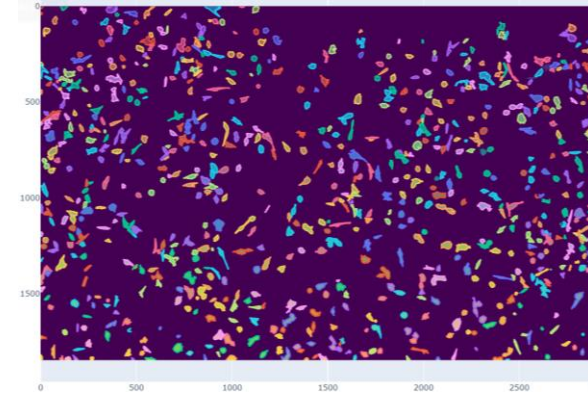
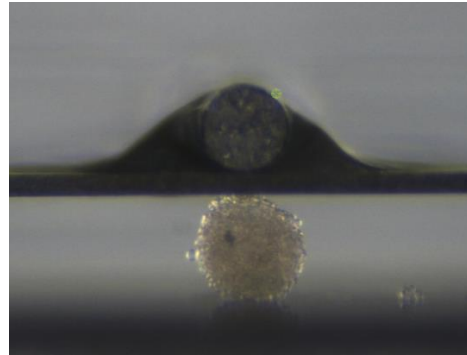




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On biomechanics and its relevance to udder research



Yifat Brill-Karniely, PhD
Institute of Animal Science
Volcani Center

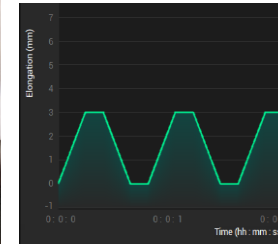




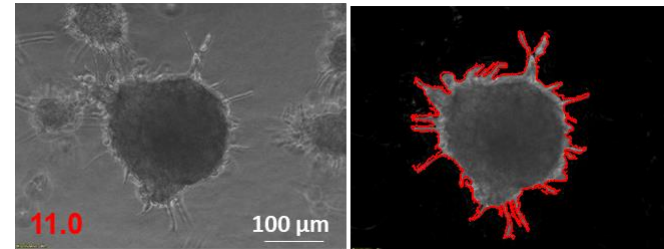
437

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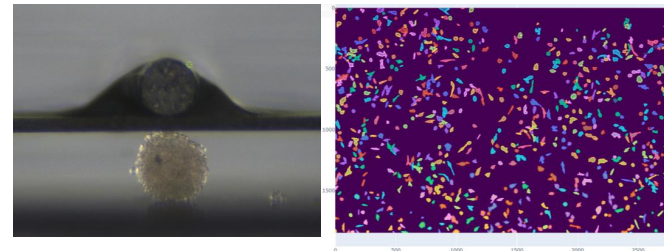
- Why are biomechanical aspects important in the study of bovine mammary glands?



- Applicative biomechanical research



- Present research and perspectives

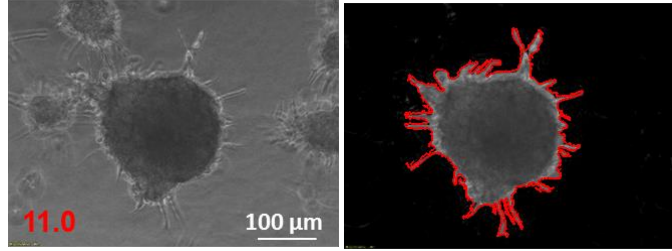




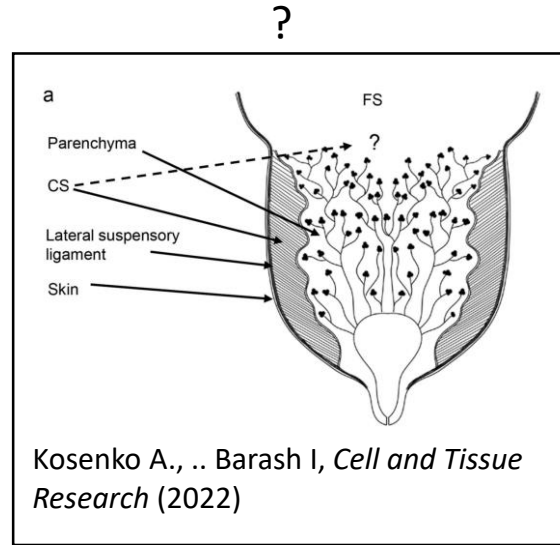
Holistic approach: biology, mechanics, structure, environment

437

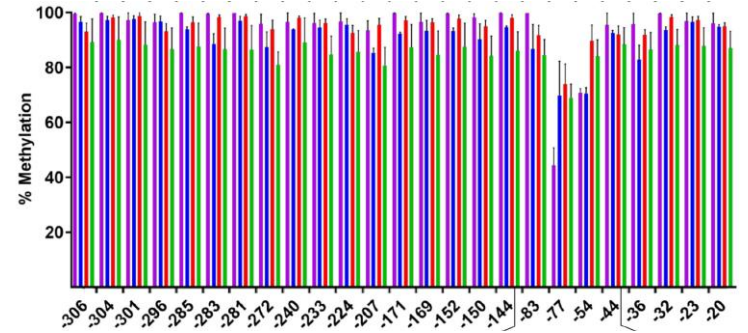
Aggregates and tissues morphology



Brill-Karniely* et al., *Science Advances* 2020

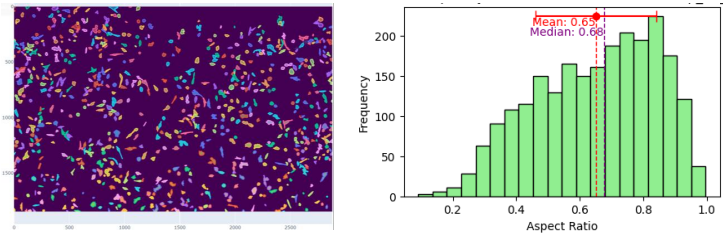


Epigenetics



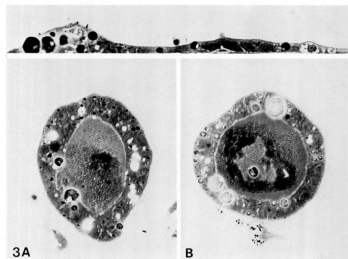
Havusha-Laufer S., .. Barash I, *Journal of Mammary Gland Biology and Neoplasia* (2020)

Cell morphology



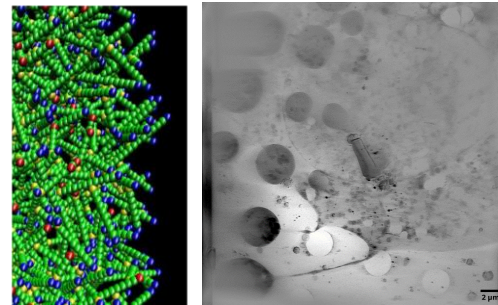
YBK lab, unpublished

Micro-environment



Bissell & Barcellos-Hoff, *J. Cell Sci. Suppl.* 1987

Intracellular dynamics



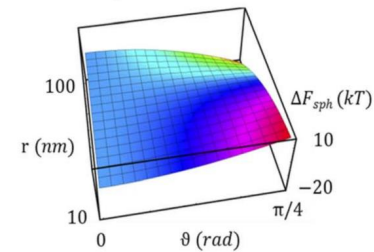
YBK thesis

YBK lab, with M. Elbaum (WIS) & S. Kapishnikov (SiriusXT), unpublished

Physical models

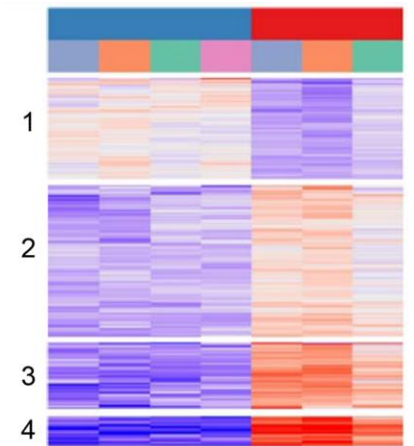
$$\frac{d\Delta F_{\text{cyl}}}{d\theta} = 2l \left(\frac{\kappa}{r} - \epsilon r \right)$$

