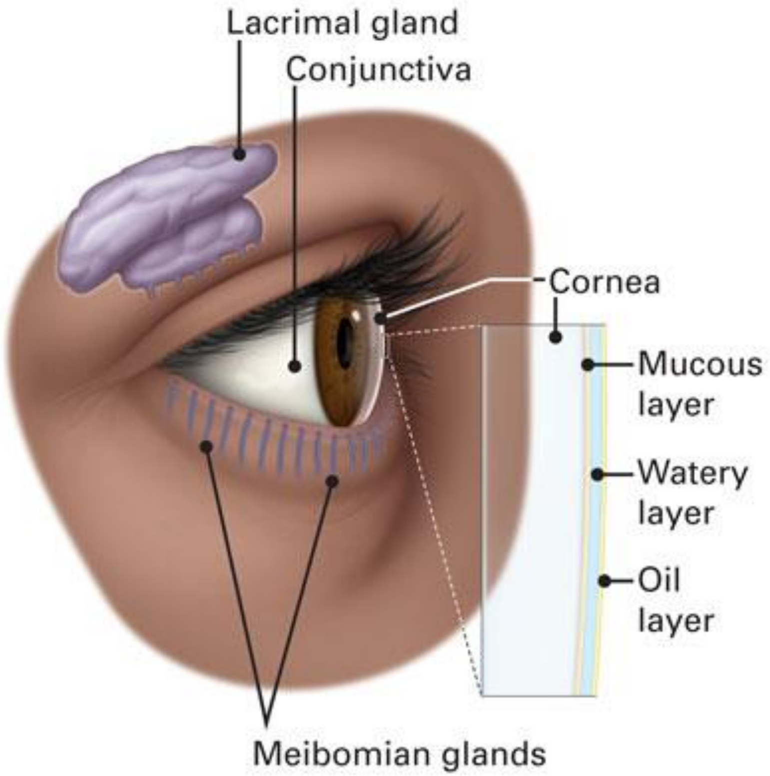
- **Mucous layer** (inner layer) – helps tears stick evenly to cornea, for a smooth optical surface
- **Watery layer** (middle layer) – provides moisture, oxygen, nutrients; flushes out debris
- **Lipid layer** – prevents evaporation of tears

- Main functions of tear film: **lubrication** (reduces friction when blinking); **protection** (traps dust & removes microorganisms); **nutrition and waste** removal

- Tears drain from eyes from the tear duct

Anatomy of the eye

Some key points



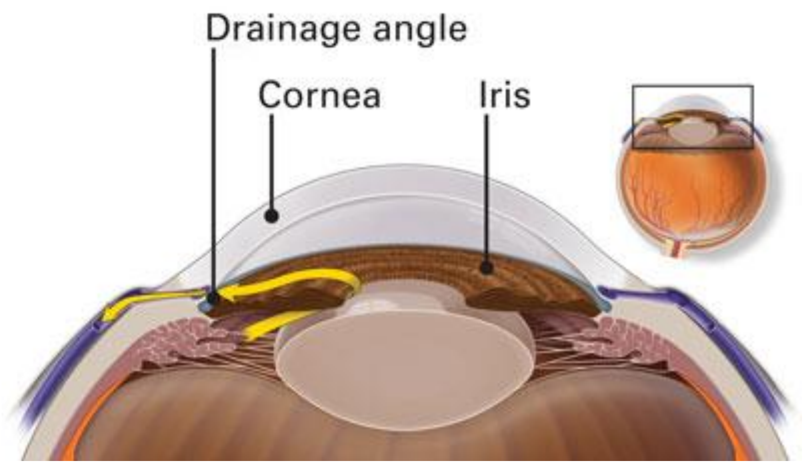
- *Tears* are critical! Lubrication, optical clarity requires smooth refractive surface, protection, cleaning, & nutrition for ***cornea that has no blood vessels***

- Tears consist of oils, water, mucous, and protective molecules

- Why blink? Spread tear film, clean surface, prevent drying, protect eye

Anatomy of the eye

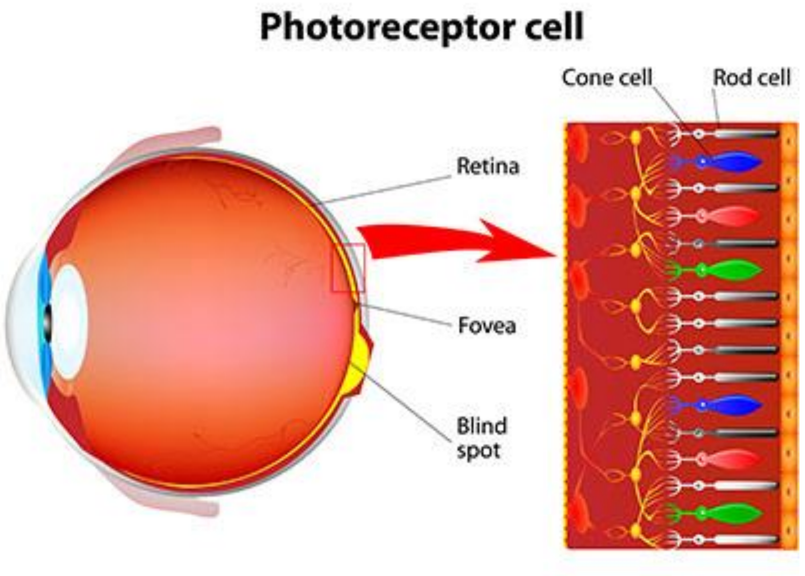
Anatomy of the eye – front of the eye



- ***Cornea***: Light first enters the eye through the cornea, the transparent, dome-shaped outer surface that helps focus incoming light.
- ***Anterior Chamber***: Just behind the cornea is the anterior chamber, filled with a clear fluid called aqueous humor. This fluid helps maintain constant eye pressure by balancing its production and drainage.
- ***Iris and Pupil***: Behind the anterior chamber lie the iris and pupil. The iris (the colored part of the eye) contains muscles that constrict or dilate to change the size of the pupil—the central opening that controls how much light enters the eye.
- ***Lens***: Directly behind the pupil is the lens, which changes shape to fine-tune focus, directing light precisely onto the retina at the back of the eye.

Anatomy of the eye

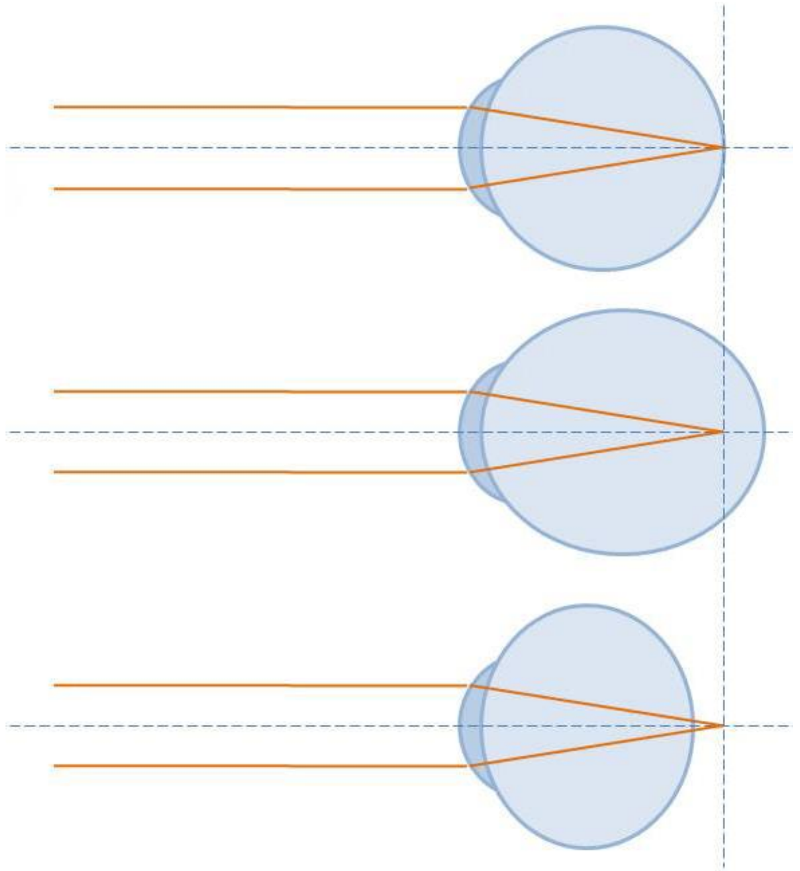
Anatomy of the eye – back of the eye



[Anatomy of the eye]

- The ***vitreous cavity*** is the large space between the lens and back of eye, filled with a cleat, jelly-like substance called the vitreous humor
- Light entering the eye is focused by the cornea and lens, then passes through the vitreous cavity to reach the ***retina***
- The ***retina*** is a thin, light-sensitive layer that lines the inner back surface of the eye
- ***Photoreceptor cells*** in the retina convert light signals into electrical impulses, which are send to the brain through the optic nerve
- There are 2 main types of photoreceptor cells:
  - Rods – detect black, white, and shades of gray; important for night and peripheral vision
  - Cones – detect color and allow for sharp central vision in bright light.

Eyesight



Correctly focused

Focused in front of retina
Near-sighted (light refracted too much)

Focal point behind retina
Far-sighted (light refracted too little)

Refractive error

OCTOBER 1, 2024 | 7 MIN READ

The Nearsightedness Epidemic Has Become a Global Health Issue

Myopia is projected to affect half of the world's population by 2050. A new report says it needs to be countered by classifying it as a disease and upping children's outdoor time

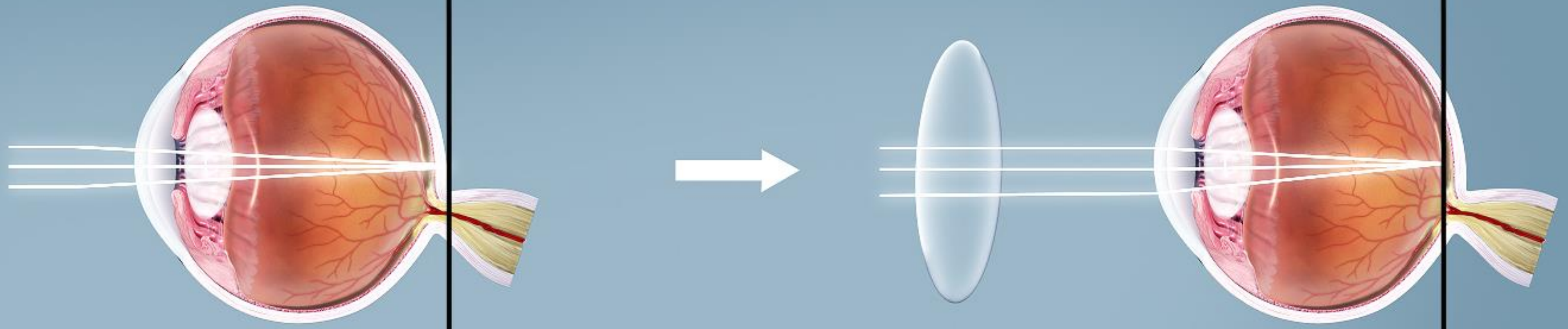
BY GARY STIX

Why? Too much time spent indoors
Outdoor light has a more varied "visual diet"

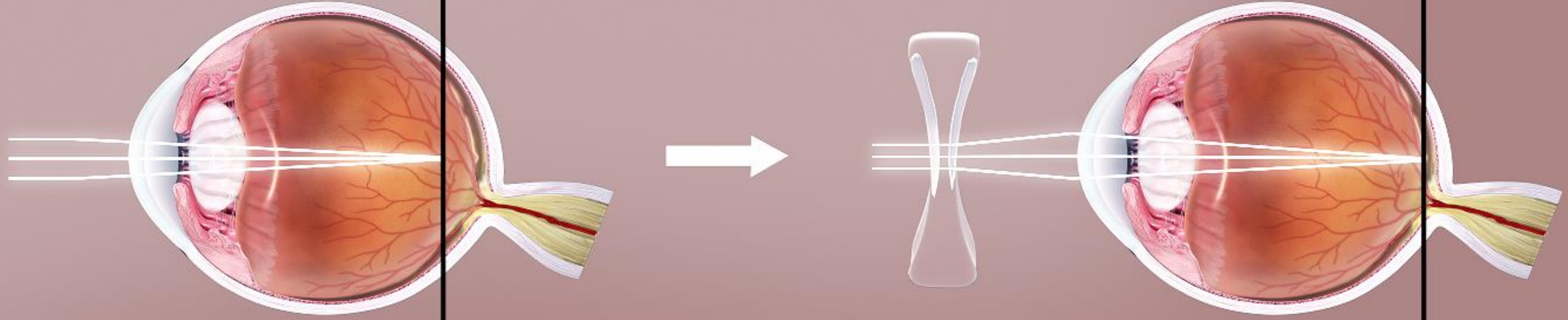
https://www.scientificamerican.com/article/nearsightedness-has-become-a-global-health-issue/

Corrective lenses

Far-sighted



Near-sighted



[Corrective lenses]

Dry eyes

- Not enough tears produced
- Tears evaporate too quickly

Symptoms

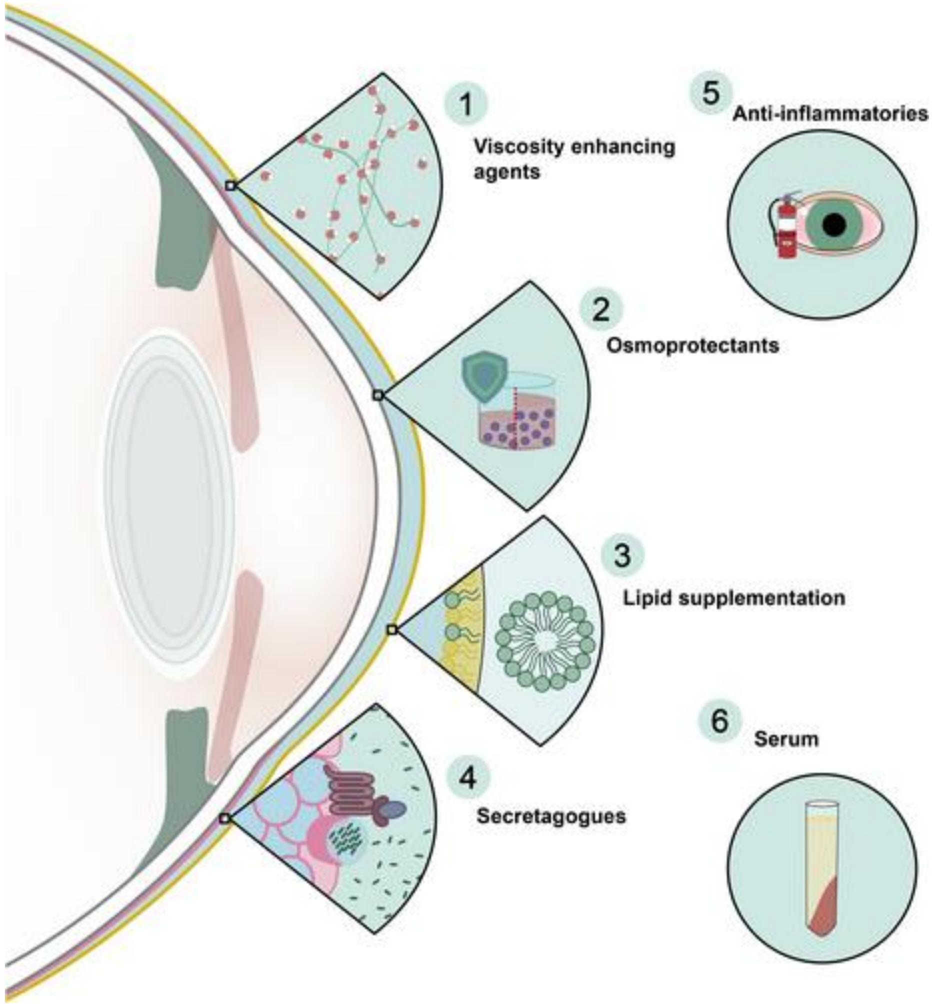
- Dryness, redness, discharge
- Blurred vision
- Tear film instability
- Increased risk to damage the ocular surface