$$\kappa/\epsilon = 2250 \text{ nm}^2$$



Brill-Karniely* et al., *Nanoscale Adv.* 2022

Genetics

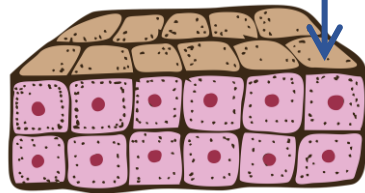
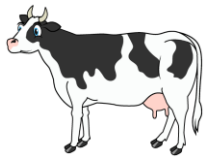
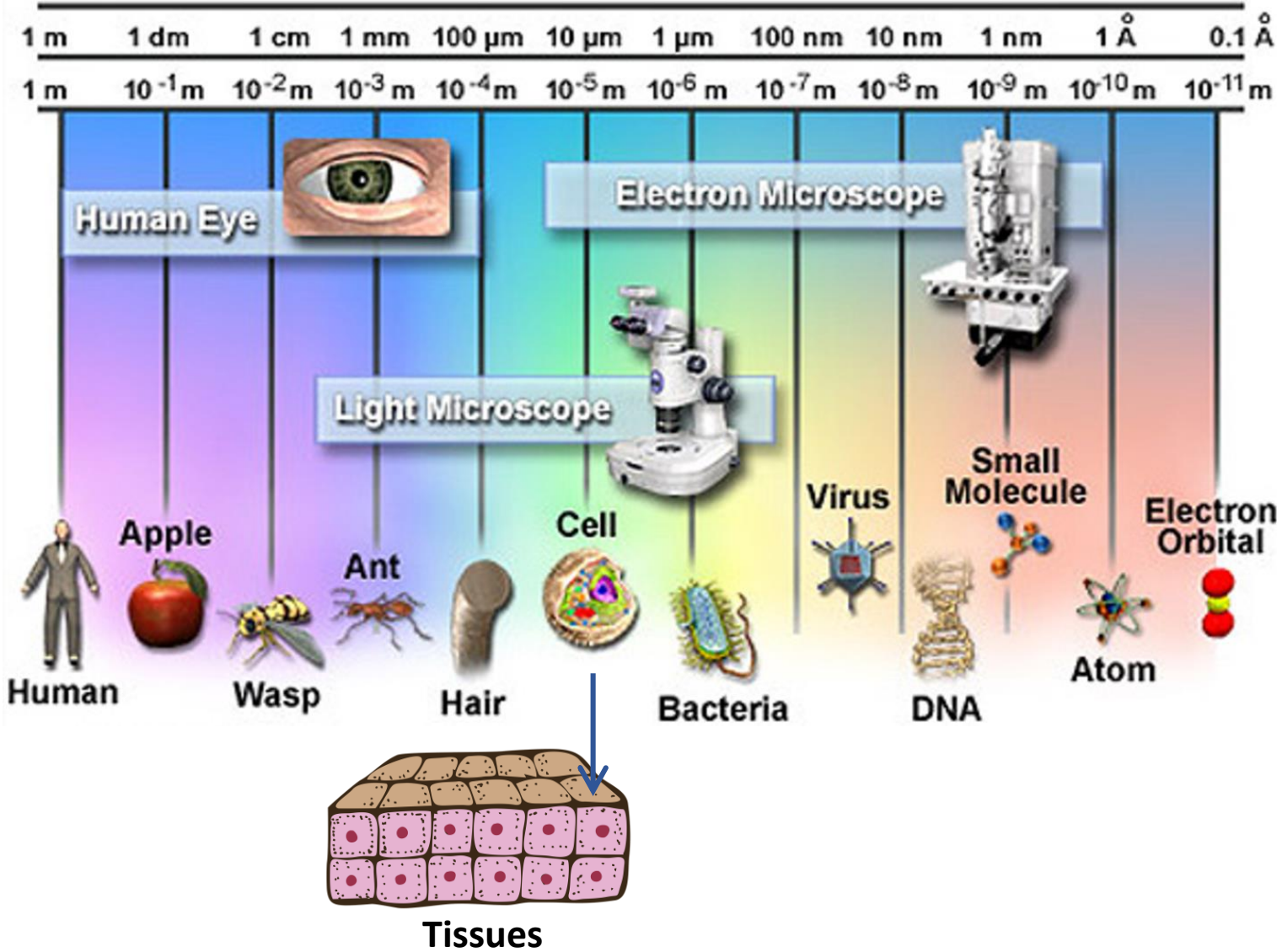


Kosenko A., .. Barash I, *Cell and Tissue Research* (2022)



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Relative Sizes and Detection Devices

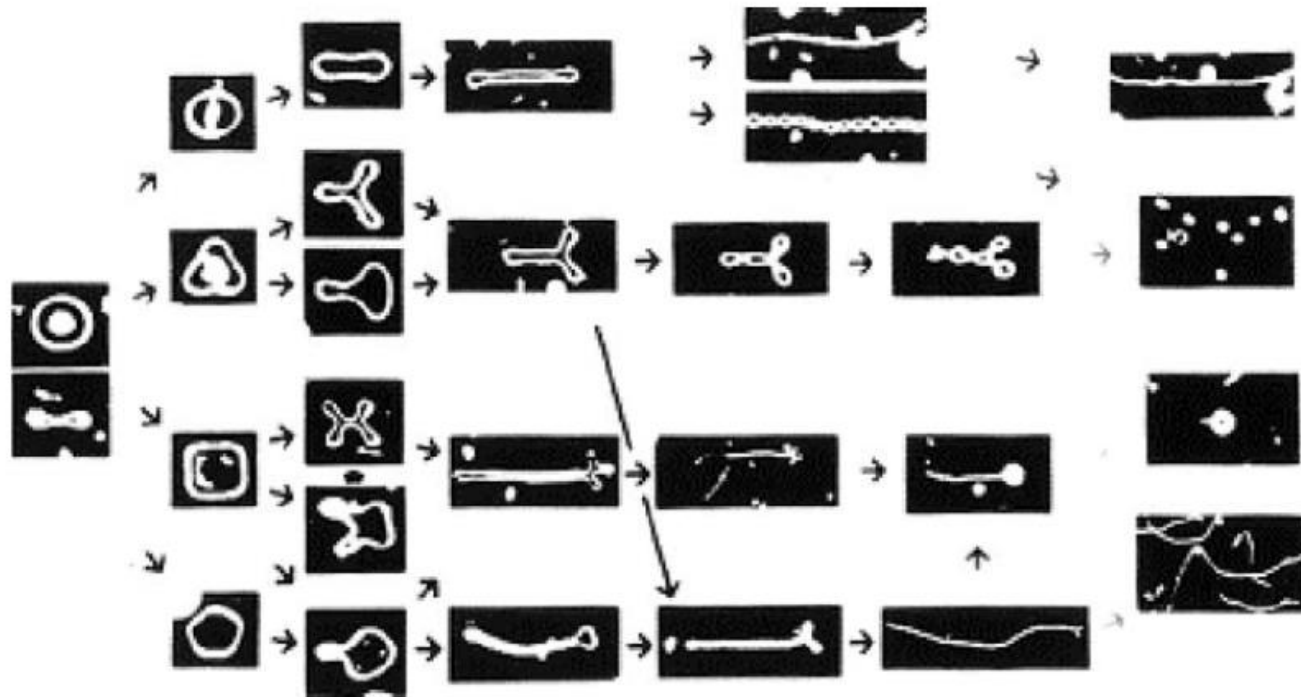
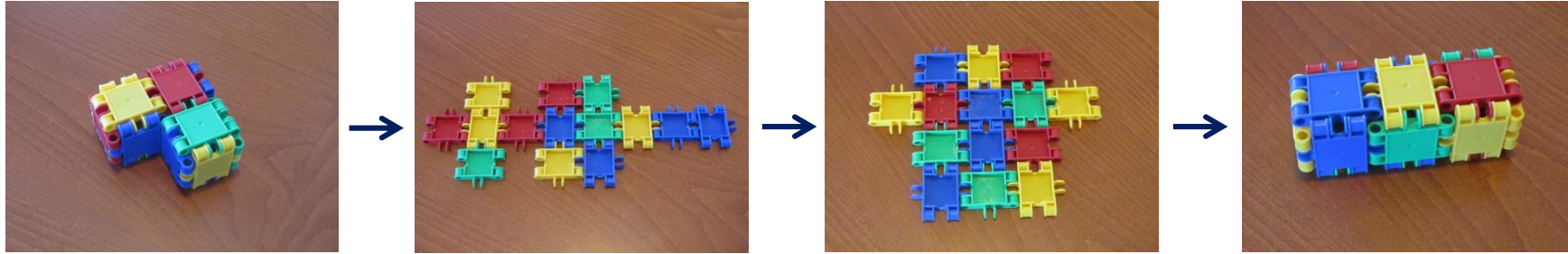


Tissues



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Same composition – different structure and function



H. Hotani J. Mol. Biol. (1984)

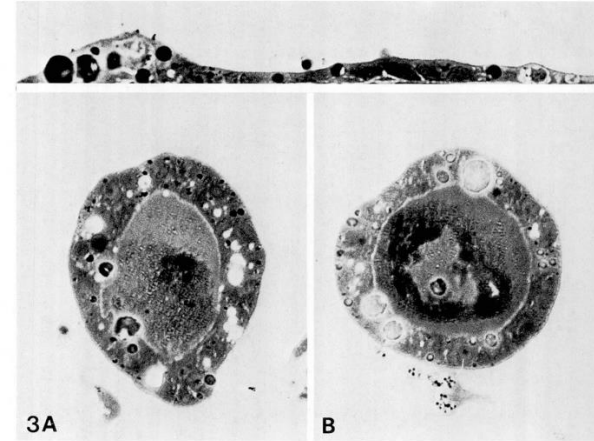


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Form ↔ Function



Mina J. Bissell, Berkeley U.