Causes

- Age
- Various deficiencies/illnesses
- Side effects of medications
- Laser surgery
- Contact lenses
- Screen use (we blink less)

https://onlinelibrary.wiley.com/doi/full/10.1111/aos.15675

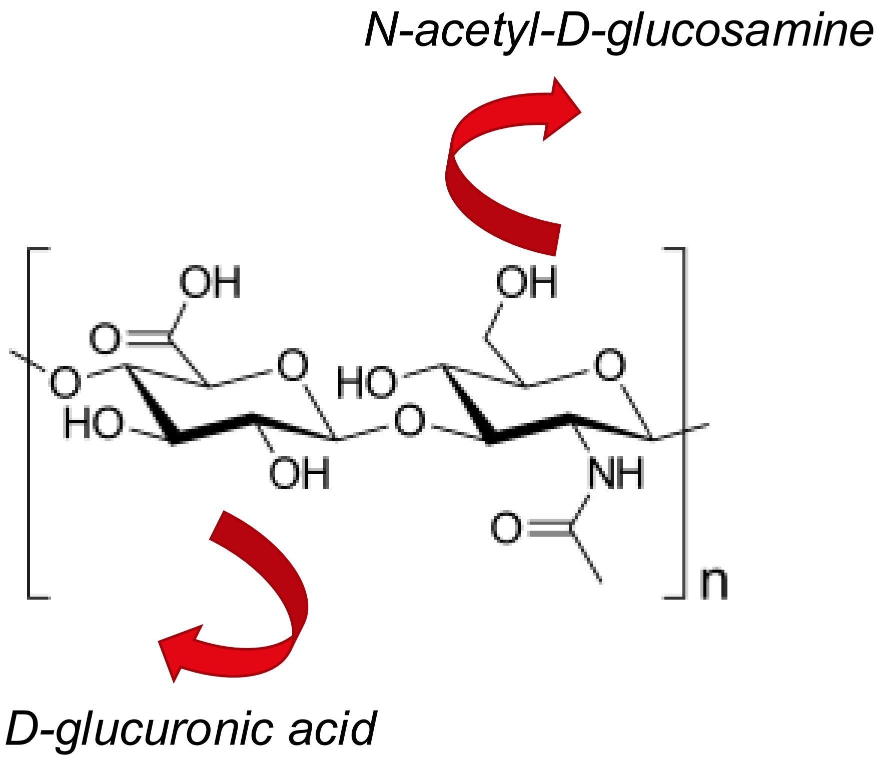
Dry eyes – topical treatments



- Natural and synthetic polymers and emollients
- Benefits to ocular surface:
  - Improved viscosity
  - Improved surface adhesion
  - Improved tear-film distribution, lubrication, retention time
  - Decreased evaporation

https://onlinelibrary.wiley.com/doi/full/10.1111/aos.15675

Hyaluronic acid



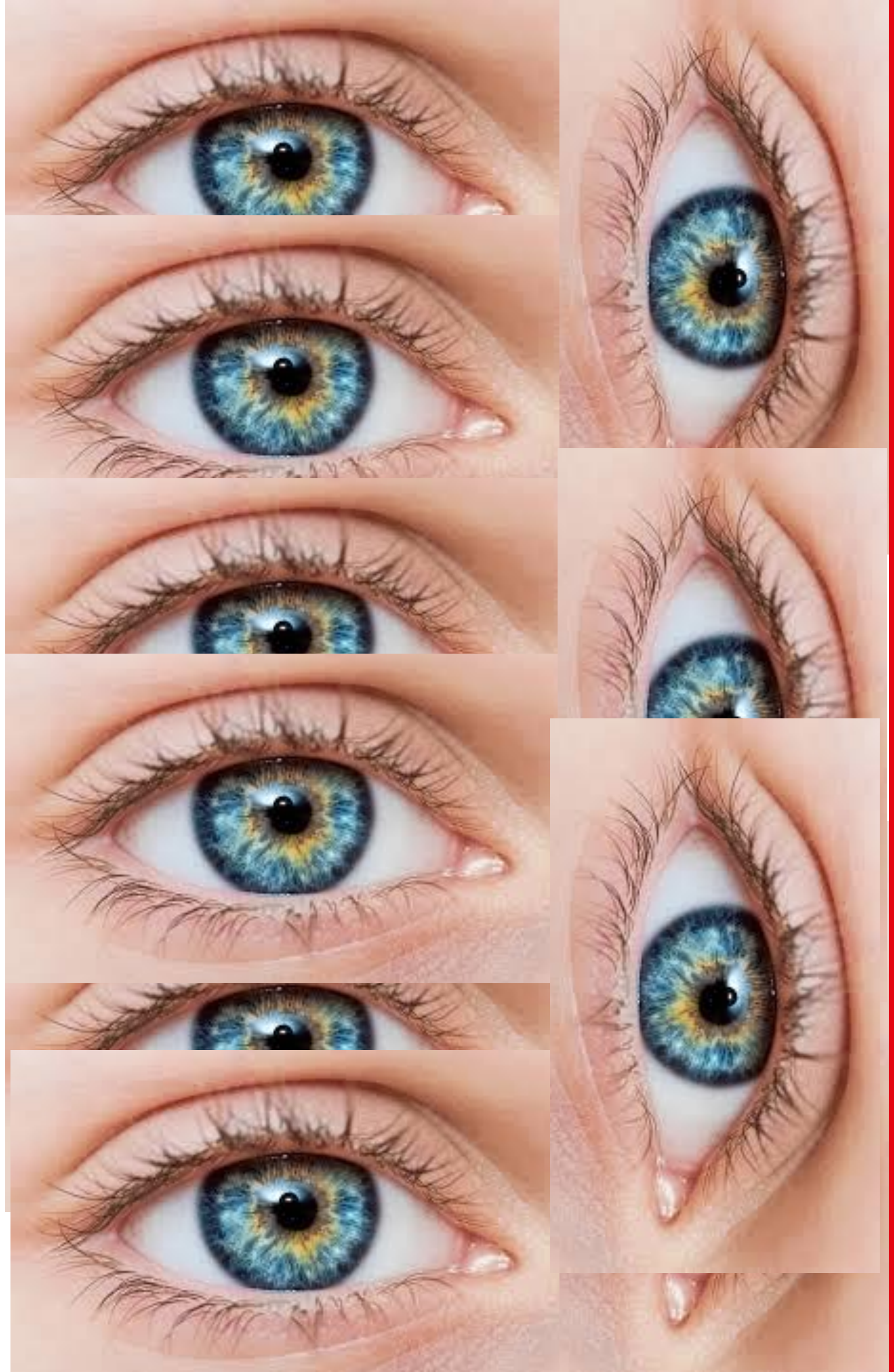
- Anionic, non sulfated, glycosaminoglycan
- Distributed widely throughout connective, epithelial, and neural tissues
- Used medically to treat osteoarthritis of the knee, wound healing, as a cosmetic filler, and to treat dry eye
- Described as "**goo**" molecule until late 1970s – ubiquitous polymer in ECM
- Role in lubrication and tissue repair, etc.,

https://onlinelibrary.wiley.com/doi/full/10.1111/aos.15675

Hyaluronic acid for dry eye

- Naturally occurring (including in vitreous humor, cornea, and tear film)
- Varying molecular weights
- Properties for dry eye treatment: water retention and lubrication, reduces shear force on ocular surface, provides anti-inflammatory and antioxidant effects
- HA drops are often used as a control when assessing the safety and efficacy of new dry eye treatment options due to long history of safety and efficacy in opthamology

https://onlinelibrary.wiley.com/doi/full/10.1111/aos.15675
https://www.nature.com/articles/s41598-022-21330-0



Self-lubricating, Living Contact Lenses

Onto the paper…

ADVANCED MATERIALS

JOURNAL METRICS >

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- 2023 IF = 27.4
- 2023 acceptance rate = 21%
- 2023 submission to first decision = 14 days
- 2023 submission to acceptance = 74 days

RESEARCH ARTICLE
Editor's Choice
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Self-Lubricating, Living Contact Lenses

*María Puertas-Bartolomé, Izabook Gutiérrez-Urrutia, Lara Luana Teruel-Enrico, Cao Nguyen Duong, Krupansh Desai, Sara Trujillo, Christoph Wittmann, and Aránzazu del Campo**

2024
Cited 26 times

The increasing prevalence of dry eye syndrome in aging and digital societies compromises long-term contact lens (CL) wear and forces users to regular eye drop instillation to alleviate discomfort. Here a novel approach with the potential to improve and extend the lubrication properties of CLs is presented. This is achieved by embedding lubricant-secreting biofactories within the CL material. The self-replenishable reservoirs autonomously produce and release hyaluronic acid (HA), a natural lubrication and wetting agent, long term. The hydrogel matrix regulates the growth of the biofactories and the HA production, and allows the diffusion of nutrients and HA for at least 3 weeks. The continuous release of HA sustainably reduces the friction coefficient of the CL surface. A self-lubricating CL prototype is presented, where the functional biofactories are contained in a functional ring at the lens periphery, outside of the vision area. The device is cytocompatible and fulfils physicochemical requirements of commercial CLs. The fabrication process is compatible with current manufacturing processes of CLs for vision correction. It is envisioned that the durable-by-design approach in living CL could enable long-term wear comfort for CL users and minimize the need for lubricating eye drops.

management, digital medicine, and communication.[1] The transfer of this vision into widely accepted user products demands CL materials with the highest and most durable comfort.[2] In soft CLs, user comfort depends on the capacity of the CL material to retain moisture, provide high lubrication, and avoid adsorption of tear fluid molecules on the CL surface, among other factors.[3] Wettability and water retention in CLs have been significantly improved in commercial CLs by grafting hydrophilic polymer layers, surfactants, or lipids on the surface of the lens (e.g., MoistureSeal, Aquaform or Hydraluxe technologies, among others).[4] Alternative academic approaches have been recently suggested based on embedded electronics[5] or engraved microchannels[6] to transport and retain tear fluid at the eye–lens interface.

RESEARCH ARTICLE
Editor's Choice
ADVANCED MATERIALS
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Self-Lubricating, Living Contact Lenses

*María Puertas-Bartolomé, Izabook Gutiérrez-Urrutia, Lara Luana Teruel-Enrico, Cao Nguyen Duong, Krupansh Desai, Sara Trujillo, Christoph Wittmann, and Aránzazu del Campo**

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INM Leibniz Institute for New Materials

Saarland University

- Collaboration between research institute and university
- Two university departments: Chemistry and Systems Biotechnology
- Prof (del Campo) is doubly affiliated

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Dynamic Biomaterials

See! Research is fun!

Prof. Dr. Aránzazu del Campo

Head of Dynamic Biomaterials
Telefon: +49 (0)681-9300-510
E-mail: Aranzazu.DelCampo@leibniz-inm.de

More information

We study and orchestrate how synthetic materials interact with living cells. We engineer cell-instructive environments and material-based solutions for zero-waste therapeutic solutions.

Our group develops hydrogel materials with programmed and tunable properties designed to encapsulate and instruct living cells. We study how living cells and inert matter interact and how these interactions can be exploited to direct cellular functions and ultimately result in therapeutic advantages. We cooperate with synthetic biologists, biophysicists, drug developers and clinicians to explore the application potential of our developments, with a focus on new materials for ophthalmic drug delivery. We contribute to INM's competence fields opto-interactive and bio-intelligent materials. Our research addresses biomedical needs.

- Interactions between synthetic materials and living cells
- Why? Therapeutic

Institute CEO; publicly funded

Aránzazu del Campo

FOLGEN

Scientific Director & CEO, INM-Leibniz Institute for New Materials
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Hydrogels for cell encapsul…

TITEL	ZITIERT VON	JAHR
SU-8: a photoresist for high-aspect-ratio and 3D submicron lithography A del Campo, C Greiner Journal of micromechanics and microengineering 17 (6), R81	1107	2007
Advances in colloidal assembly: the design of structure and hierarchy in two and three dimensions N Vogel, M Retsch, CA Fustin, A Del Campo, U Jonas Chemical reviews 115 (13), 6265-6311	856	2015
Contact shape controls adhesion of bioinspired fibrillar surfaces A Del Campo, C Greiner, E Arzt Langmuir 23 (20), 10235-10243	580	2007

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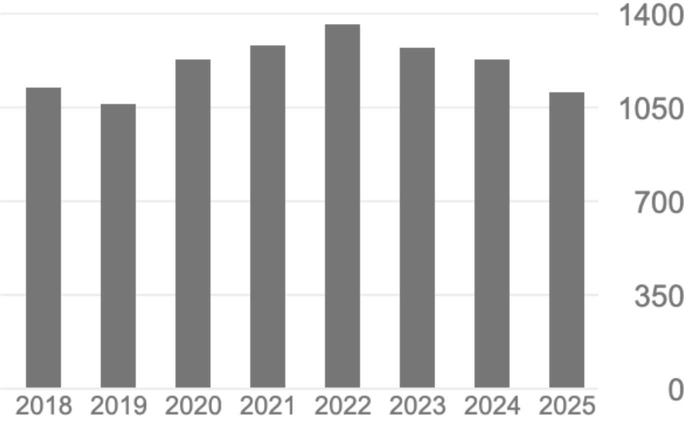
i10-index	150	120



2026

Quantification of collagen matrix deposition in 2D cell cultures: a comparative study of existing assays

Hambardzumyan, Syuzanna | Kasper, Jennifer Y. | Del Campo, Aránzazu

Biomaterials Advances , 2026, 178 214436.
https://www.sciencedirect.com/science/article/pii/S2772950825002638?via%3Dihub

2025

A practical workflow for cytocompatibility assessment of living therapeutic materials

Mekontso Ngaffo, Joelle A. | Farrukh, Usama | Trujillo, Sara | Del Campo, Aránzazu

Biomaterials Advances , 2025, 169 214182.
https://www.sciencedirect.com/science/article/pii/S2772950825000093?via%3Dihub

Segmented, Side-Emitting Hydrogel Optical Fibers for Multimaterial Extrusion Printing

Kafrashian, Zahra | Brück, Stefan | Rogin, Peter | Usama Bin Farrukh, Hafiz Syed | Pearson, Samuel | Del Campo, Aránzazu

Advanced Materials , 2025, 37 (4), 2309166.
https://onlinelibrary.wiley.com/doi/10.1002/adma.202309166

- They already have 2026 paper ?
- Lots of inspiring studies that can be used for your poster inspiration!

Living contact lenses – abstract/introduction

Why even do this study?

- Dry eye syndrome! Oh non! (It’s serious)
- Compromises long term-contact lens wear
- Users require eye drops to alleviate discomfort

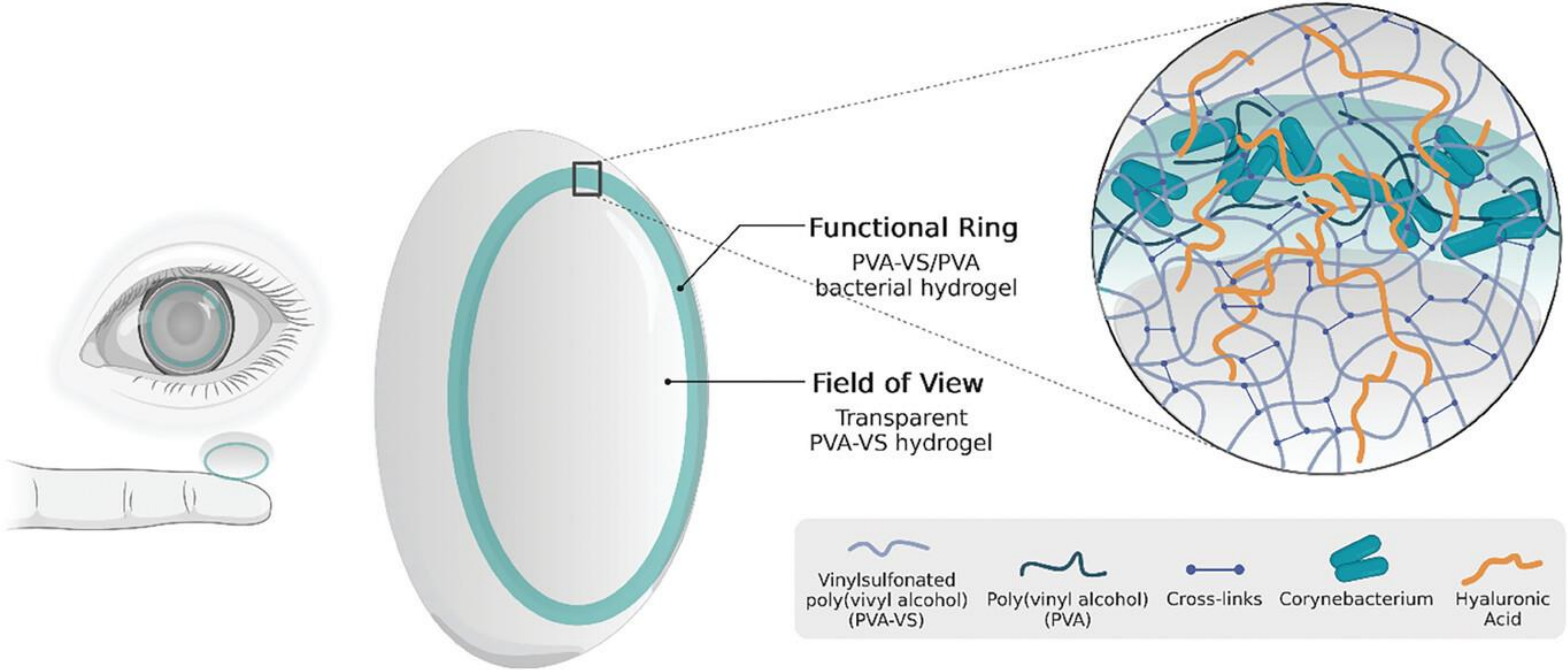
Living contact lenses – abstract/introduction

Hint!
Biofactory = bacteria

So, what did they do?

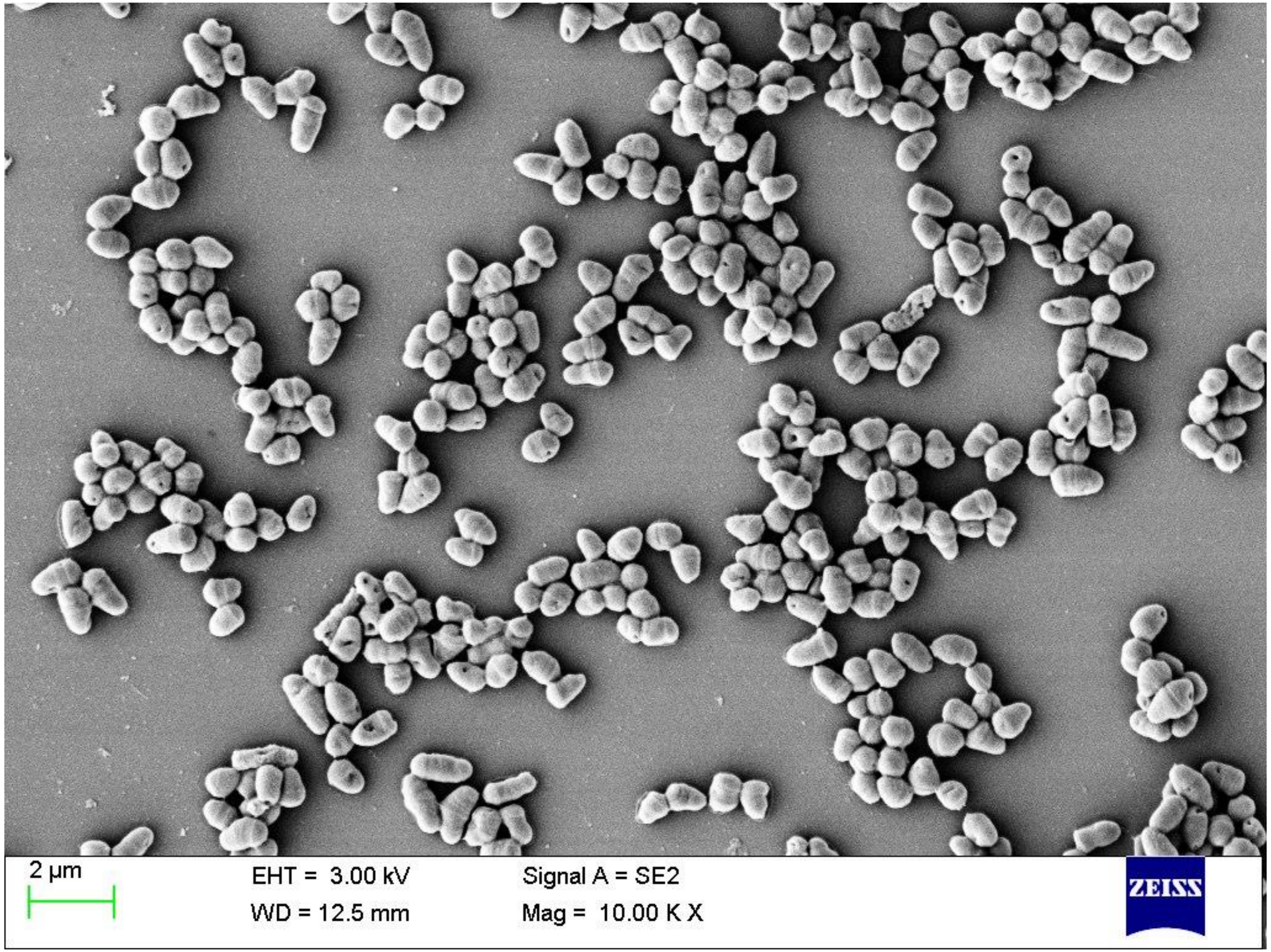
- Embedded a lubricant secreting “biofactory” with the CL
- Self-replenishable reservoirs that autonomously produce and release HA
- Hydrogel matrix of CL regulates the growth of the “biofactories” and HA production, and allows the diffusion of nutrients and HA for at least 3 weeks
- Continuous release of HA reduces the friction coefficient of the CL surface
- Prototype is presented, where the “biofactories” are contained in a functional ring at the lens periphery, outside of the vision area

Living contact lenses – abstract/introduction



Living contact lenses – results

[C. glutamicum](#) [Prospective bacterial and fungal sources of HA 2022](#)



- *Corynebacterium glutamicum*
- Gram-positive
- Rod-shaped
- Used for large scale production of various organic chemicals, such as organic acids, alcohols, amino acids
- No endotoxins
- GRAS

- *C. glutamicum* DSM 20300
- Model for *Corynebacterium mastitidis*, a taxonomically related commensal microbe of the human eye
- Wild-type genetically engineered to secrete HA

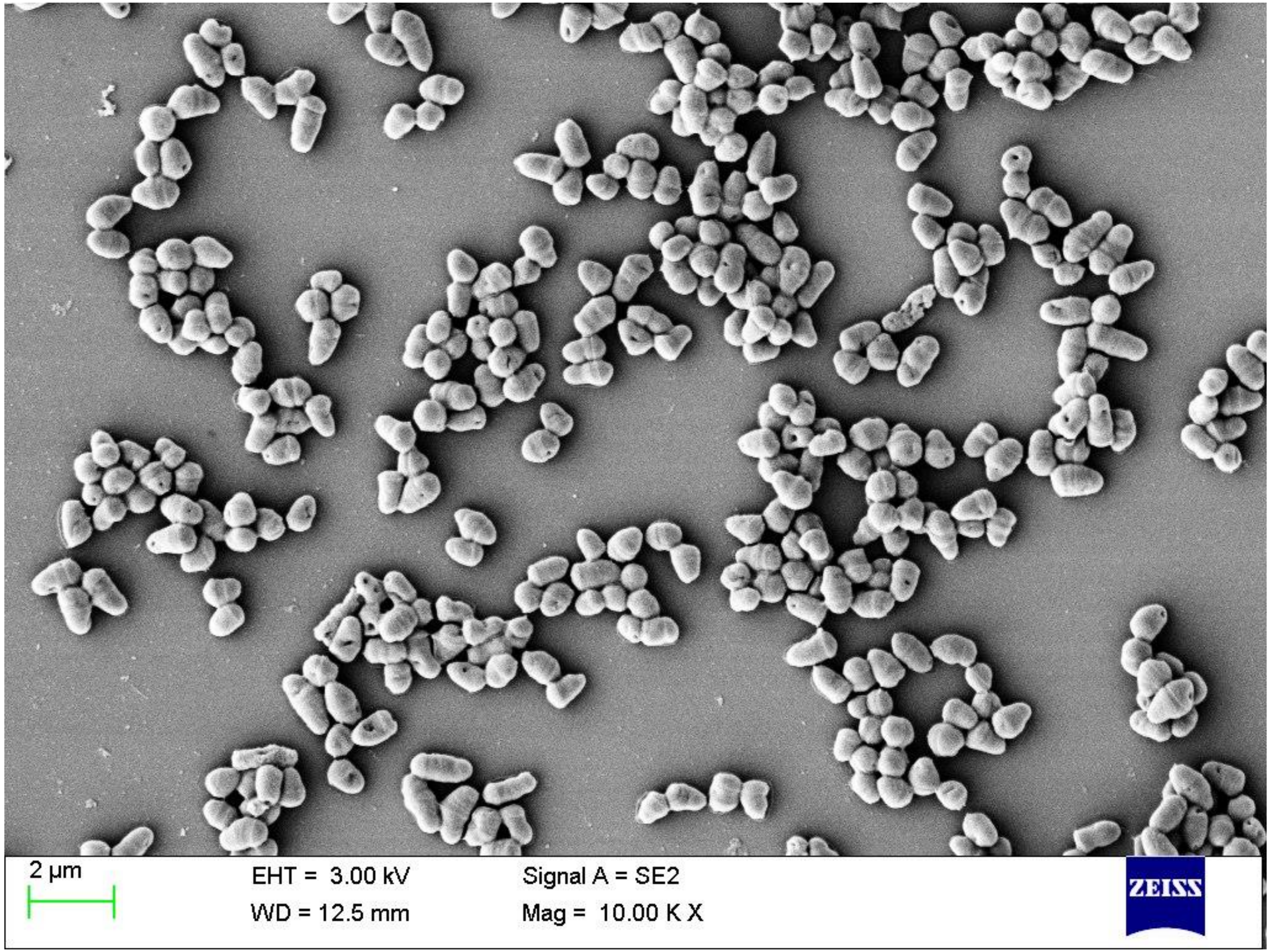
GRAS = Generally recognized as safe

"**GRAS**" is an acronym for the phrase **G**enerally **R**ecognized **A**s **S**afe. Under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act (the Act), any substance that is intentionally added to food is a food additive, that is subject to premarket review and approval by FDA, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use, or unless the use of the substance is otherwise excepted from the definition of a food additive.

https://www.fda.gov/food/food-ingredients-packaging/generally-recognized-safe-gras

Living contact lenses – results

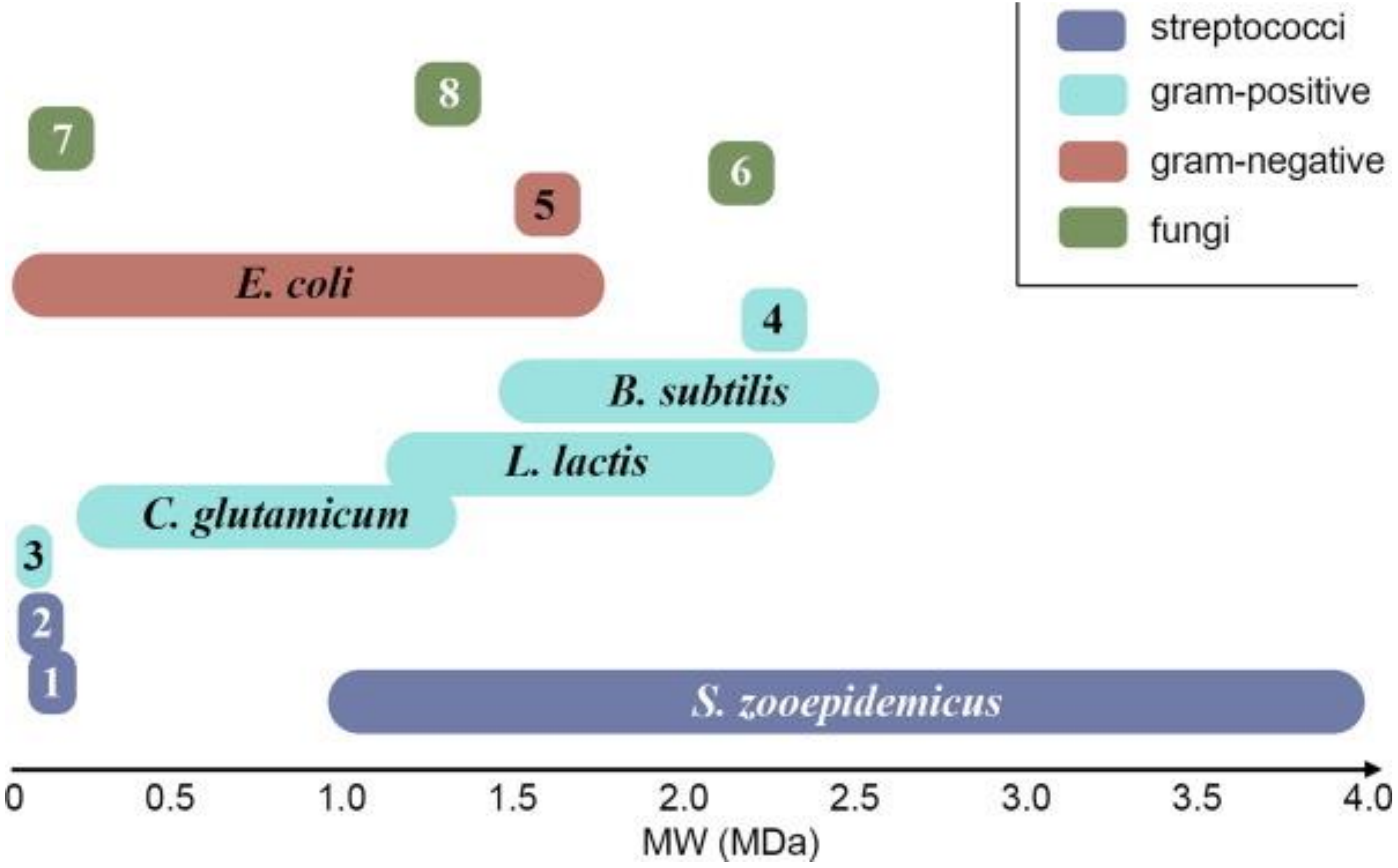
C. glutamicum   Prospective bacterial and fungal sources of HA_2022



- *C. glutamicum* DSM 20300
- Model for *Corynebacterium mastitidis*, a taxonomically related commensal microbe of the human eye
- Wild-type genetically engineered to secrete HA

HA MWs produced from various sources

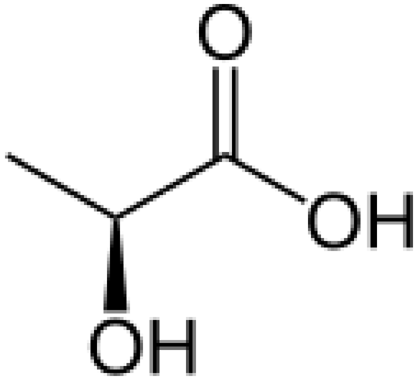
Prospective bacterial and fungal sources of HA 2022

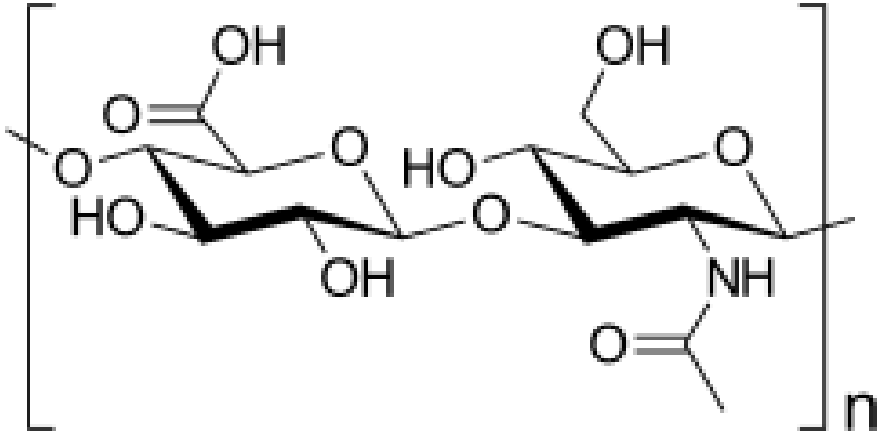


Genetic engineering

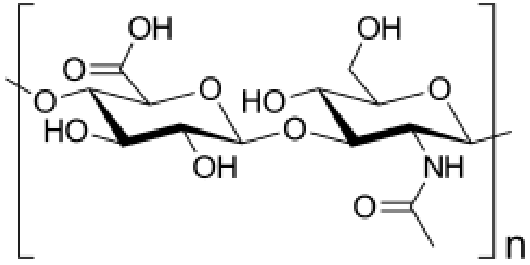
- **Step 1**: Eliminate native *ldhA* gene encoding **lactate dehydrogenase** to prevent accumulation and secretion of lactate under oxygen-limiting conditions (mutant *C. glutamicum ΔldhA)*

- *Why?* Oxygen permeability is limited in the contact lens hydrogel. Normally lactate would be produced by the bacteria in oxygen limiting conditions. Lactate is associated with pH lowering metabolic biproducts and the acidification is irritating and should be avoided.