Bissell & Barcellos-Hoff, *J. Cell Sci. Suppl.* 1987

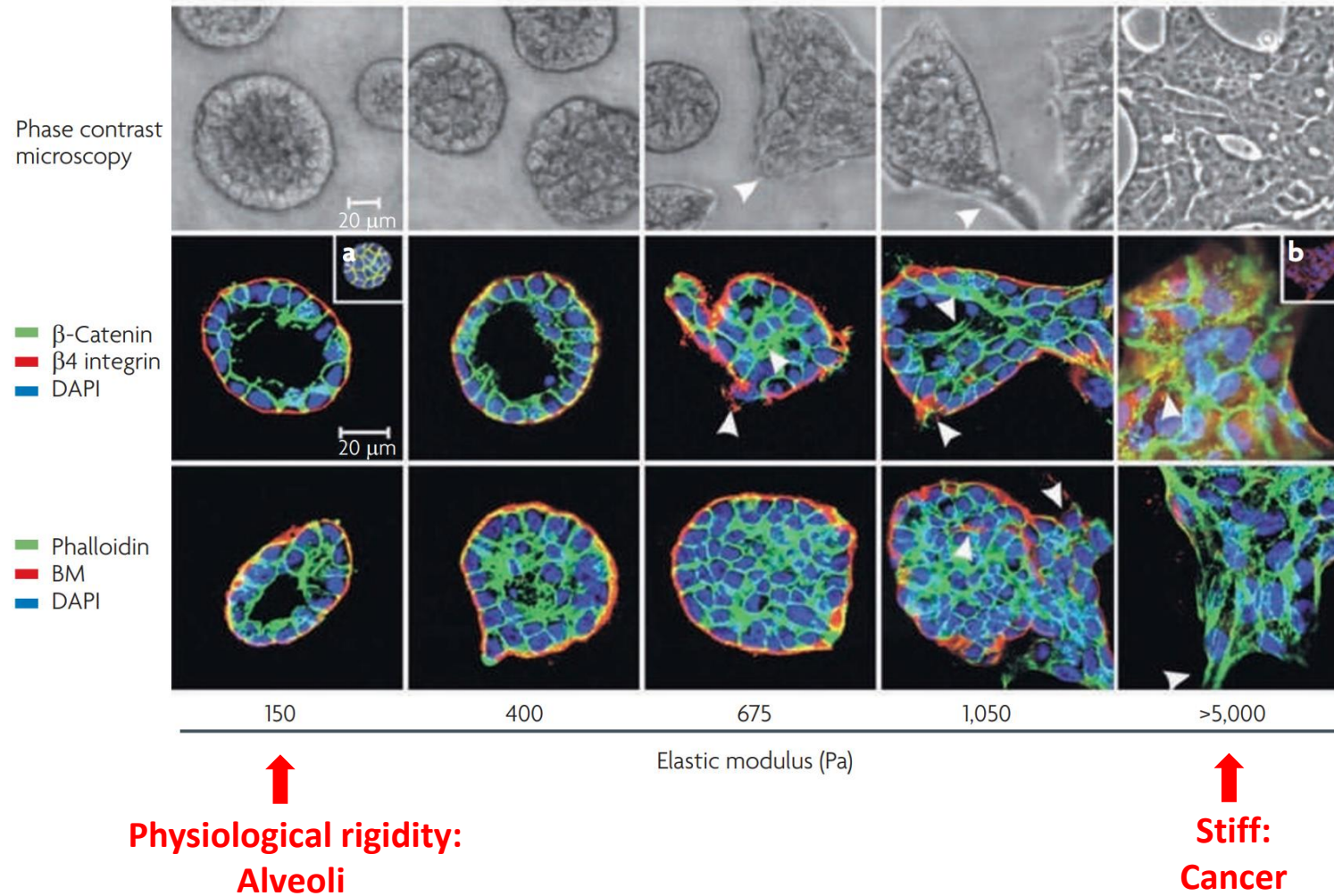
The basic functional unit for expression of milk proteins:

Mammary epithelial cells + ECM scaffold.



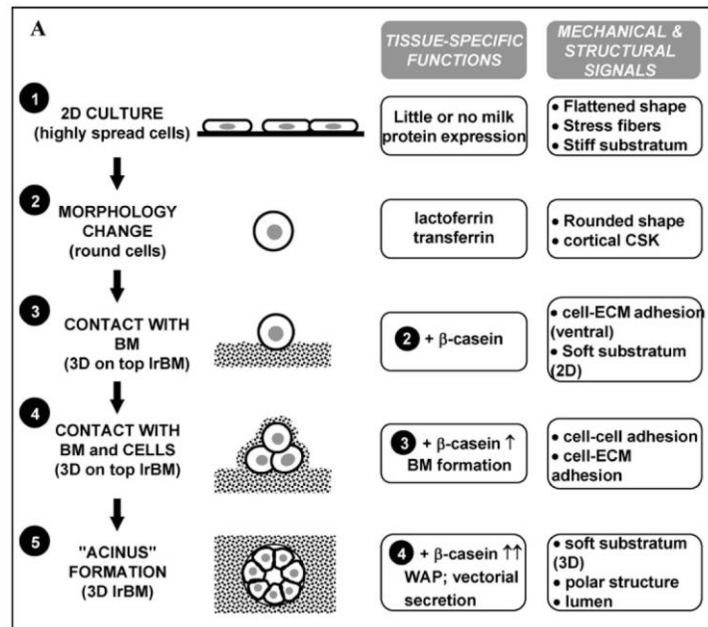
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Importance of mechanical environment

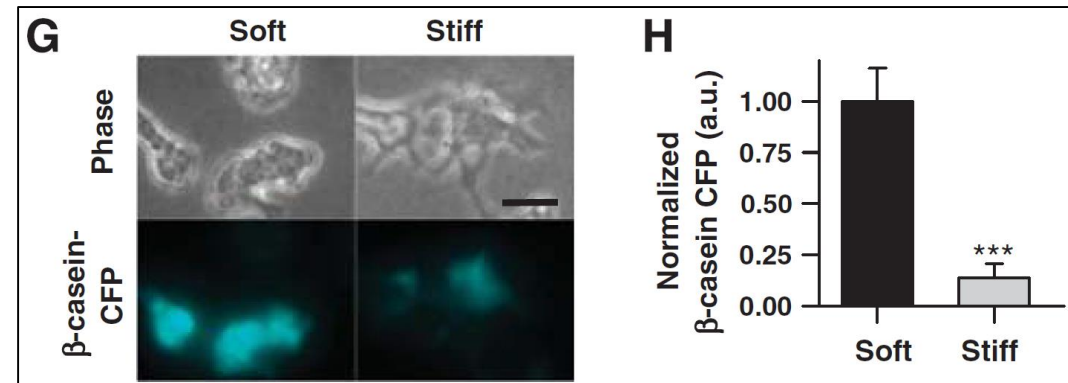




Importance of mechanical environment



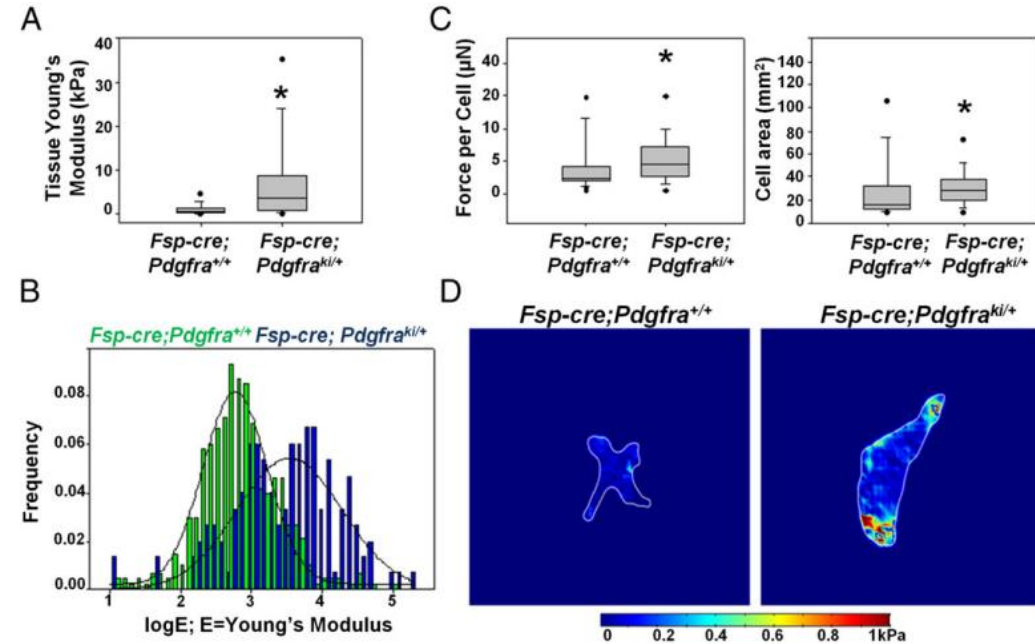
Alcaraz et al., *Journal of Mammary Gland Biology and Neoplasia* 2004