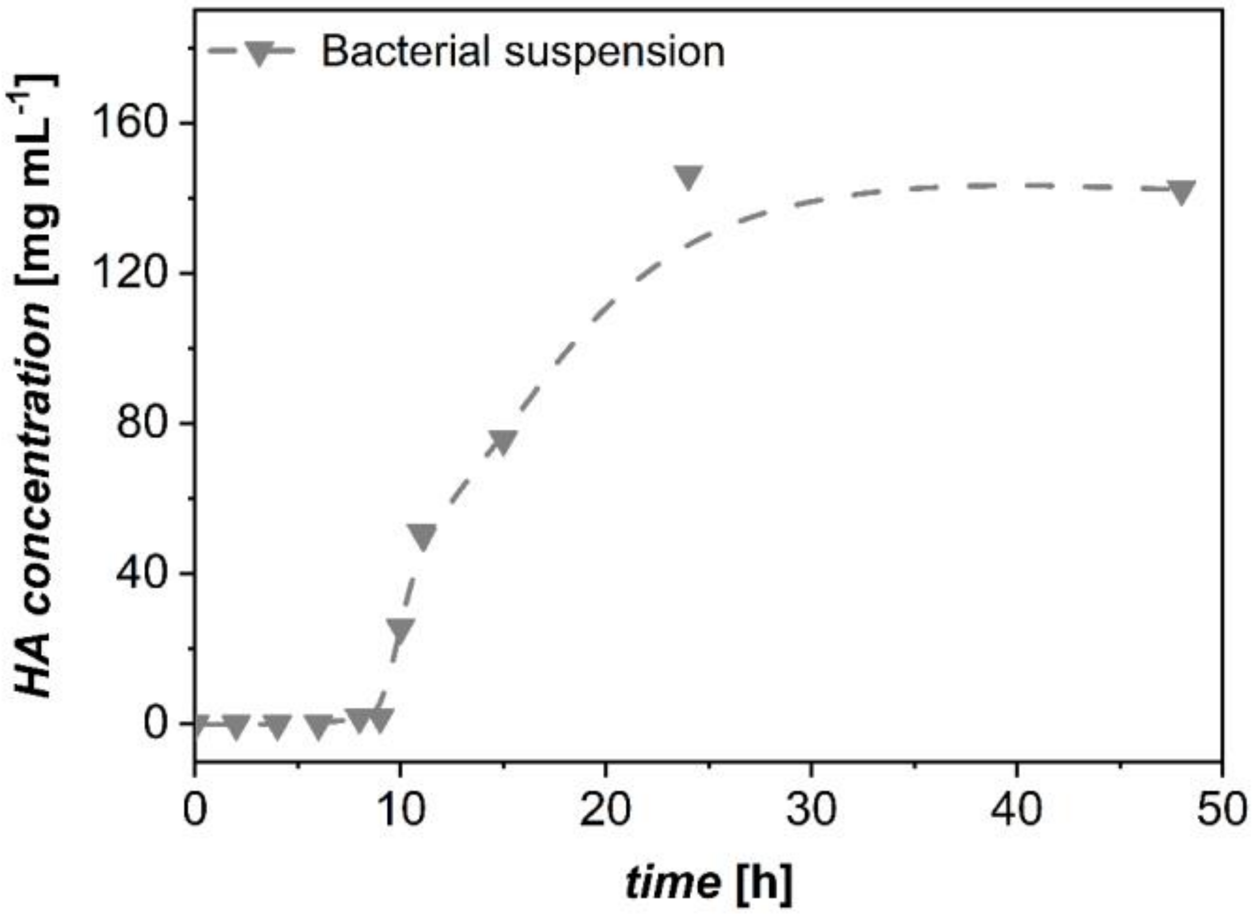
- **Step 2**: Inserted the *hasAB* operon from *Streptococcus equisimilis*, which encodes **hyaluronan synthase (*HasA*)** and **UDP-glucose dehydrogenase (*HasB*)**, the two key enzymes for HA synthesis.



- Two activated sugar monomers are needed for HA: N-*acetylglucosamine* (GlcNAc) and *glucuronic acid* (GlcA) (look at structure)
  - ***HasA*** – Hyaluronan synthase is the enzyme that polymerizes HA
  - ***HasB*** – UDP-glucose dehydrogenase converts UDP-glucose into UDP-glucuronic acid (limiting!)
  - UDP-GlcNAc is available in eye

- A **constitutive promoter (*Ptuf*)** was placed upstream of *hasAB*; "constitutive" means it is always ON, ensuring continuous transcription of both genes in tandem.

- **Operon layout**: ON switch (*Ptuf*) → gene 1 (*hasA*) → gene 2 (*hasB*)

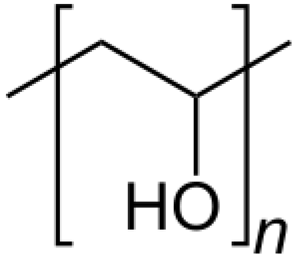


Genetic engineering seems to work!

- Showing that HA is produced in suspension culture
- Seems to need about 10 h

Figure S1: Cumulative HA concentration released in the medium from suspension culture of the engineered HA producer *C. glutamicum*. No medium change was performed during the incubation time. HA concentration was measured by GPC analysis of the supernatant.

Living contact lenses – the hydrogel – material part



PVAc　　　　Ethanol

$$[CH_2CH(OAc)]_n + C_2H_5OH \rightarrow$$
$$[CH_2CH(OH)]_n + C_2H_5OAc$$

PVA　　　　Ethyl acetate

- Based on polyvinyl alcohol
- Water soluble
- Synthetic
- Highly used in different areas
- Biocompatible hydrogels, also used in contact lenses

- Not produced by monomer polymerization – monomer vinyl alcohol is thermodynamically unstable
- Produced by the hydrolysis of polyvinyl acetate
- Properties defined by MW and degree of deacetylation
- More hydrolysis = water soluble; and vice versa

PVA or PVOH

Living contact lenses – the hydrogel

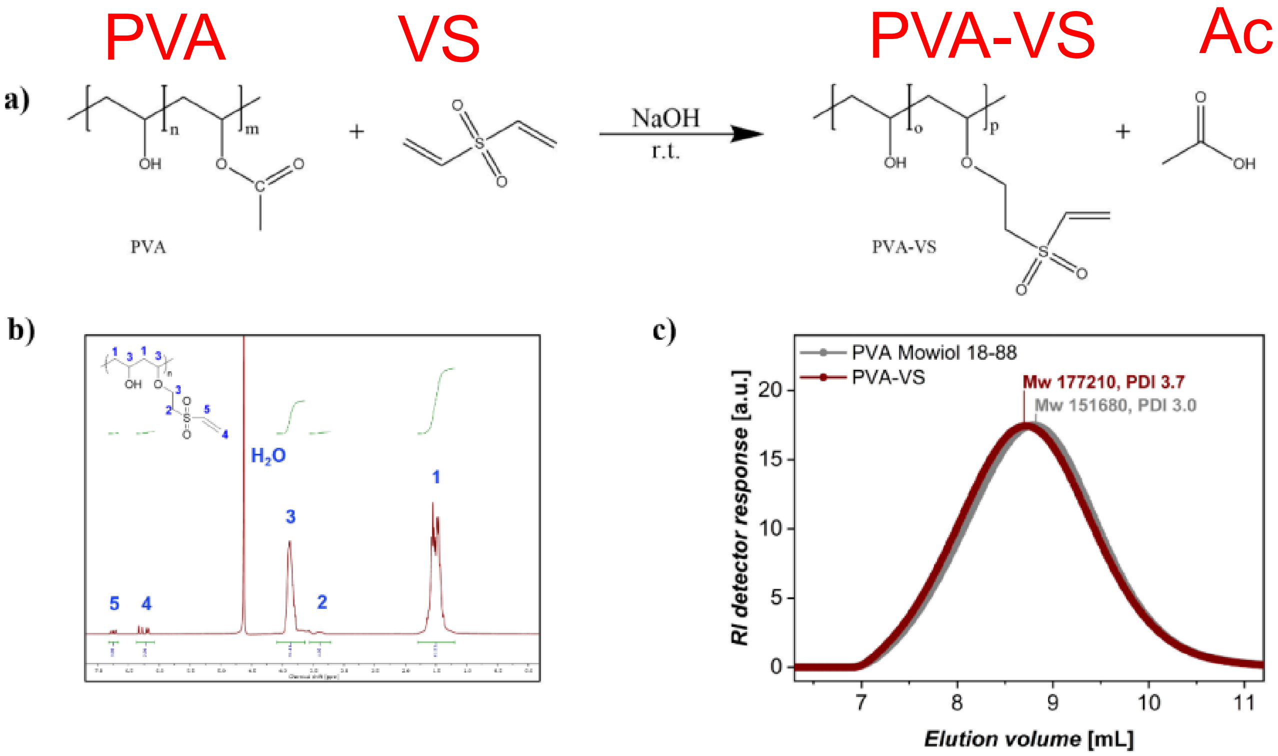


Figure S2: a) Chemical functionalization of PVA with divinylsulfone (DS) to form vinyl sulfonated poly(vinyl alcohol) (PVA-VS). **b)** [1]H-NMR spectrum of PVA-VS in D_2O. The integrals of the vinyl signals indicate a 1.5 ±0.2% degree of VS modification. **c)** GPC elugram of PVA (Mowiol 18-88) and PVA-VS showing no significant changes in the molecular weight distribution after the VS-functionalization reaction.

- Hydrogels contained PVA and modified PVA-vinyl sulfone (VS)
- Is PVA-VS ok for contact lenses?
- PVA-VS can be crosslinked with light with LAP as photoinitiator
- Non-crosslinkable PVA is included to modulate the porosity of the hydrogels
- Screening results: 5-10% w/v PVA-VS with 1.5% degree of VS functionalization gives mechanically stable and transparent hydrogels
- Bacteria could grow in these gels (data not shown)

EPFL

Living contact lenses – the hydrogel

Table 1. Physicochemical properties of PVA-VS/PVA hydrogels and the commercial PVA-based Focus Dailies CL (Alcon) measured in STF.

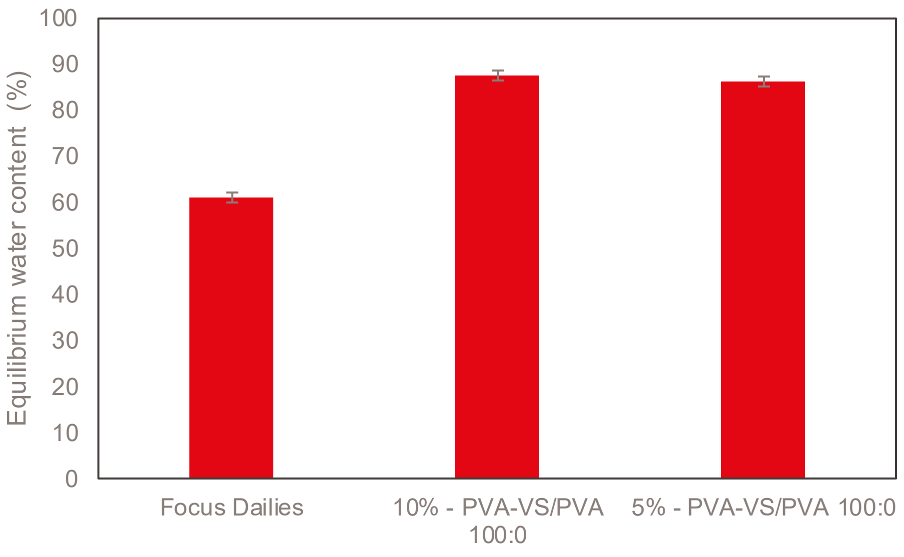
Material	Polymer content [% w/v]	Equilibrium water content (EWC) [%]	Oxygen permeability D_k [barriers][a)]	Water contact angle [°]	Transmittance [%][b)]	Refractive index	Storage modulus G' [kPa][c)]
Focus Dailies	–	61 ± 3	19 ± 2	28 ± 4	>99	1.380	15.6 ± 0.2
PVA-VS/PVA 100:0	10	87.5 ± 0.9	53.9 ± 2.4	29 ± 3	99.1 ± 0.5	1.336	17.9 ± 0.1
PVA-VS/PVA 100:0	5	86.1 ± 0.6	50.9 ± 1.5	23 ± 7	98.4 ± 0.6	1.334	2.2 ± 0.3
PVA-VS/PVA 99:1	5	86.6 ± 1.1	52.1 ± 2.8	22 ± 3	98.4 ± 0.3	1.333	1.6 ± 0.2
PVA-VS/PVA 95:5	5	85.3 ± 0.5	49.4 ± 1.1	23 ± 1	98.7 ± 0.8	1.334	1.5 ± 0.1

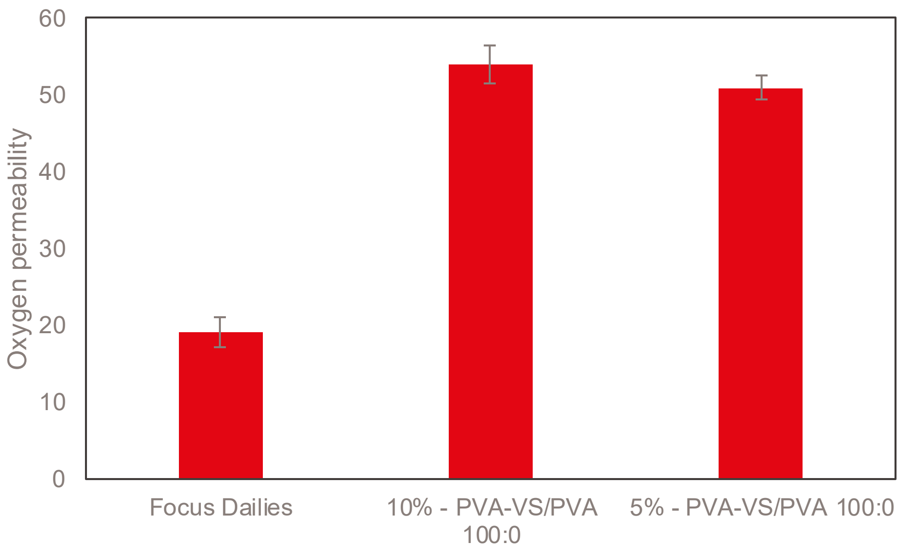
[a)] Calculated from EWC measurements; [b] Value at 600 nm; [c)] Obtained from time sweep measurements.

- [a)] Calculated from EWC measurements;
- [b] Value at 600 nm;
- [c)] Obtained from time sweep measurements.

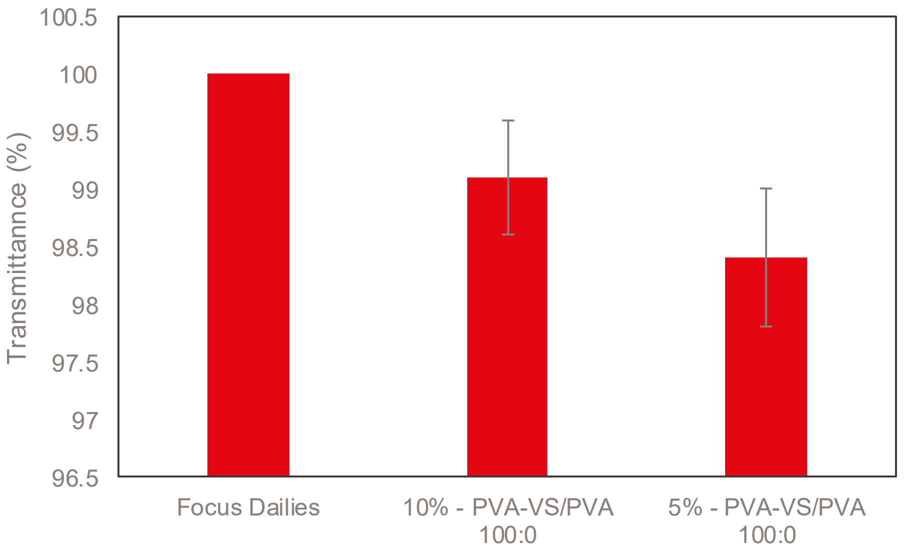
Big table of properties, not super visual – can I make it clearer?

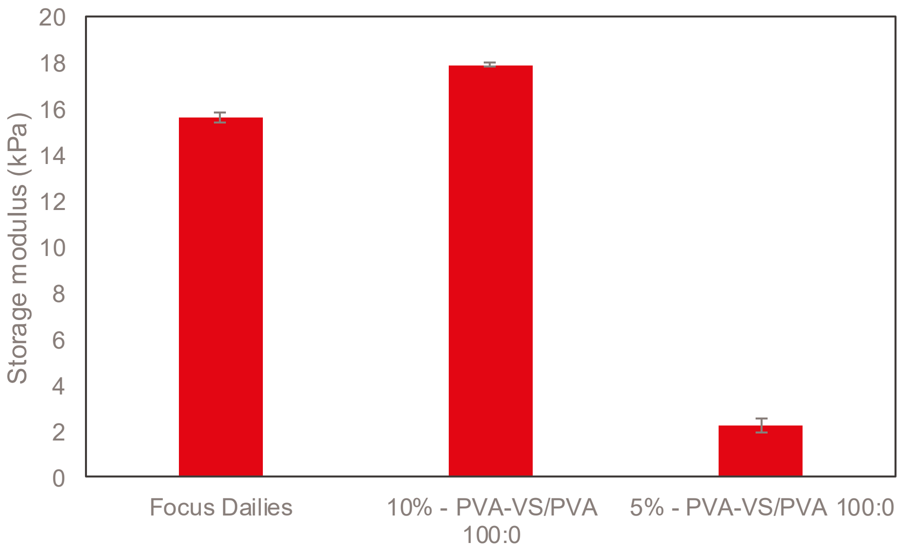
Living contact lenses – effect of polymer content





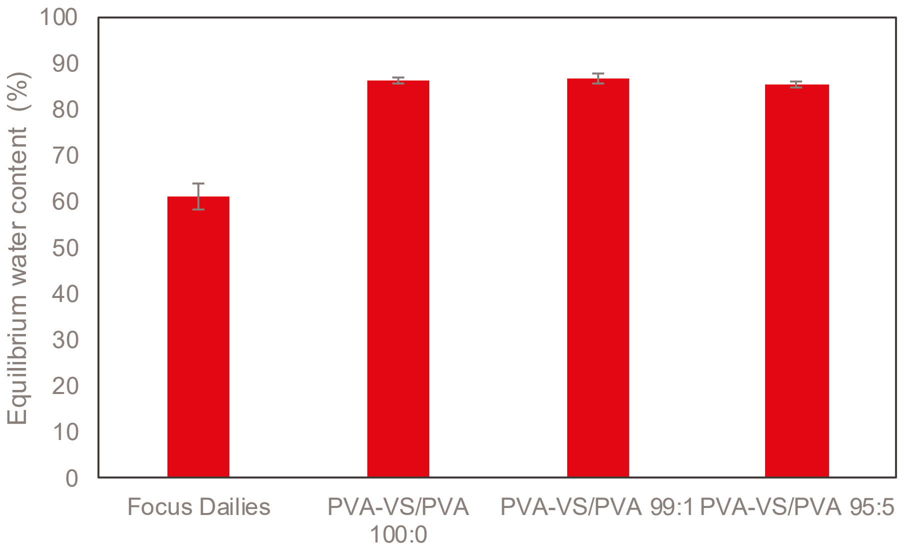
5 or 10% polymer in hydrogel

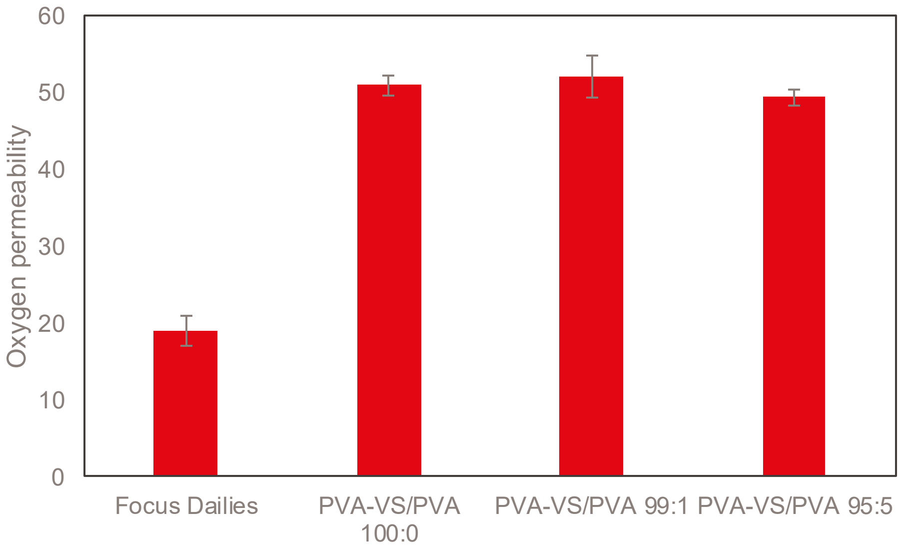


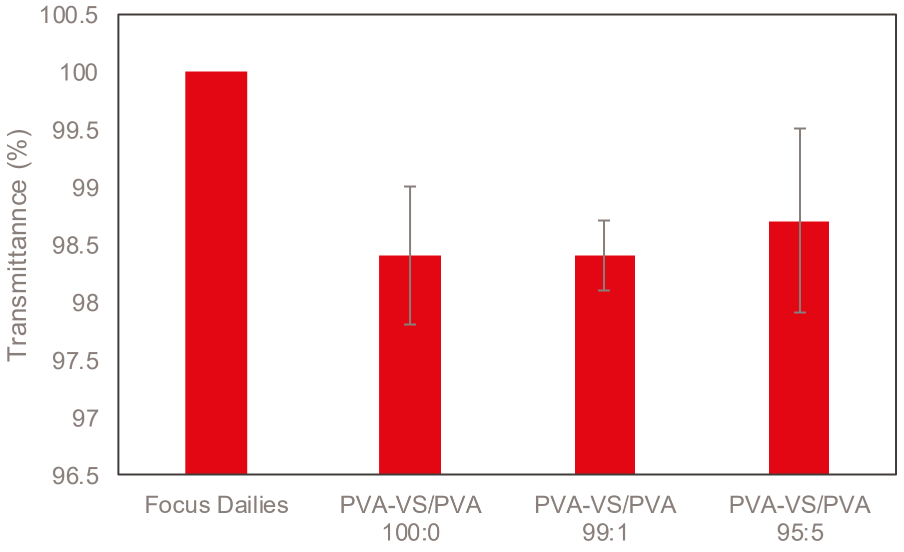


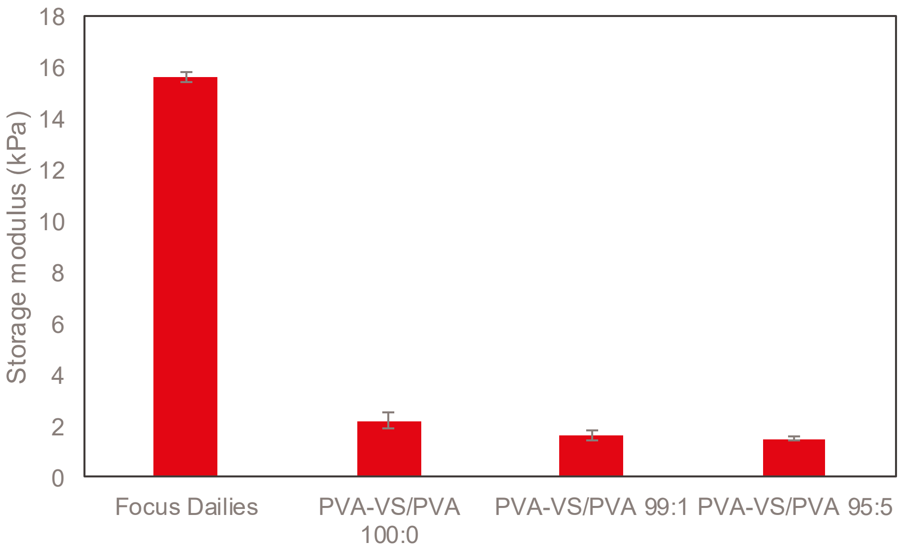
- Only see effect of 5 vs.10% in G'

Living contact lenses – effect of free PVA





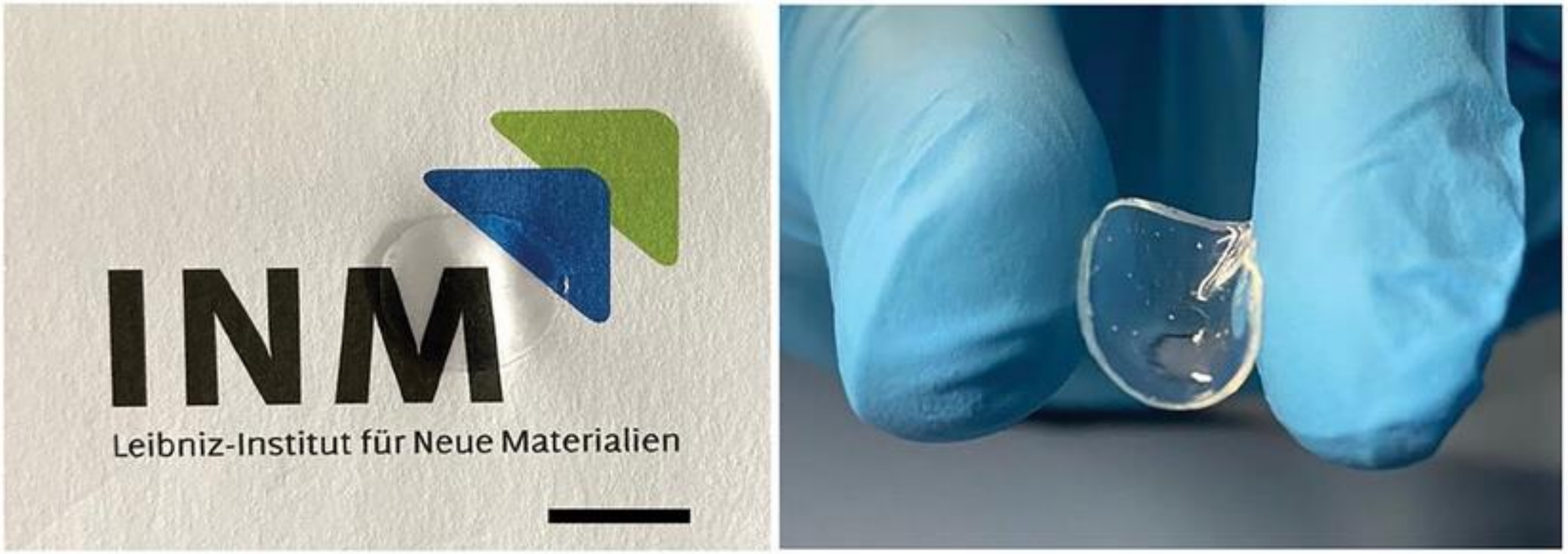




5% total solids; 0. 1 or 5% free PVA

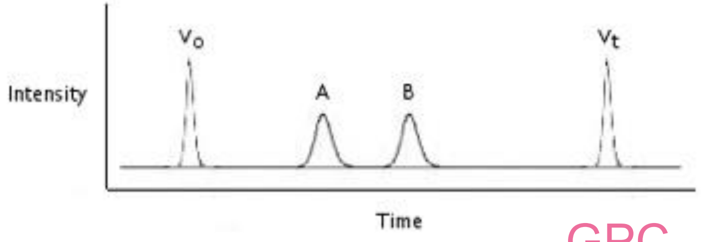
- All at 5%
- No big diff
- Softer than commercial but higher permeability and less chance of contamination by toxic monomers
- Soft is good for bacteria

Transparent & soft lenses - 5% free PVA



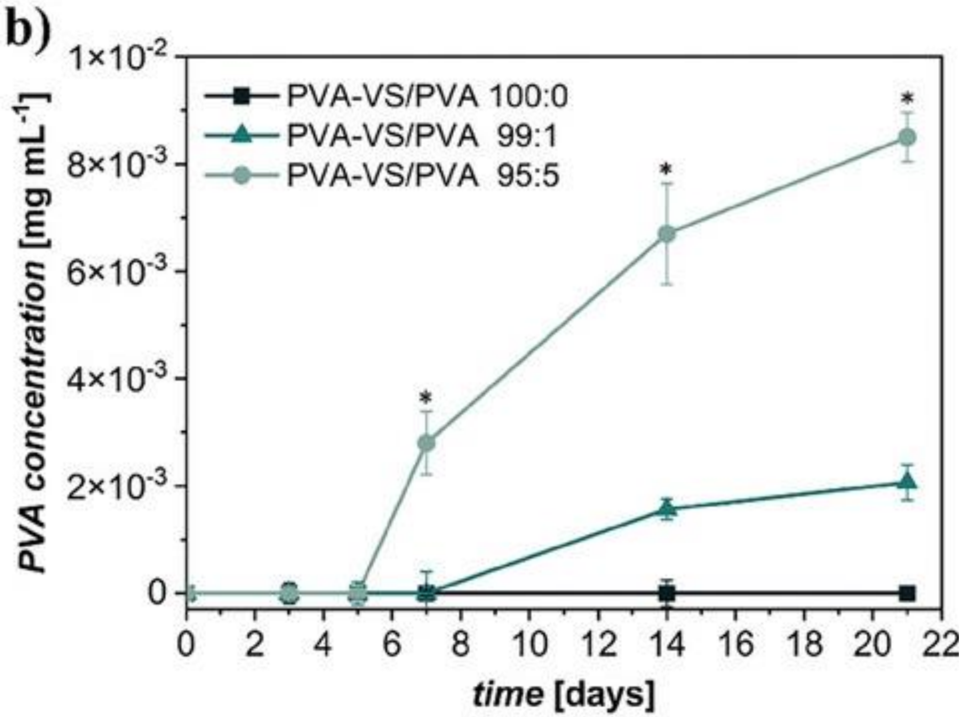
- PVA-VS/PVA 100:0 hydrogel discs
- Scale = 1 cm

PVA leaching

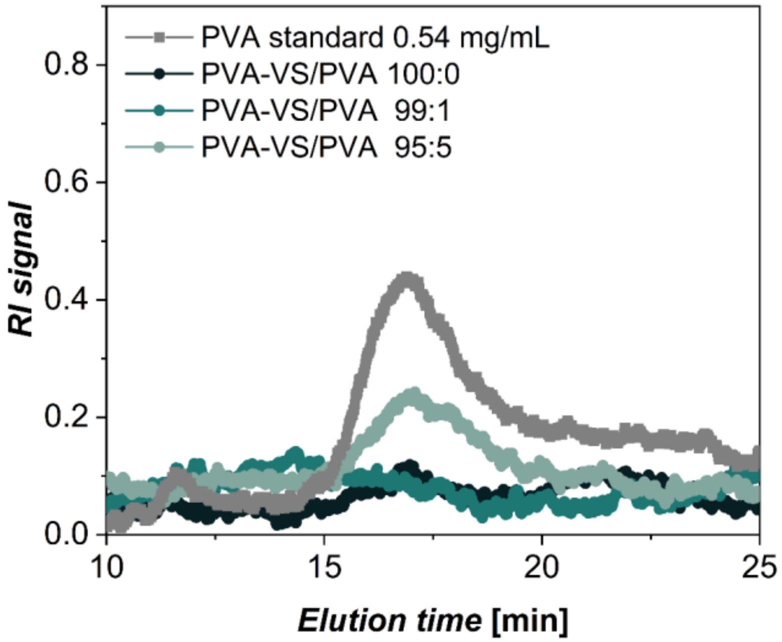


GPC

PVA release in STF (simulated tear fluid) at 30 °C for 3, 5, 7, 14, and 21 days



GPC (gel permeation chromatography) of supernatant

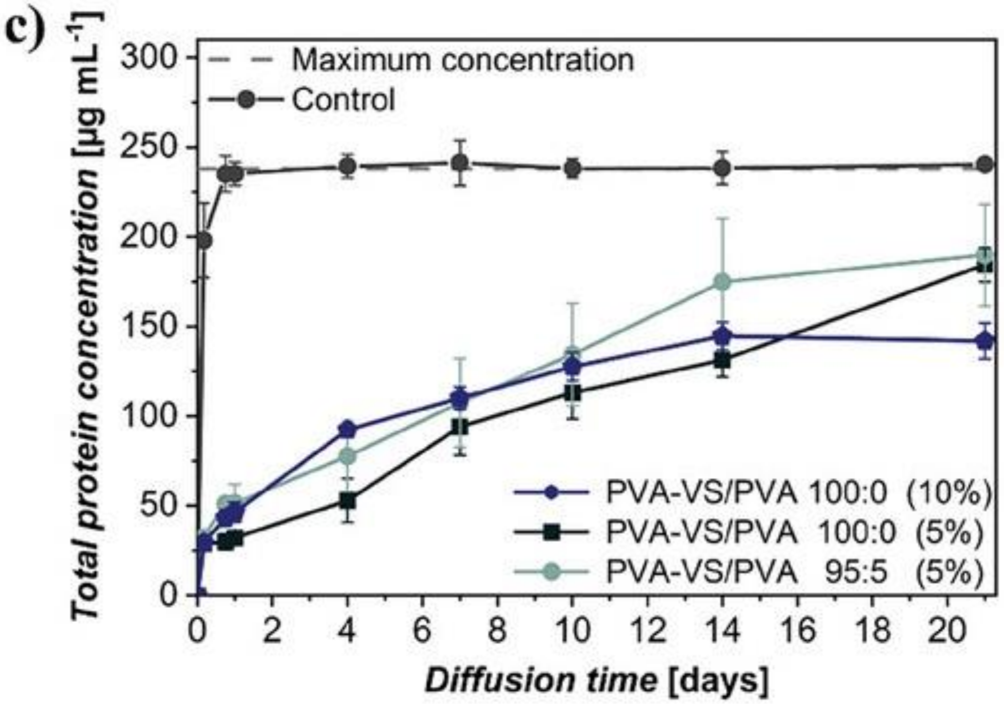


- No PVA release in 100-0 (no free PVA)
- <25% PVA loss in 1% and 5% free PVA - mostly entrapped