Alcaraz et al., *The EMBO Journal* 2008



Mammary gland function is correlated with cell and tissue rigidity

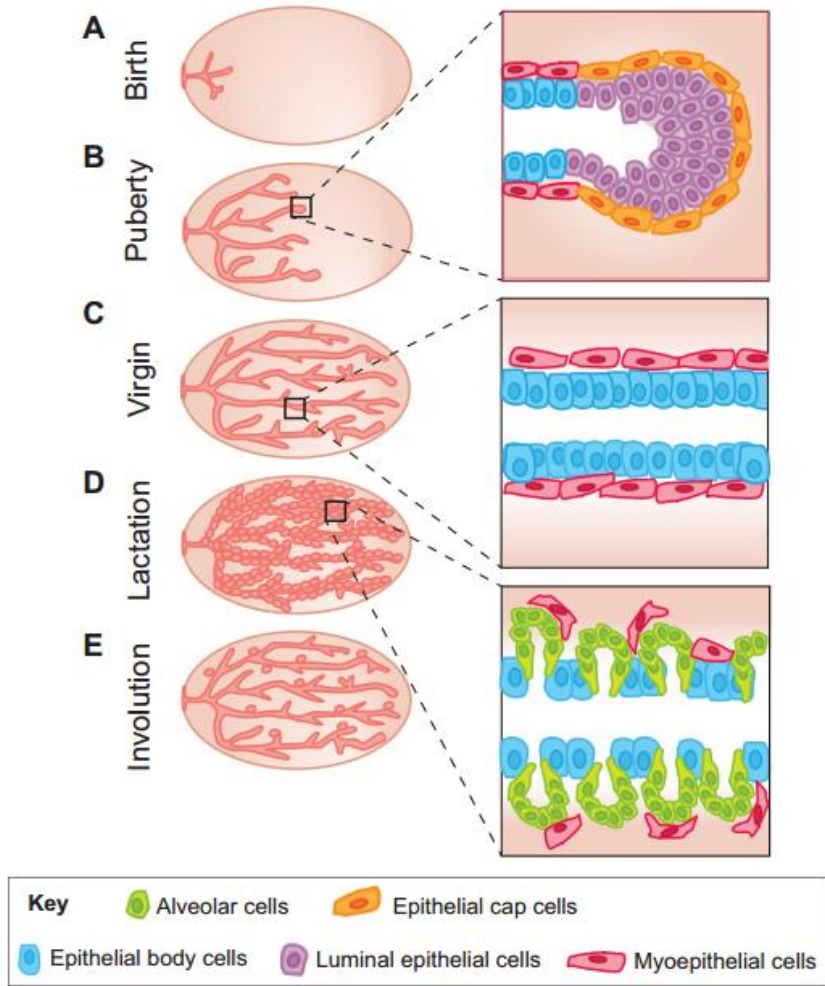


Hammer et al., *Neoplasia* 2017

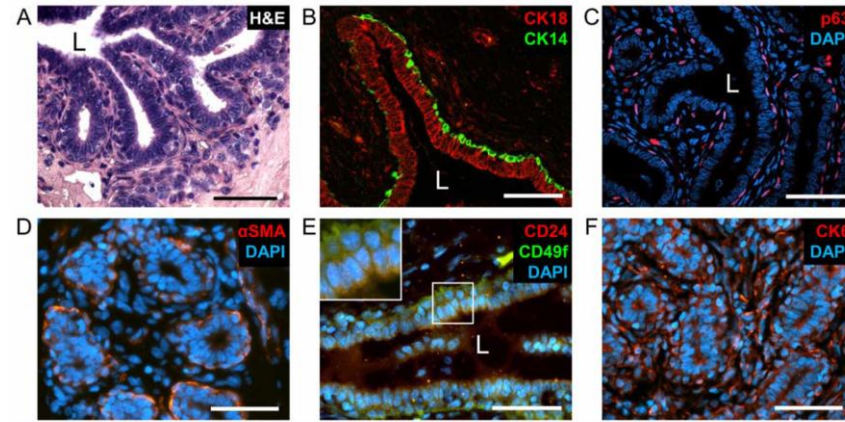


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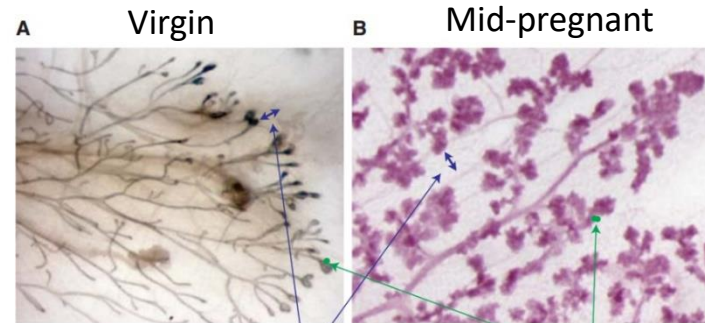
Massive physical alterations of mammary glands during development



Inman, ..., Bissell, *Development* 2015



Rauner & Barash, *PLoS ONE* 2012



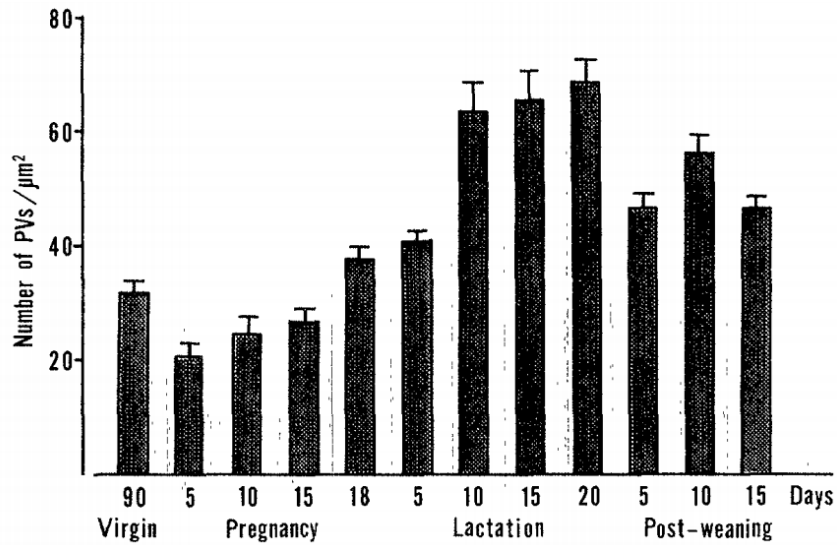
Long-range endocrine: E2, Pg, g/c, Prl
 Stromal/epithelial: ARreg, FGF, HGF, IGF
 Cell adhesion: e.g. integrin, cadherin

Muschler & Streuli, *CSH Perspect Biol* 2010

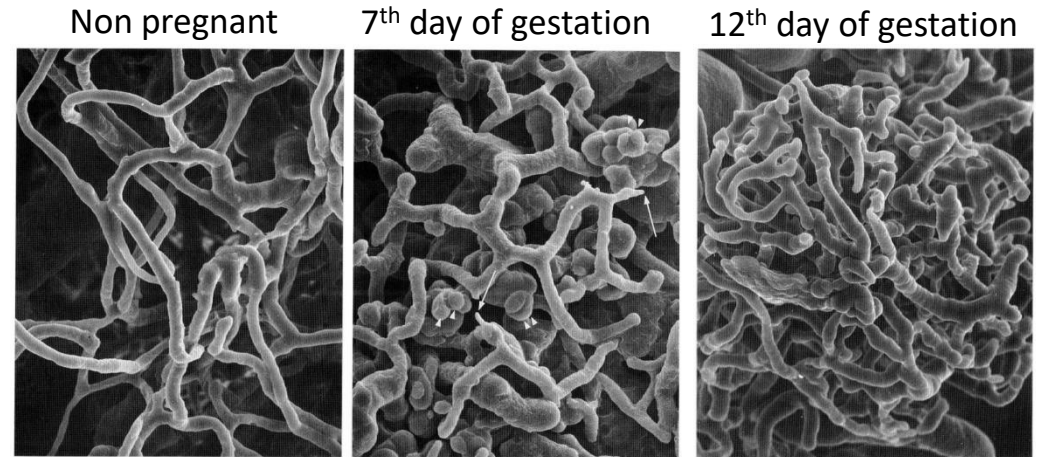


Massive physical alterations of mammary glands during development

Change in vascular density: more than 3 fold



Matsumoto et al., *J. of Vet. Med. Sci.* 1992



Yasugi et al., *Arch. Histol. Cytol.* 1989

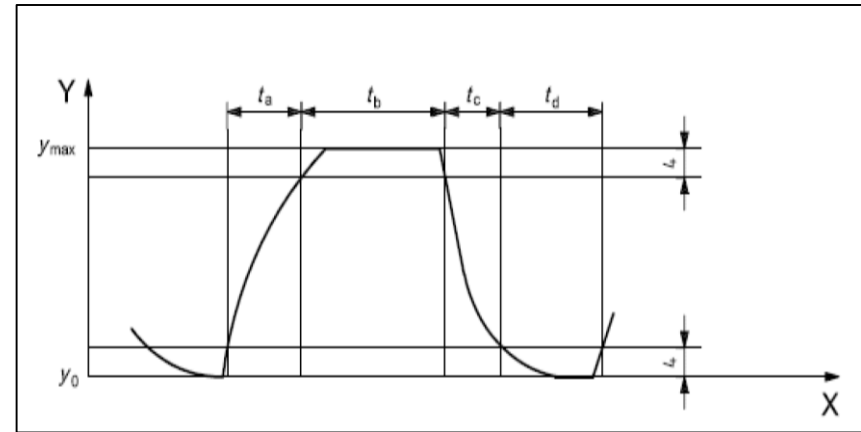


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Vacuum forces during milking



From a tour guided by Prof. Uzi Moallem (Volcani Inst.)