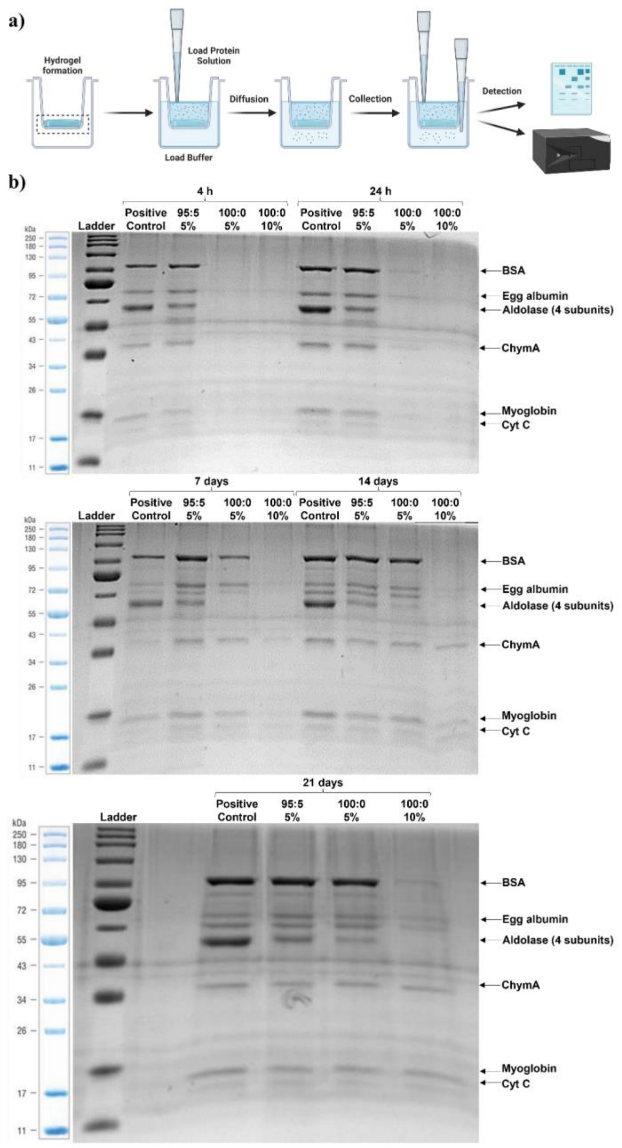
EPFL

Protein diffusion through hydrogels – 12.3-160 kDa mixture

BCA assay

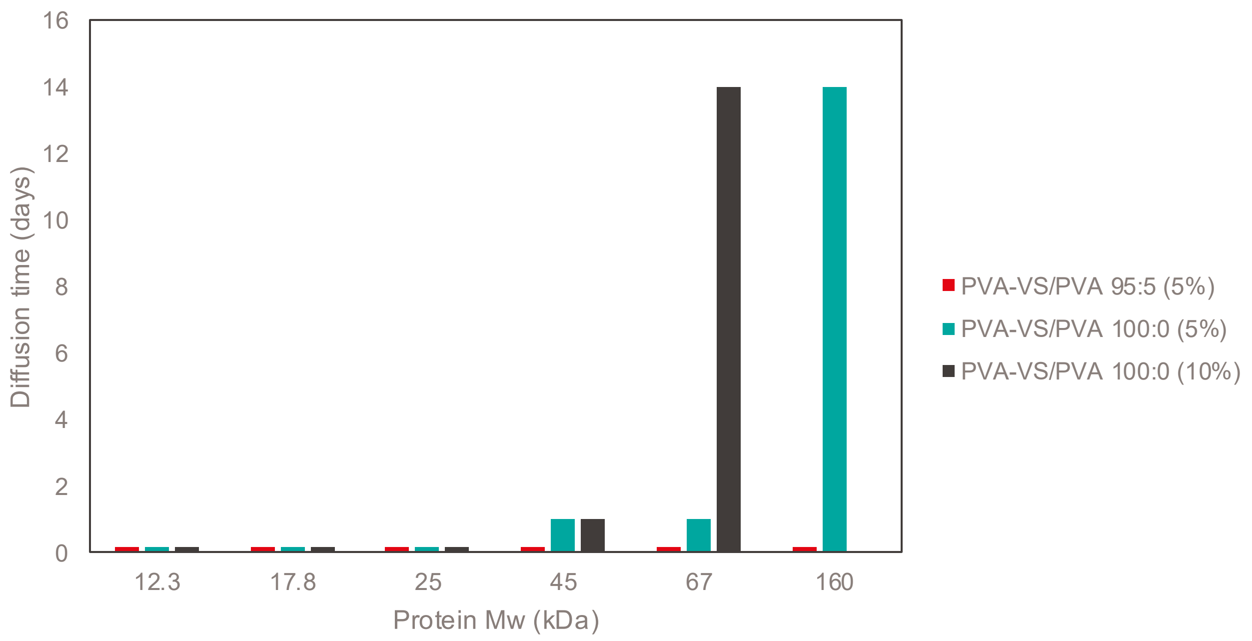


- Used BCA assay to detect total protein concentration in supernatant



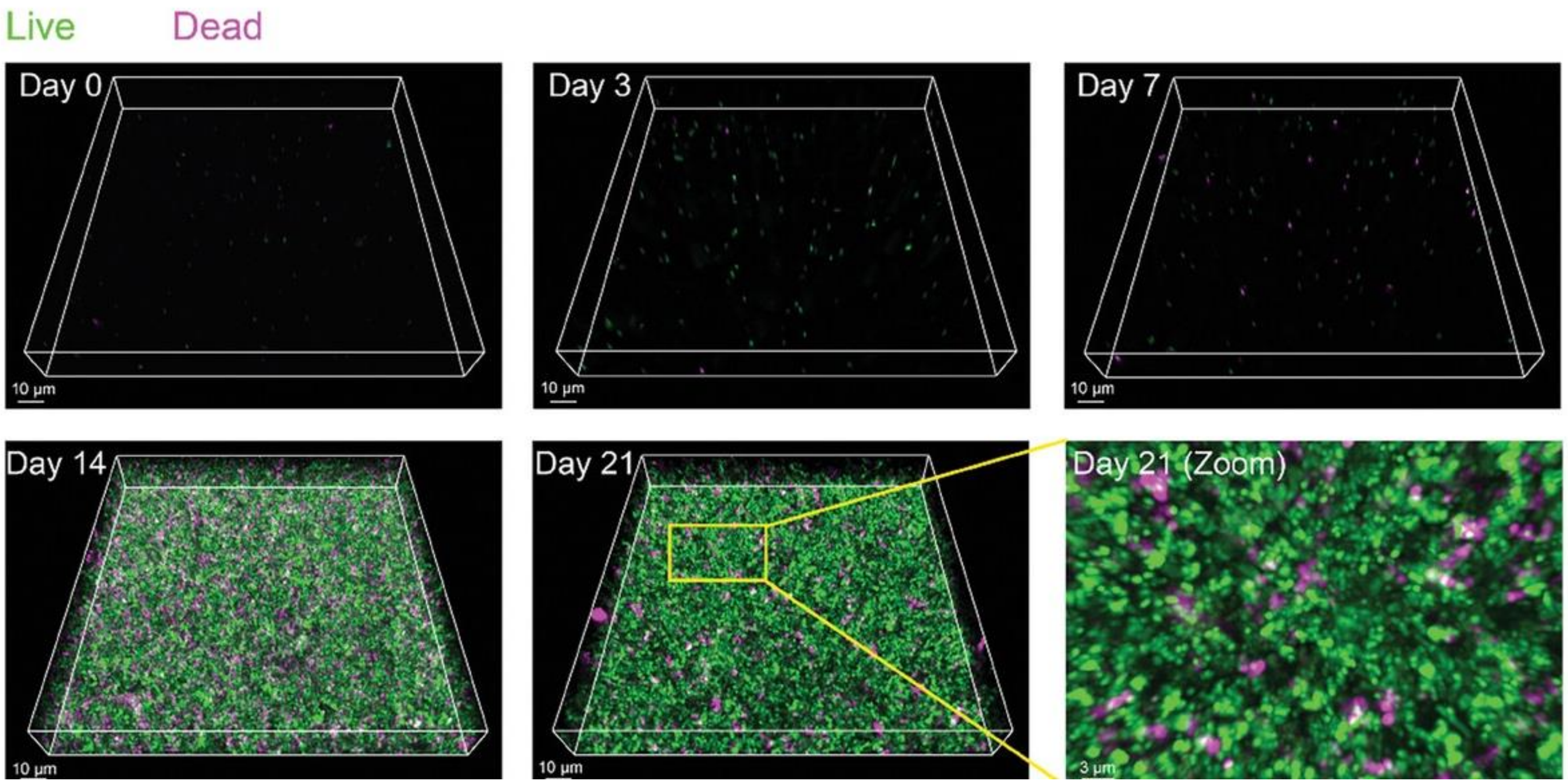
Porosity of hydrogels by diffusion

Tells us about permeability and biocompatibility of hydrogel & also to be sure that HA will be able to diffuse out



- All proteins were able to diffuse through the 5% w/v hydrogels, indicating that the pores of the network are larger than 160 kDa
- Proteins with molecular weight <25 kDa diffused through the hydrogels within 4 h
- Proteins with size >25 kDa required 4 h to diffuse through the hydrogel that included non-crosslinked PVA, and 1 to 14 days when the PVA-VS content increased from 5% to 10% w/v

Living hydrogel – 5% w/v PVA-VS/PVA 95:5 (*notice free PVA*)



- Growth of bacteria in the hydrogel during incubation in **medium** for 21 days at 30 °C was monitored by fluorescence imaging after Live/Dead staining (time scale relevant to real life CL use –weekly/monthly)

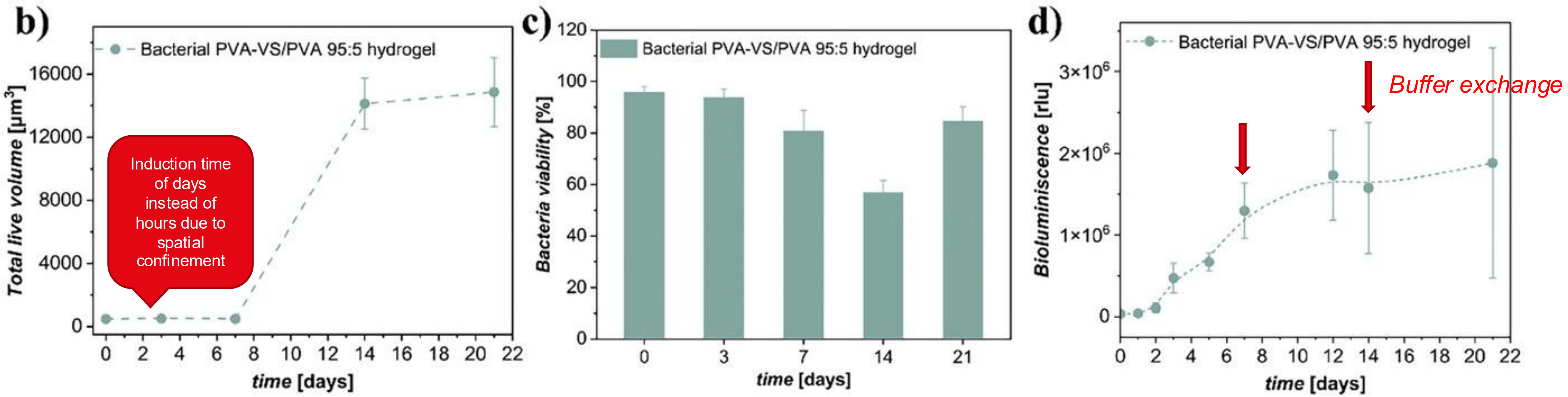
- *C. Glutamicum* mixed with hydrogel precursor solution
- Photo crosslinking in mold
- Contact time of bacteria and precursors <1 min
- They conclude that the bacteria is encapsulated and not implicated in the crosslinking chemistry
- It's alive! It grows!

Living hydrogel - 5% w/v PVA-VS/PVA 95:5

From Live/Dead

From Live/Dead

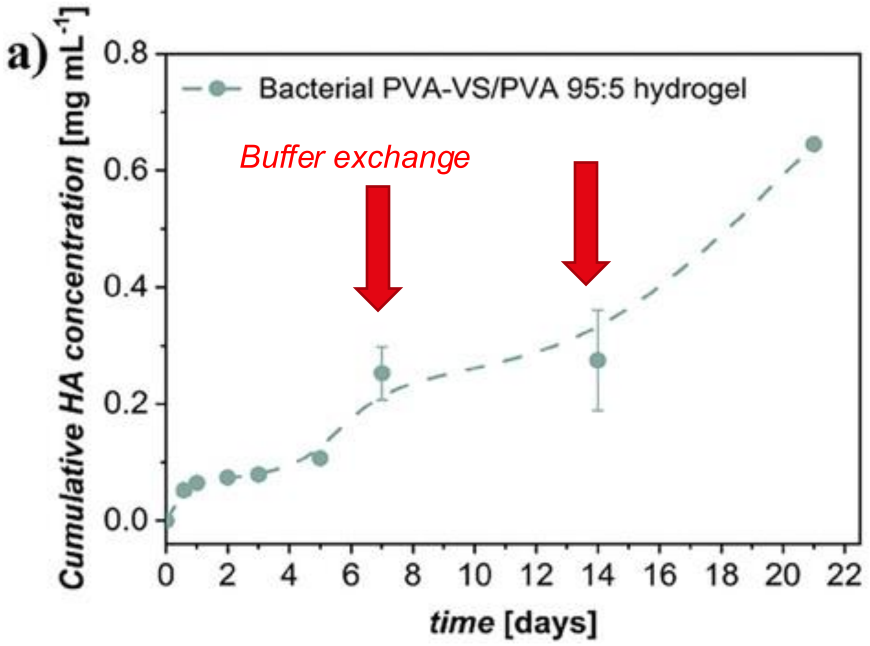
From 3D bioluminescence assay



- Estimates by image analysis show induction, growth, and steady-state over several days (b)
- Viability was high over 21 days (a, c)
- Metabolic activity by quantifying ATP in hydrogels using a 3D viability assay (d) – indicates an *increase in metabolic activity during the first week followed by a constant value at longer times*
- Conclusion – hydrogel system supports the spatially contained growth and activity of the bacteria for at least 3 weeks

Release of HA from living hydrogel - 5% w/v PVA-VS/PVA 95:5

- *medium exchange on days 7 and 14*



- GPC of supernatant
- HA with a MW of **30-70 kDa** was detected after 14 h
- *C. glutamicum* in PVA-VS hydrogels produce and release HA!