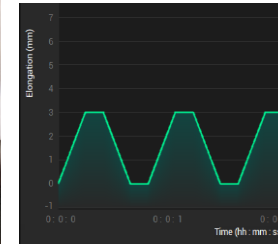
Israel recommendation for milking apparatus,
Israel Dairy Board 2007



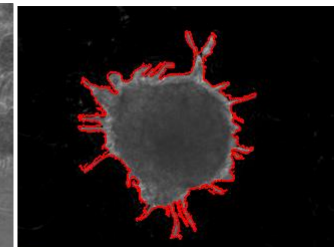
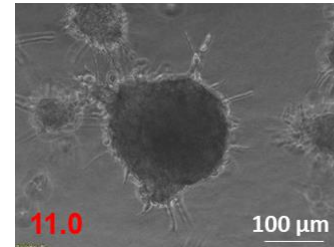
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Outline

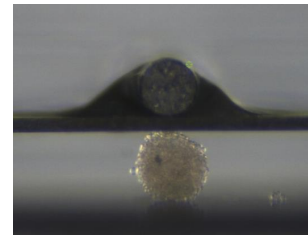
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- Applicative biomechanical research



- Present research and perspectives

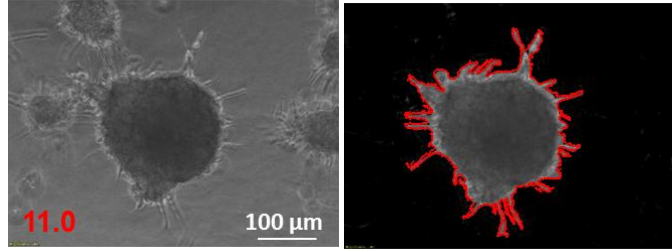




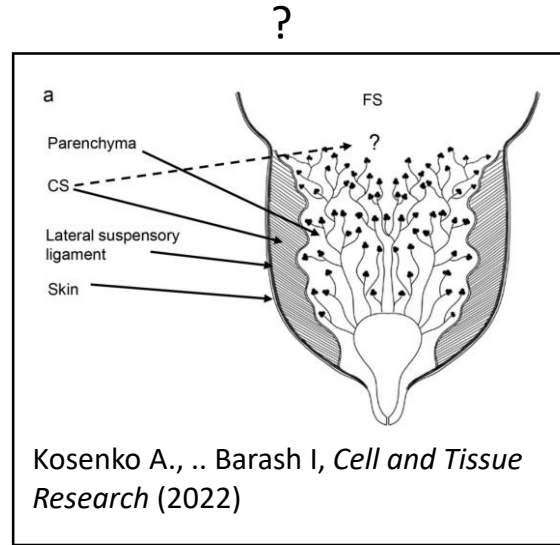
Holistic approach: biology, mechanics, structure, environment

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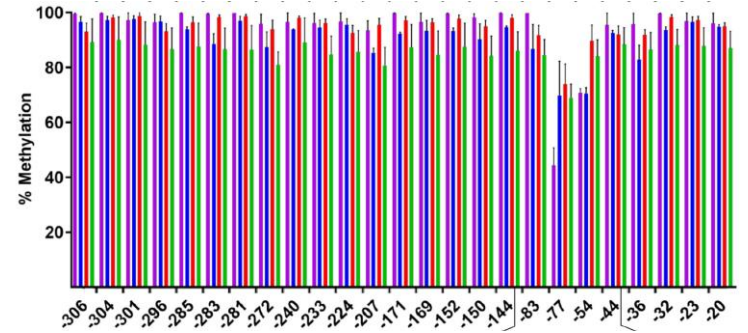
Aggregates and tissues morphology



Brill-Karniely* et al., *Science Advances* 2020

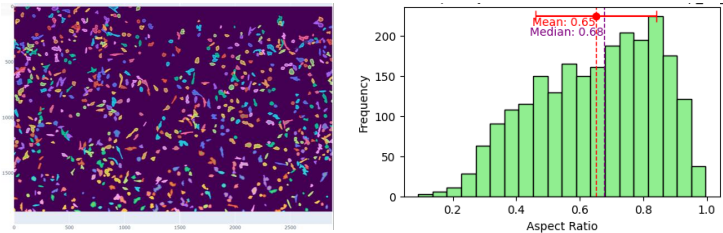


Epigenetics



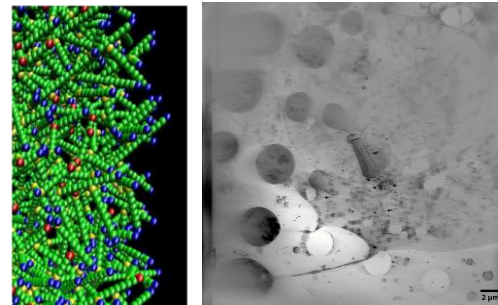
Havusha-Laufer S., .. Barash I, *Journal of Mammary Gland Biology and Neoplasia* (2020)

Cell morphology



YBK lab, unpublished

Intracellular dynamics



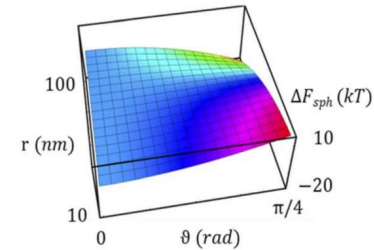
YBK thesis

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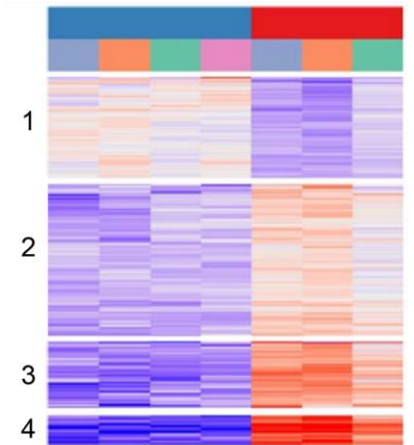
$$\frac{d\Delta F_{cyl}}{d\theta} = 2l \left(\frac{\kappa}{r} - \epsilon r \right)$$

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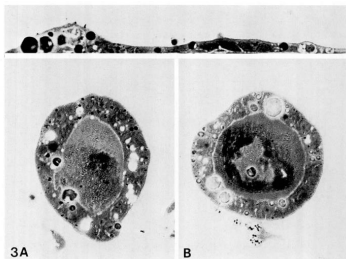
Brill-Karniely* et al., *Nanoscale Adv.* 2022

Genetics



Kosenko A., .. Barash I, *Cell and Tissue Research* (2022)

Micro-environment

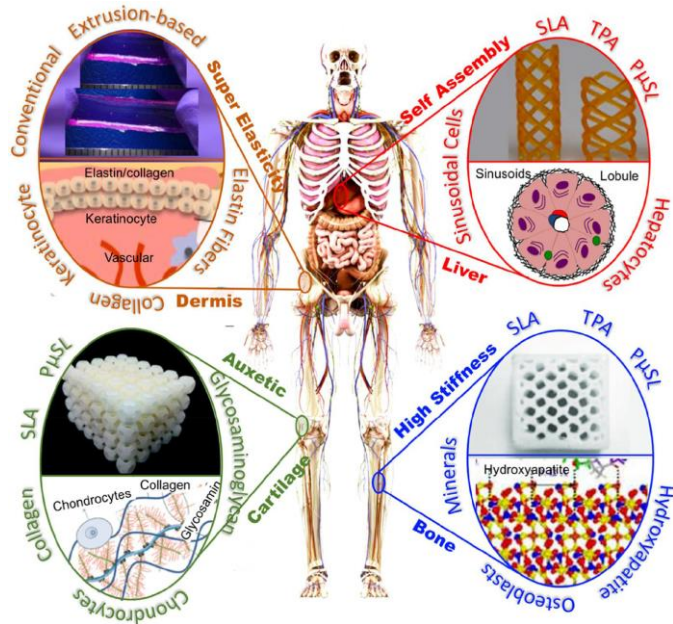


Bissell & Barcellos-Hoff, *J. Cell Sci. Suppl.* 1987



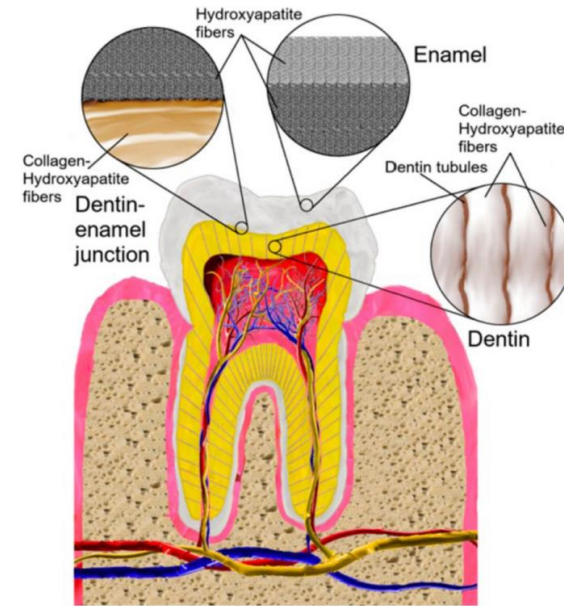
Applicative biomechanical research: tissue engineering and transplants

Tissue engineering



Dogan et al., *Applied Materials Today* 2020

Dental medicine



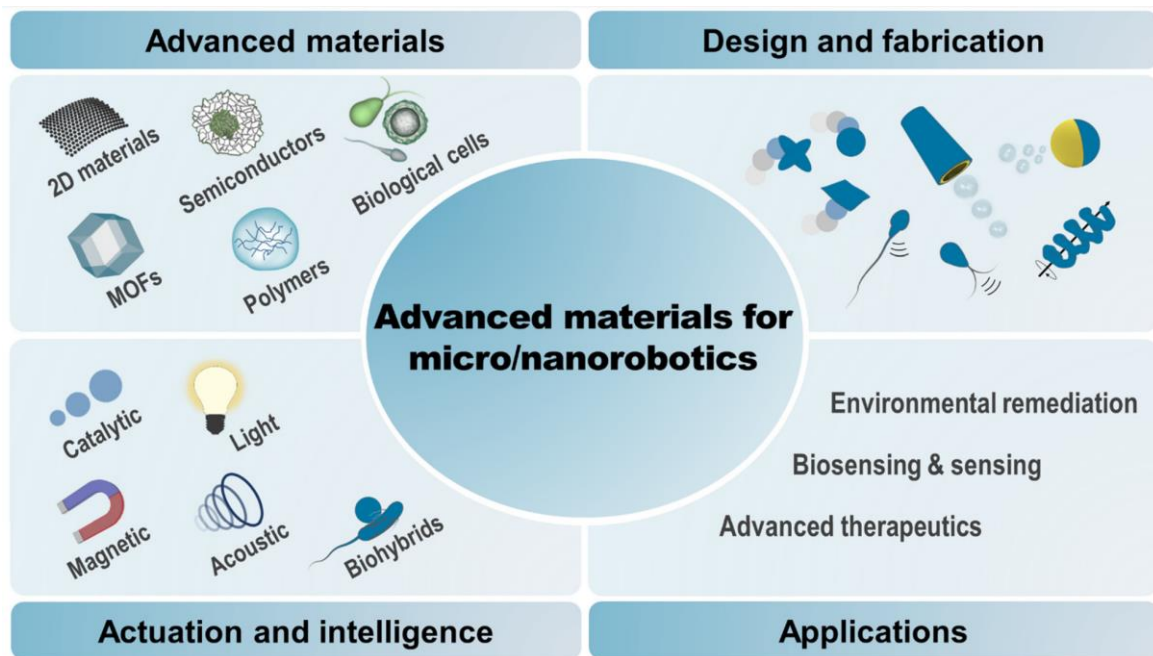
Alsuraif et al. *Beni-Suef Univ J Basic Appl Sci* 2024



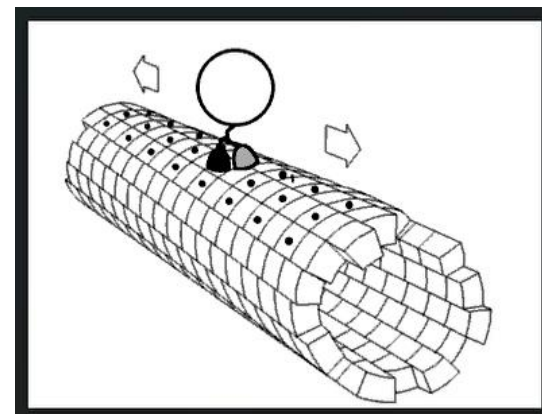
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Applicative biomechanical research: nano / micro robotics

Nano / micro robotics



Kim et al., *Chem. Soc. Rev.* 2024

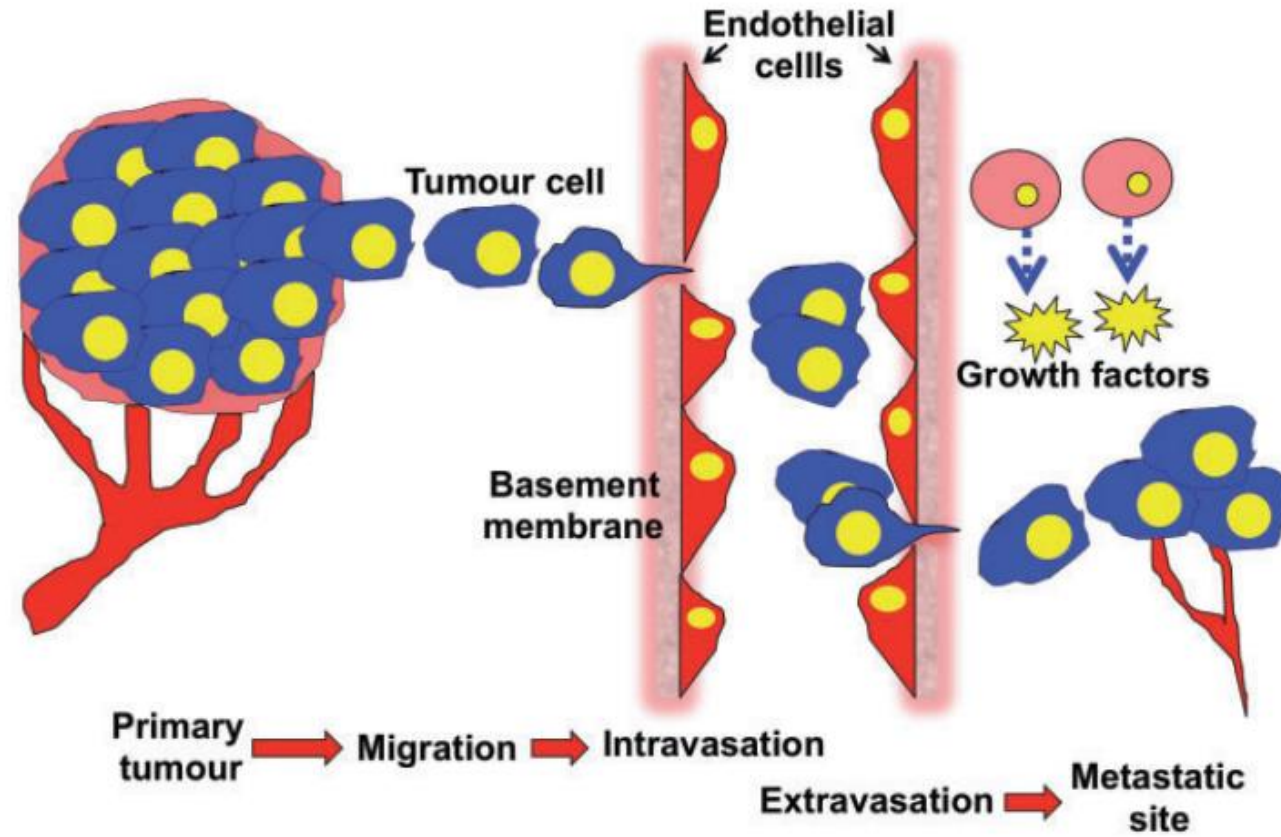


Wikipedia



Applicative biomechanical research: cancer research

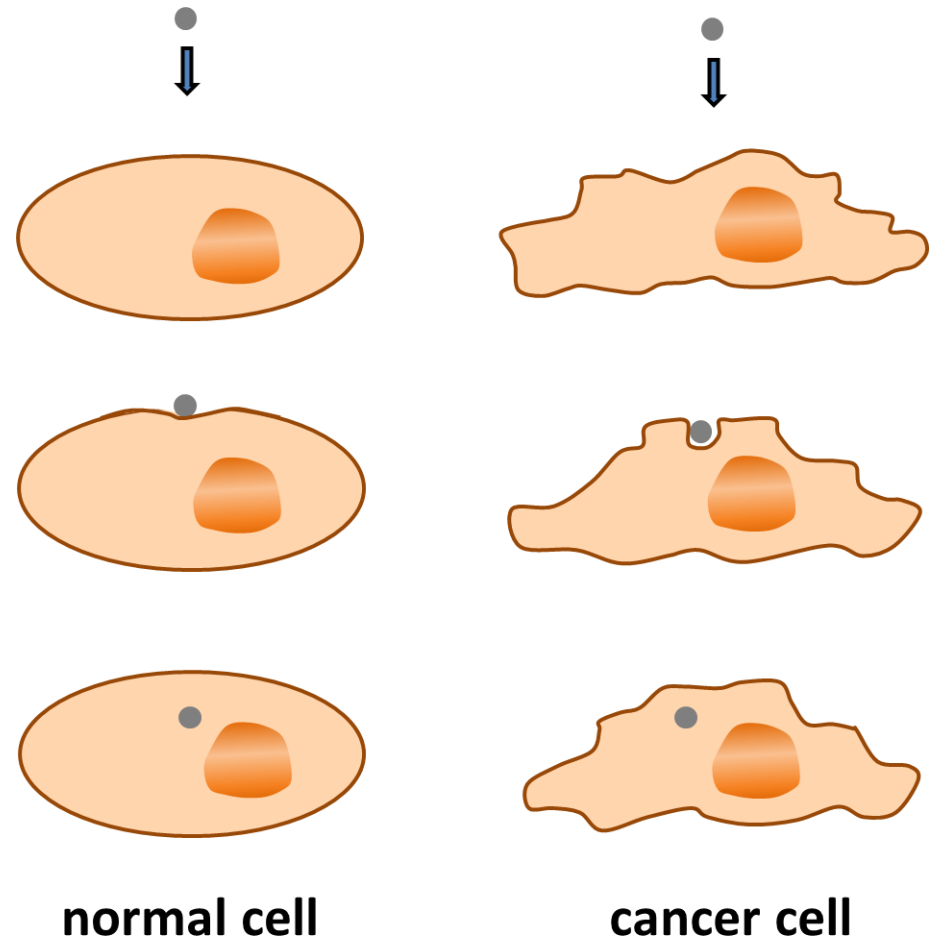
Cancer cells are more deformable than normal cells