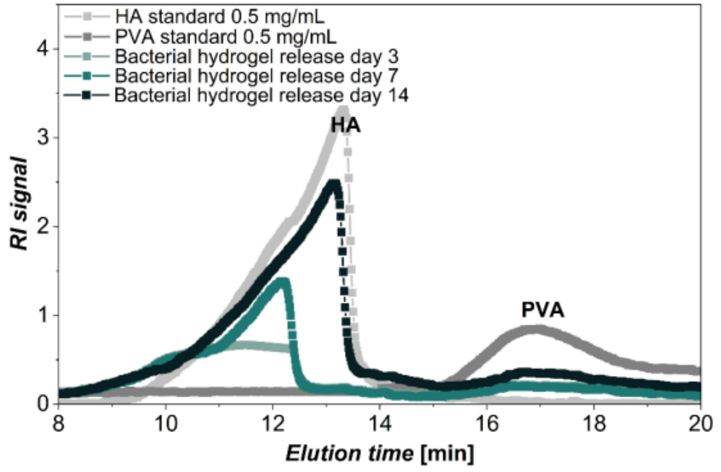
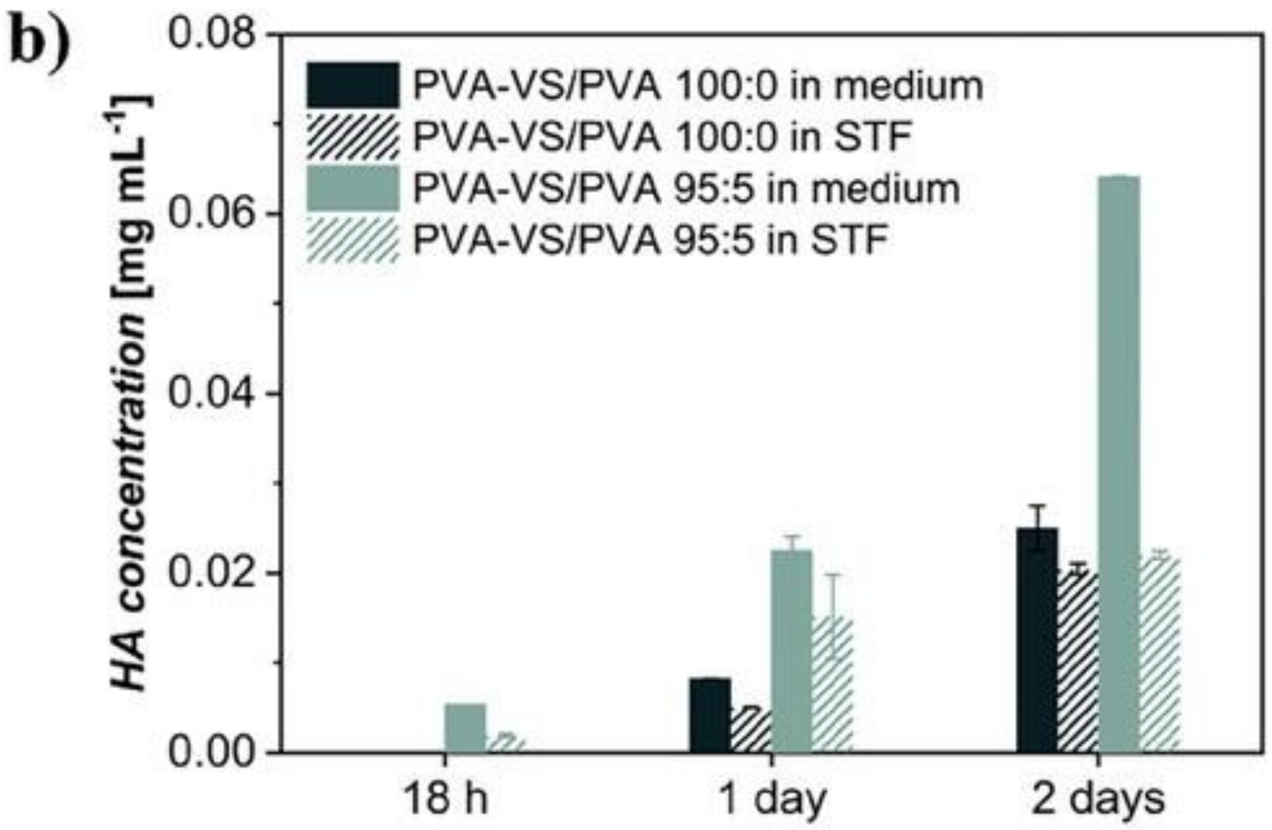


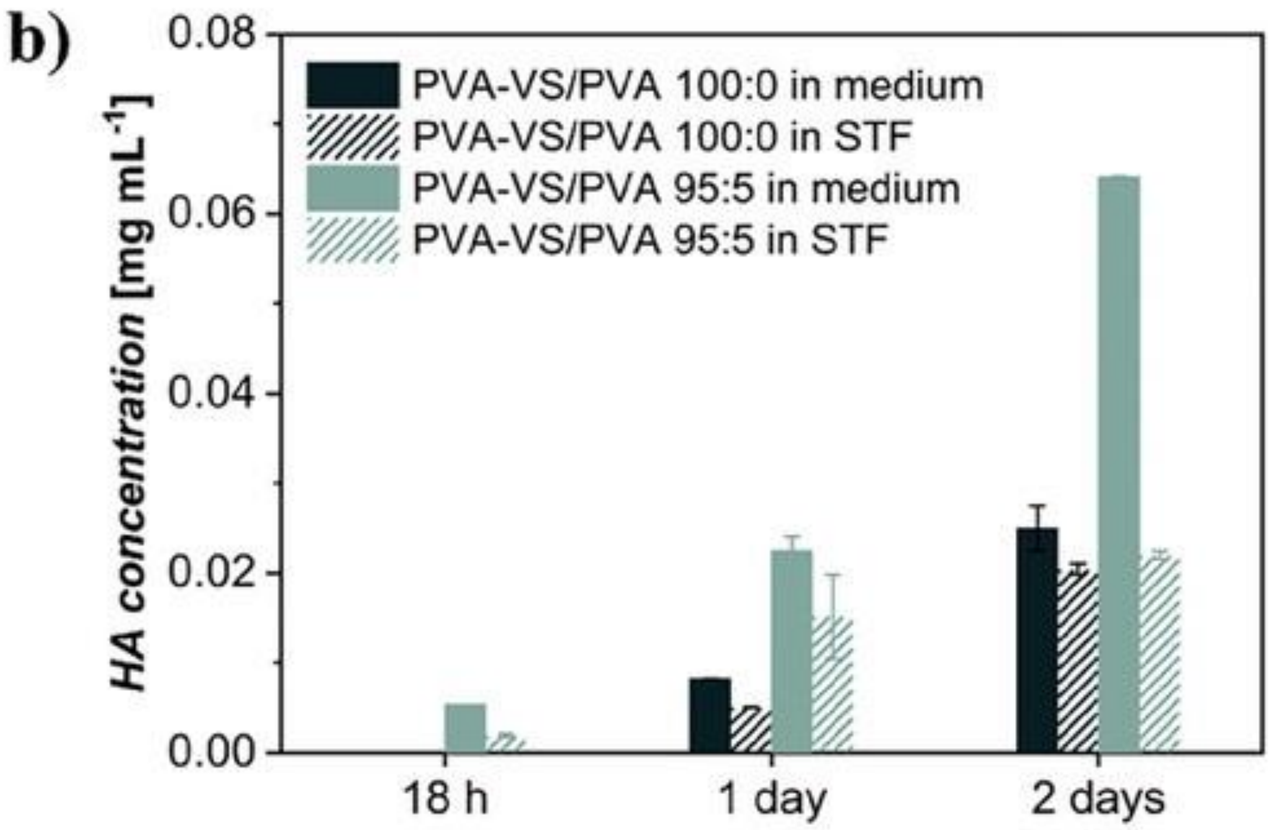
Figure S10. Representative GPC chromatograms of supernatants of PVA-VS/PVA 95:5 bacterial hydrogels after 3, 7, and 14 days of incubation. The chromatograms of standard HA (0.5 mg/mL) and PVA (0.5 mg/mL) solutions are also shown.

Release of HA from living hydrogel - 5% w/v PVA-VS/PVA 95:5



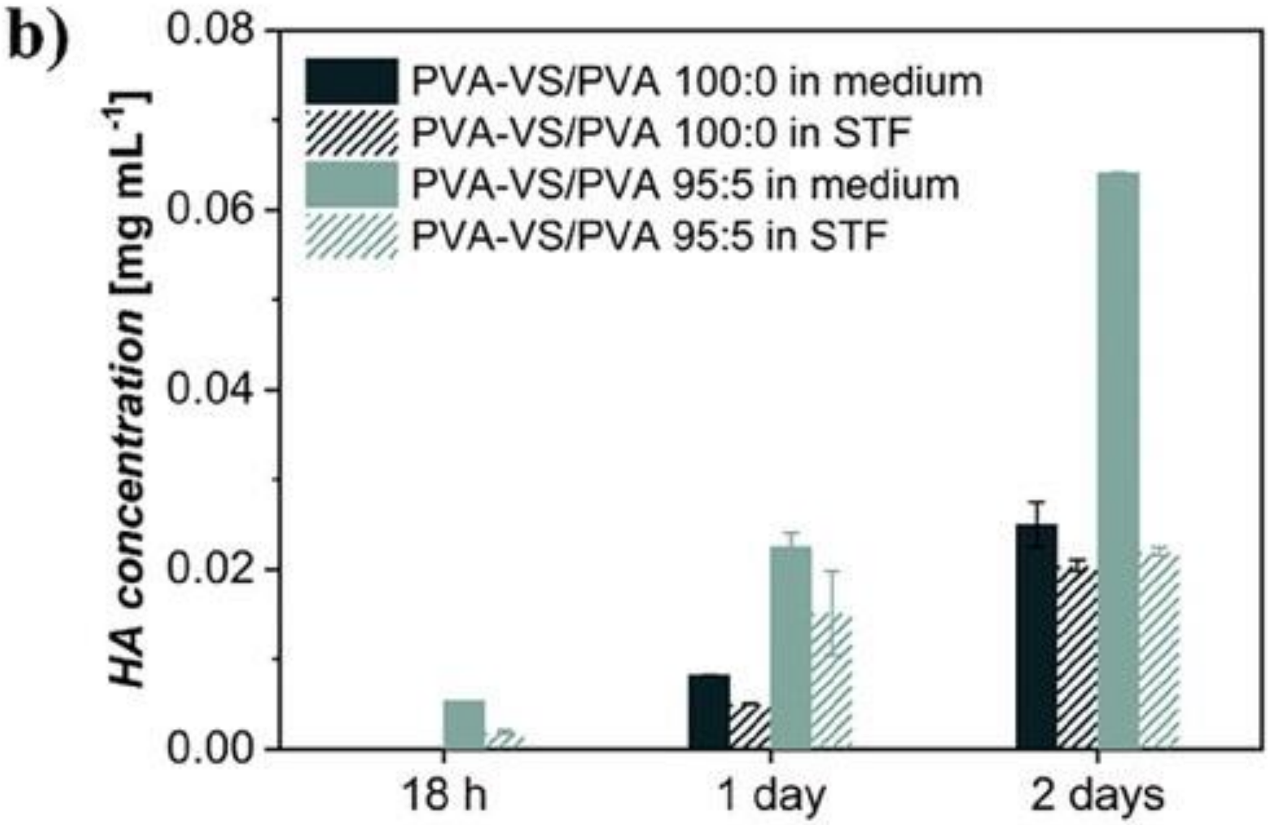
- **Key:** medium is nutritive, supports bacterial growth, whereas STF is non-nutritive
- All samples, first grown in media for 21 days; after placed in fresh media or STF
- More HA detected in nutritive medium than in STF
- Free PVA seems to help diffusion of HA

Release of HA from living hydrogel - 5% w/v PVA-VS/PVA 95:5



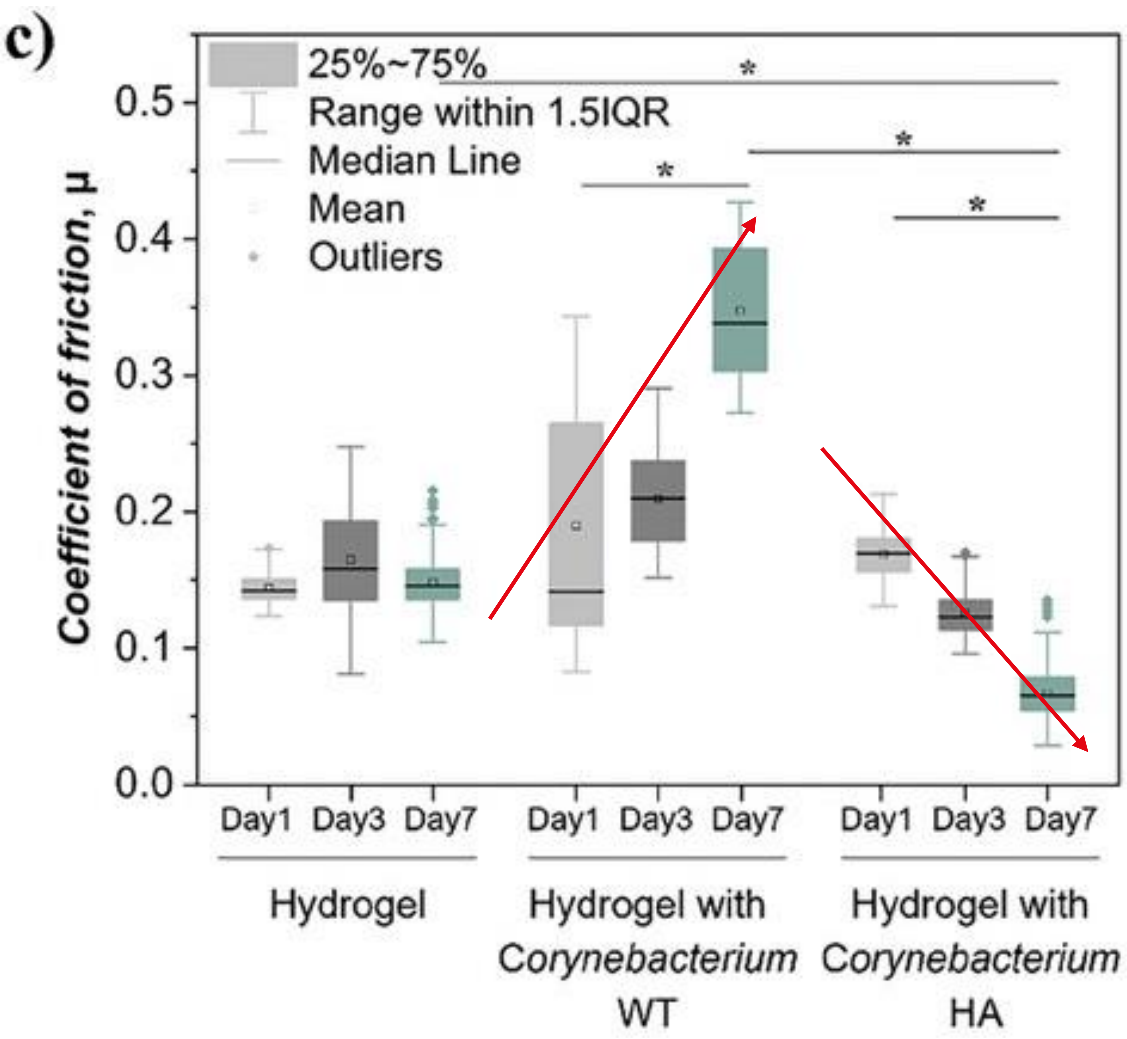
- In STF, HA is only passively released; properties of gel matter a lot here! Gel is a reservoir of HA that has already been produced, and the gel controls the rate of release!
- In nutritive media, can be 2 factors that contribute the release, easier diffusion of HA reservoir and/or continued biosynthesis of HA (can't really tell)

Release of HA from living hydrogel - 5% w/v PVA-VS/PVA 95:5



- Deep question: Why even have bacteria here?
- In STF, the situation closest to an actual eye, we have no HA secretion and likely no bacterial growth – what we do have is a preloaded reservoir of HA
- It's good the bacteria aren't growing… in your eye, but could I just add HA to the PVA hydrogel and skip the bacteria?

Self-lubrication properties of living hydrogel

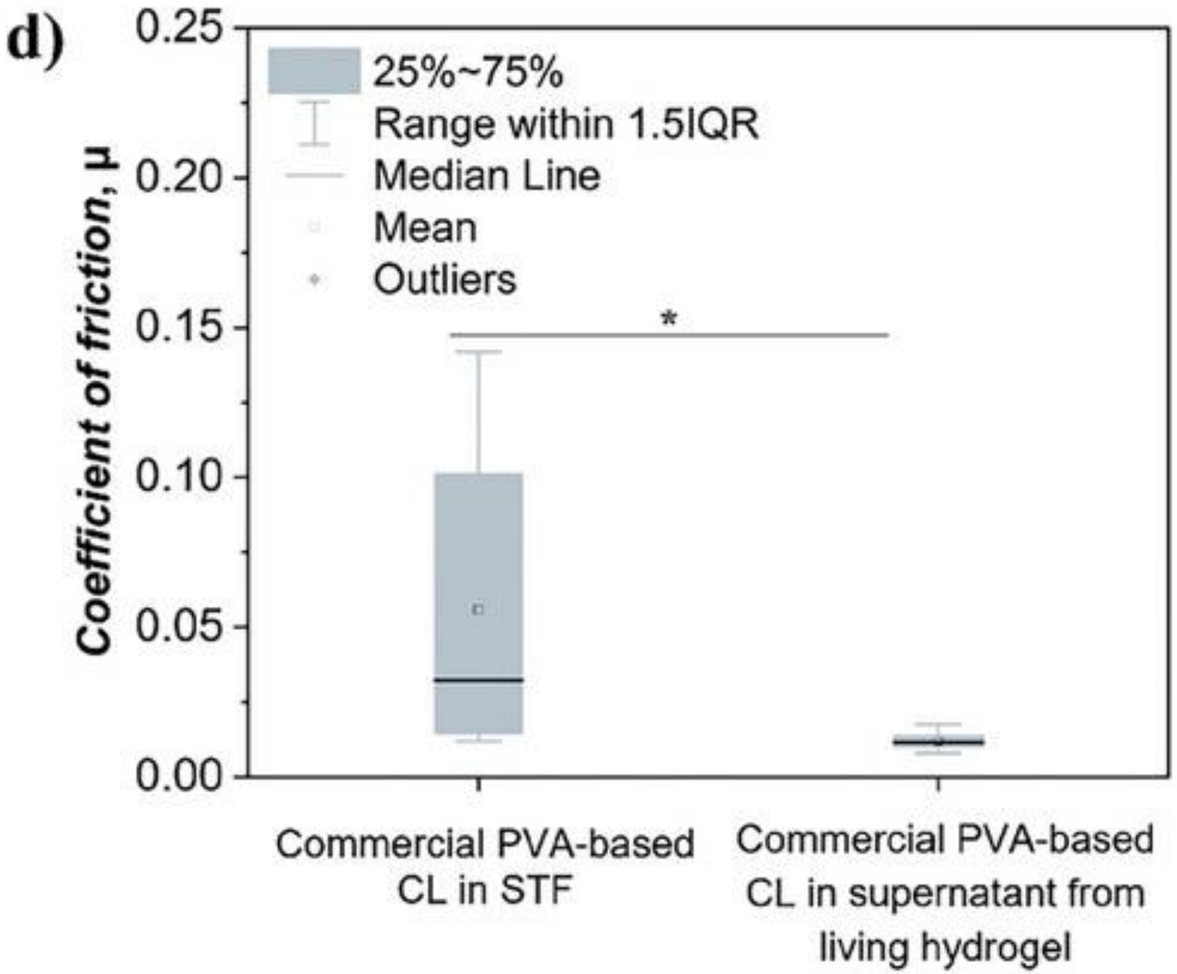


- 5% w/v PVA-VS/PVA 95:5
- Control is WT which does not produce HA and empty hydrogel
- Hydrogel disk attached to upper plate of rheometer and torque measured against steel bottom plate in the presence of the corresponding medium **supernatant** while an angular for is applied

- WT show an increase in friction coefficient, attributed to the release of metabolites and proteins that can interact with the hydrogel

- Opposite is seen for HA-containing/secreting hydrogels! Self-lubrication! (or some release of PVA)

How does a commercial hydrogel behave?

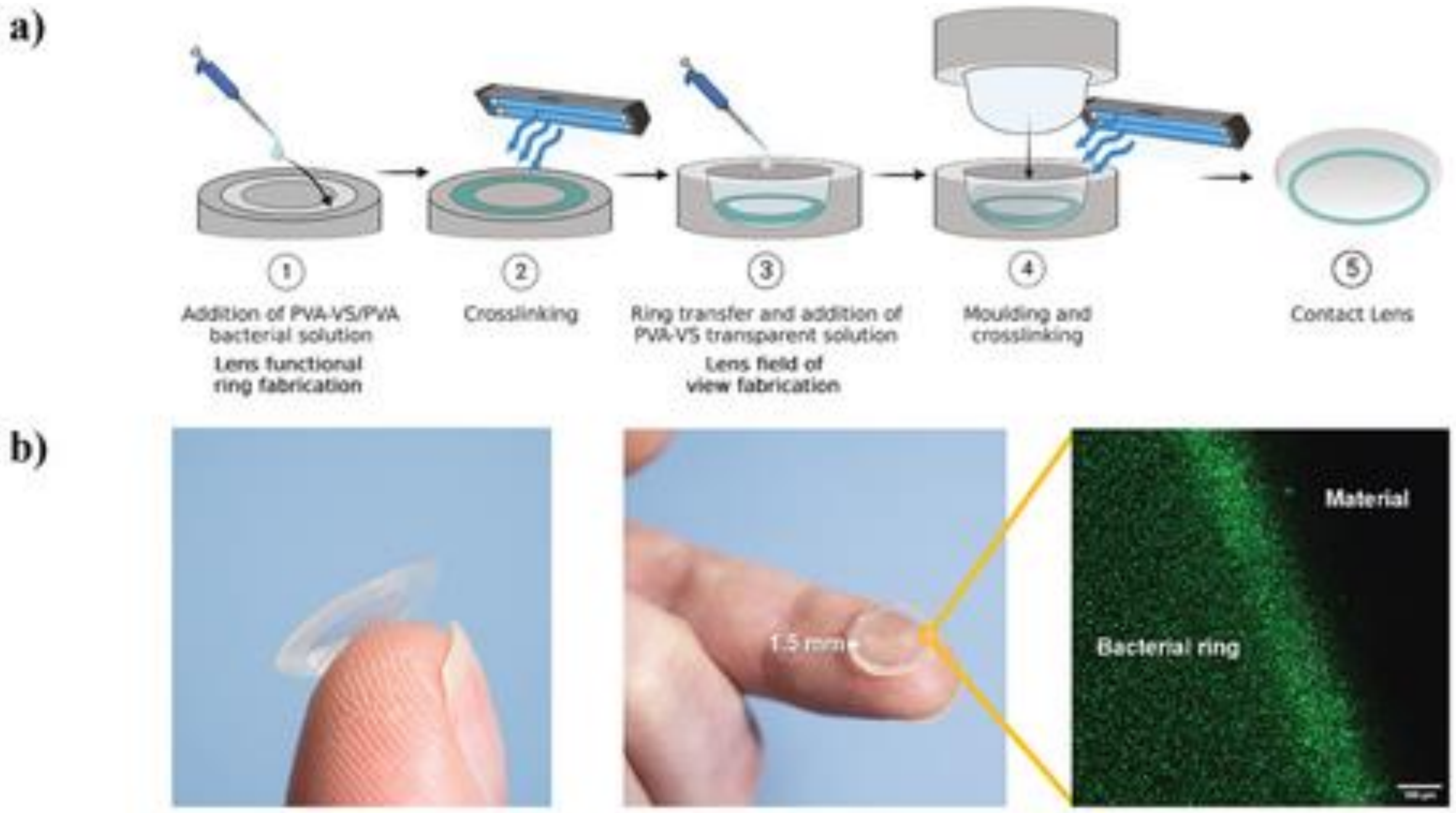


- Interesting study: took commercial contact lenses
- In the first case, measured coefficient of friction in STF
- In the second case, used the supernatant collected from the living hydrogel , and measured the commercial lens in this medium
- Lower friction! (same as previous slide); indicating that the HA secreted HA is behind the low friction coefficient, not factors related to the hydrogel

Self-lubricating CL prototype

Why a ring?

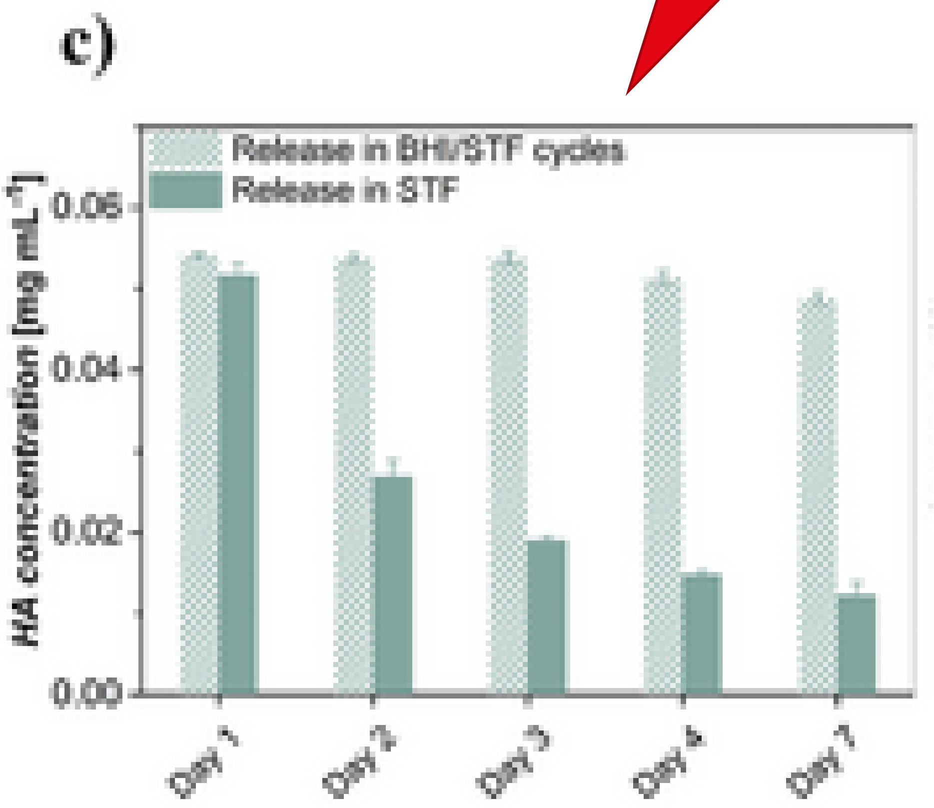
Why the different hydrogel formulations?



- 1st mold 5% hydrogel (free PVA) containing bacteria in ring (10 mm diameter)
- 2nd embed ring in 10 % hydrogel (no free PVA)
- 11 mm diameter, 1.5 mm thickness
- When incubated in medium, bacteria grew within ring, no outgrowth or leaking of bacteria

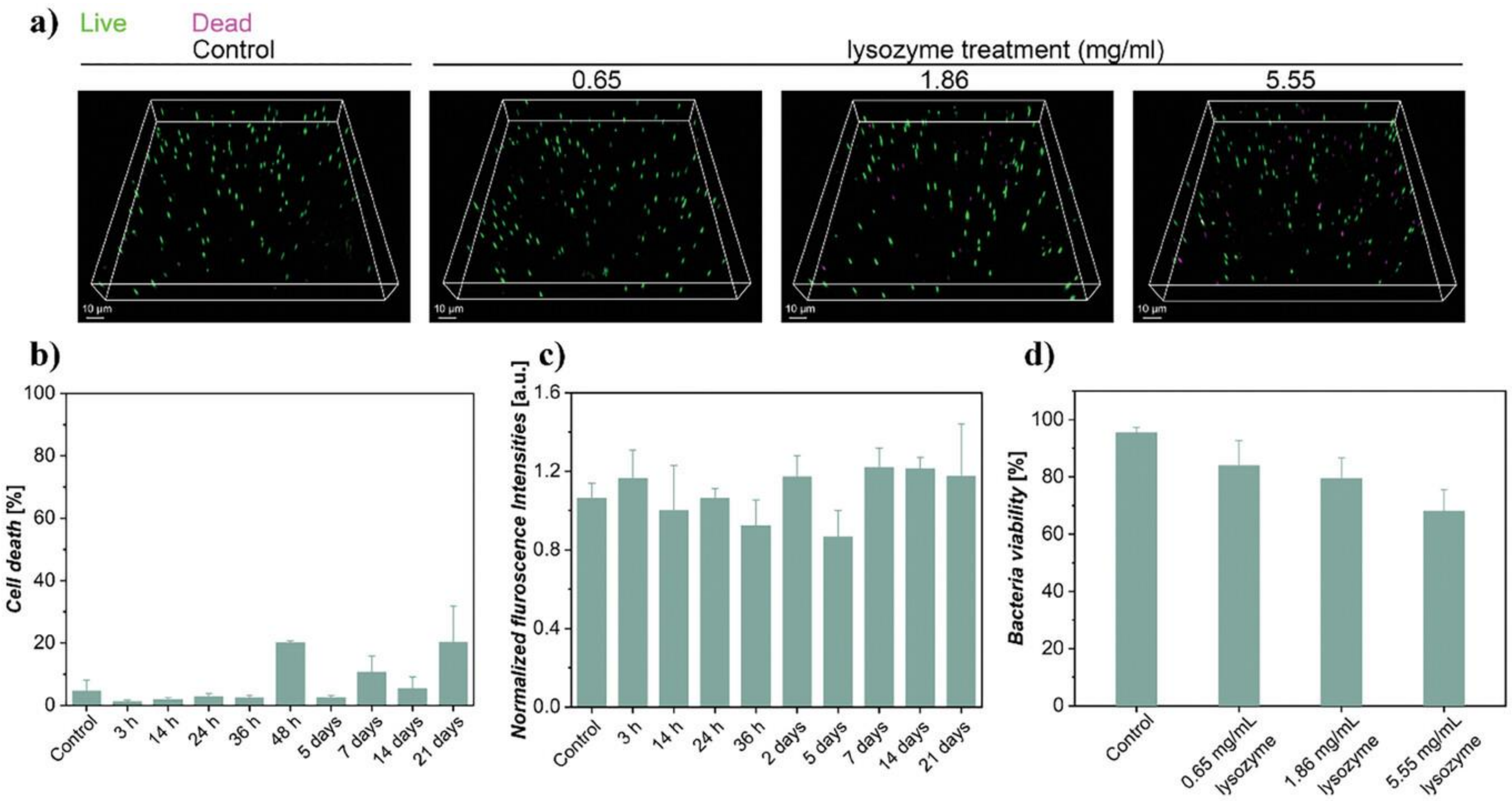
Self-lubricating CL prototype

Sustained release of a therapeutic!



- Release measured by supernatant GPC in media
- 1st case: Release in STF over days, measured after 24 hours (solid bars)
- 2nd case: cyclic 16 h in media, and 8 hours in STF (dotted bars)
- In the first case, HA decreases over time due to lack of nutrients in medium
- In second case, constant release of HA over 7 days due to exposure to nutrients which sustains HA production
- Scenario – overnight incubation (16 h), daily release (8 h) = **dailies! Now we have a reason to use bacteria!**

Cytocompatibility with mouse fibroblastic cells

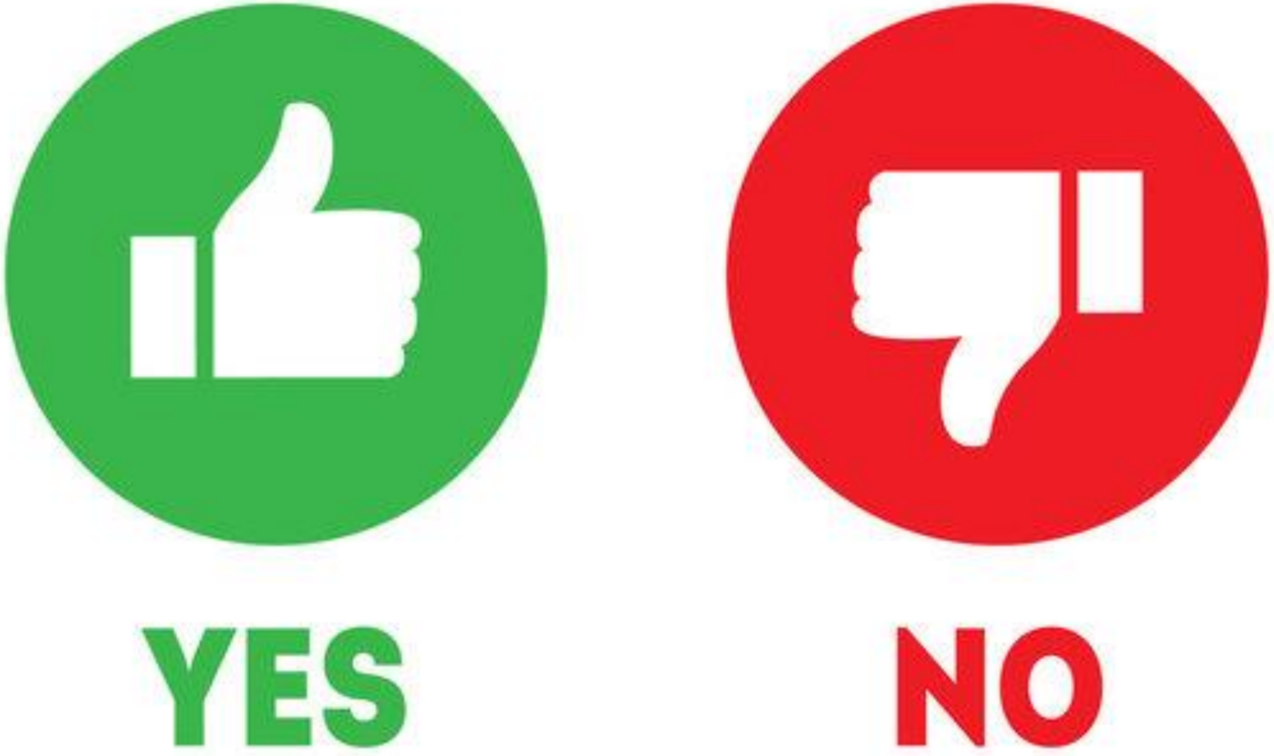


Conclusions

Why say bacteria? It's a biofactory!

- Self-lubricating living CL based on "embedded biofactories programmed to continuously produce and release HA", a natural lubricant
- Based on PVA-VS; at 5% this hydrogel can be mixed with "biofactories", and after crosslinking it supports viability and metabolic activity for at least 3 weeks
- 7-day HA release in tunable and sustained manner
- Interesting for future CL applications, but more studies needed to fully understand control/release profiles, etc.,

Did you like this paper? Why or why not? (a useful, medical application?)



Take-aways

- Recall: proof-of concept
- What did they prove?
- You can genetically engineer bacteria to produce HA
- You can encapsulate the bacteria in a hydrogel and provided the properties are appropriate and the media conditions are nutritive; the bacteria can stay alive, grow, and secrete HA
- In the eye, or STF, you might expect the bacteria to be dormant, no HA is produced, but was already produced us passively secreted into the eye
- If you take your lenses off at night and your soaking solution is nutritive, you might replenish the HA in the lenses while you sleep
- Built a cool prototype, with bacteria confined, out of sight
- Showed no cytoxicity