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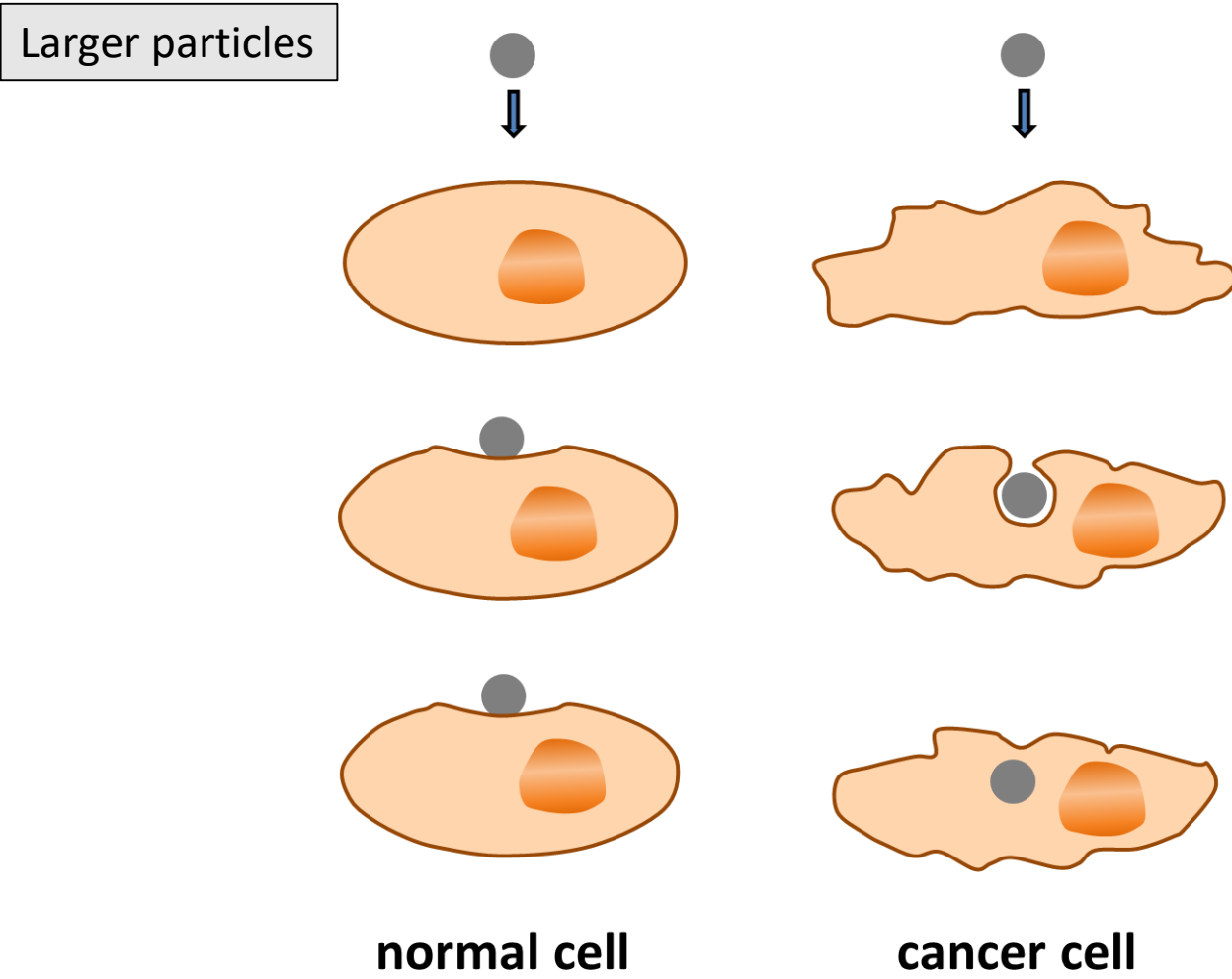
Mechanical targeting in cancer therapy





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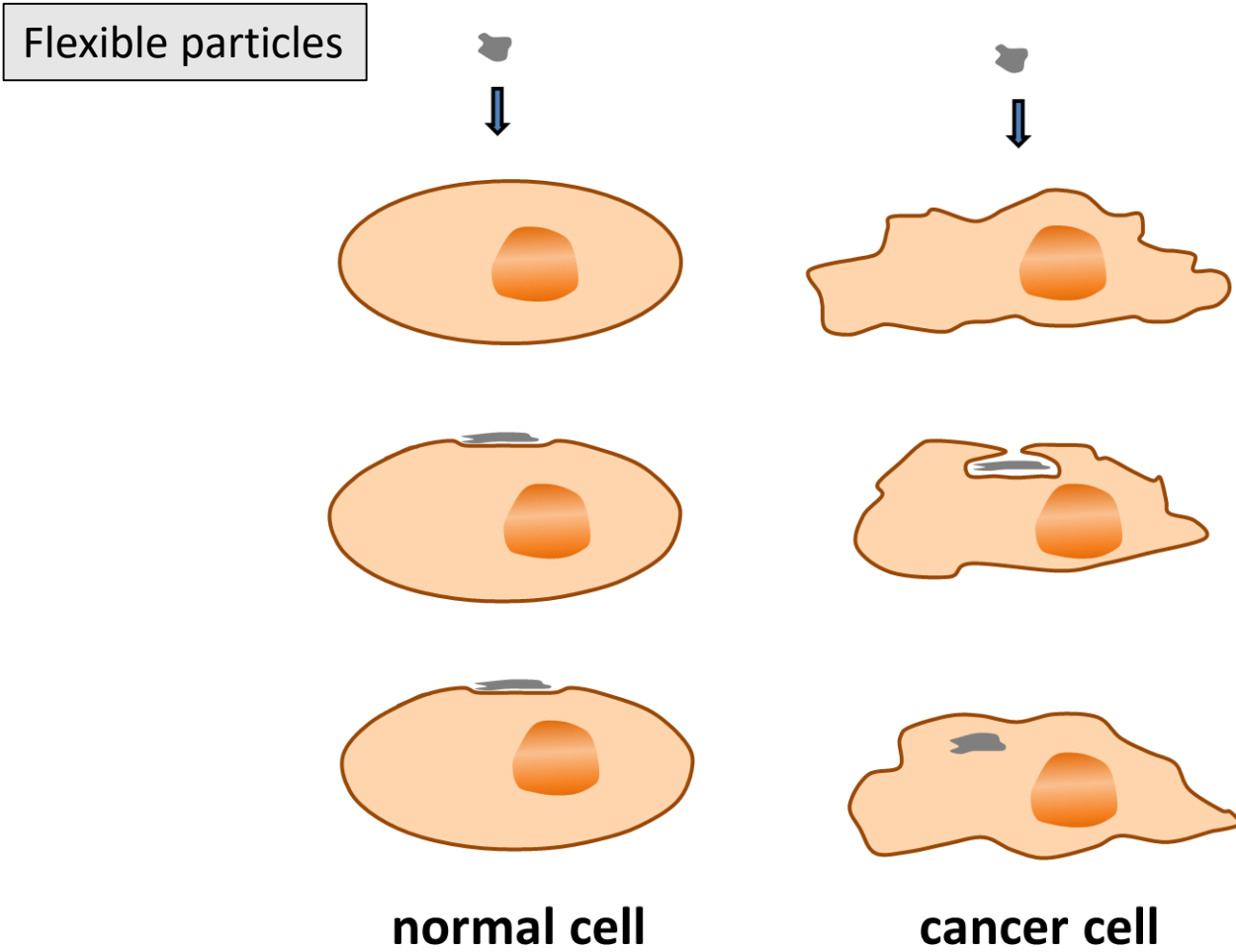
Mechanical targeting in cancer therapy





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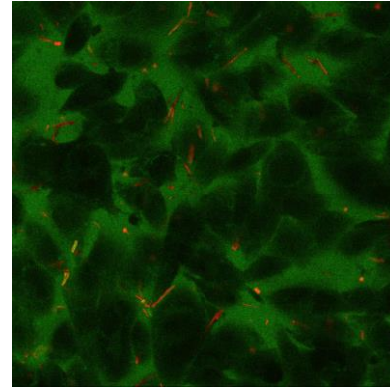
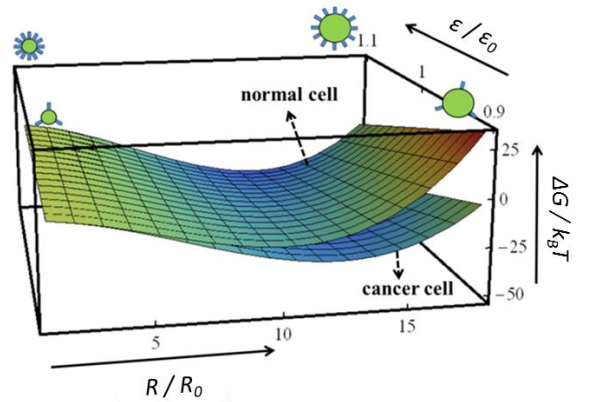
Mechanical targeting in cancer therapy



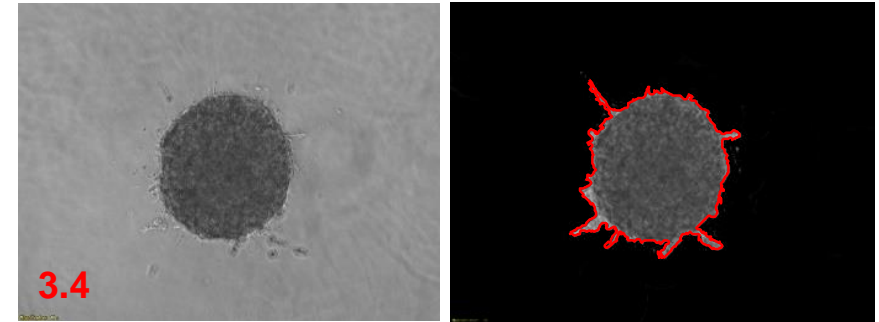


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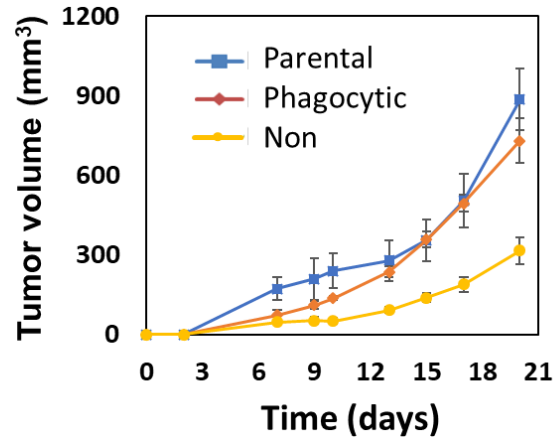
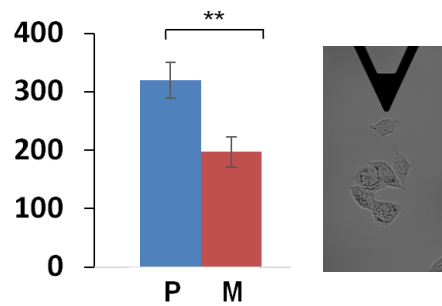
Mechanical targeting in cancer therapy



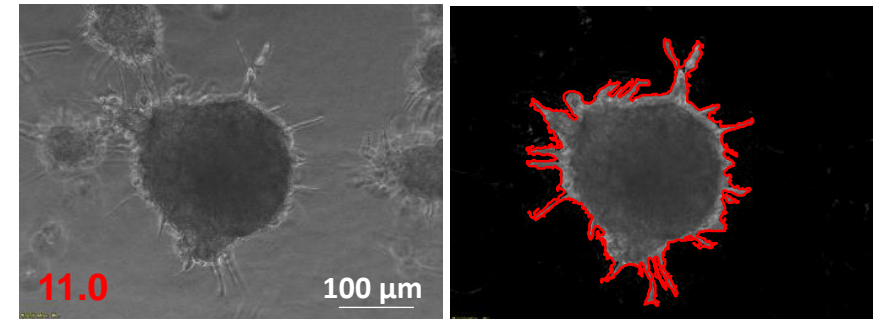
Primary



Young's modulus / Pa



Metastatic

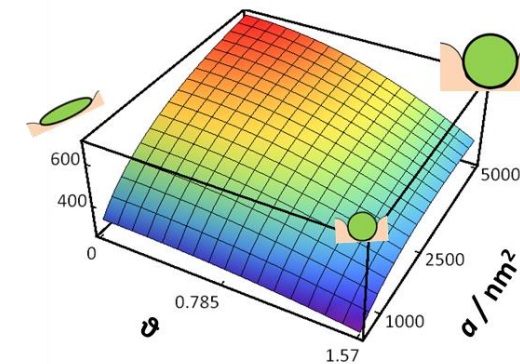
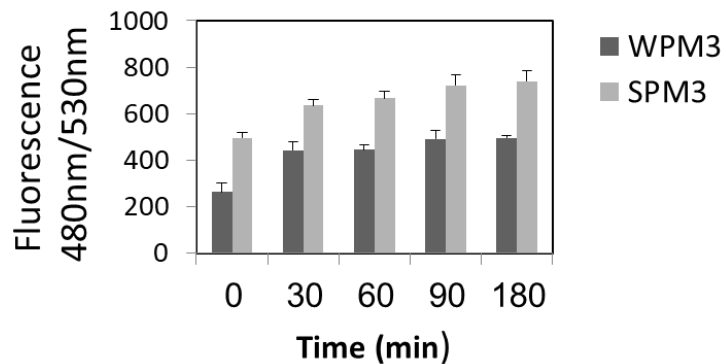
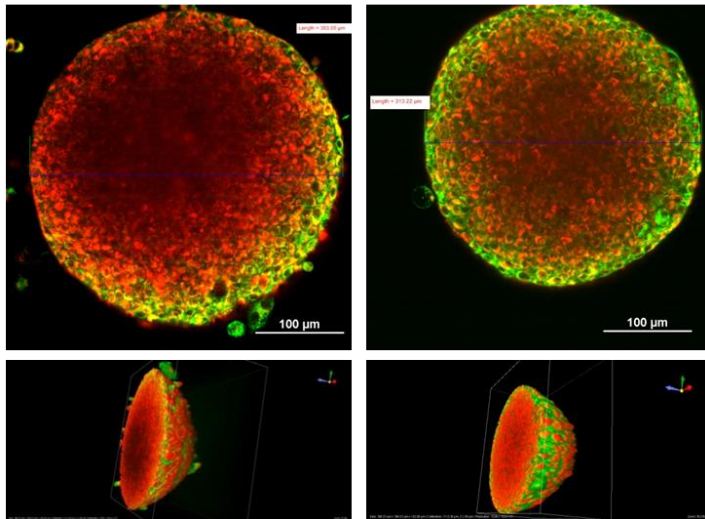




Mechanical targeting in cancer therapy

Flexible (WPM)

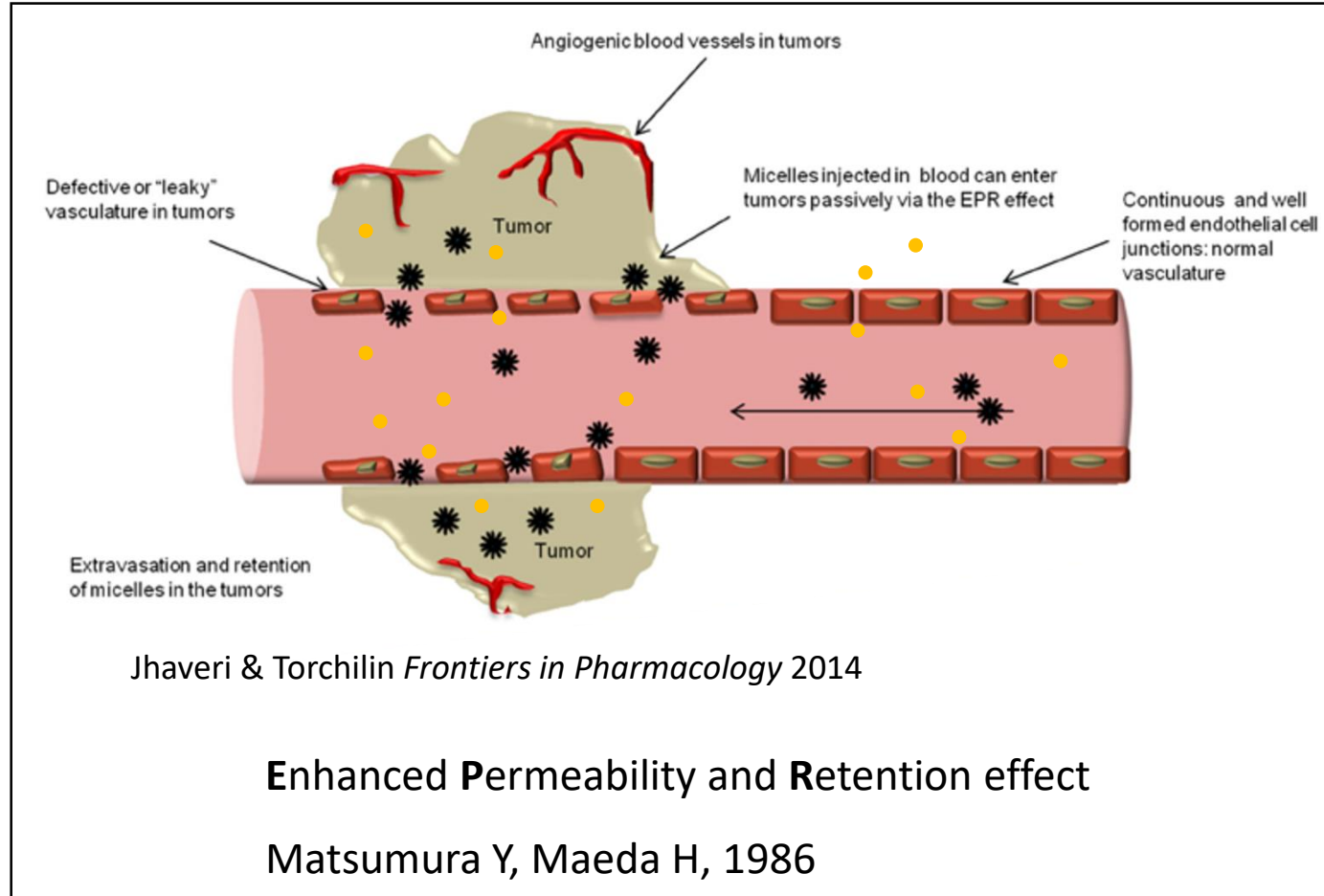
Rigid (SPM)



$$\Delta F = -\varepsilon \cdot a + 2\kappa_c(1 - \cos\theta) + \kappa_r \sqrt{\frac{2a}{\pi(1 - \cos\theta)}} \cdot \sin\theta$$



The Enhanced Permeability and Retention effect

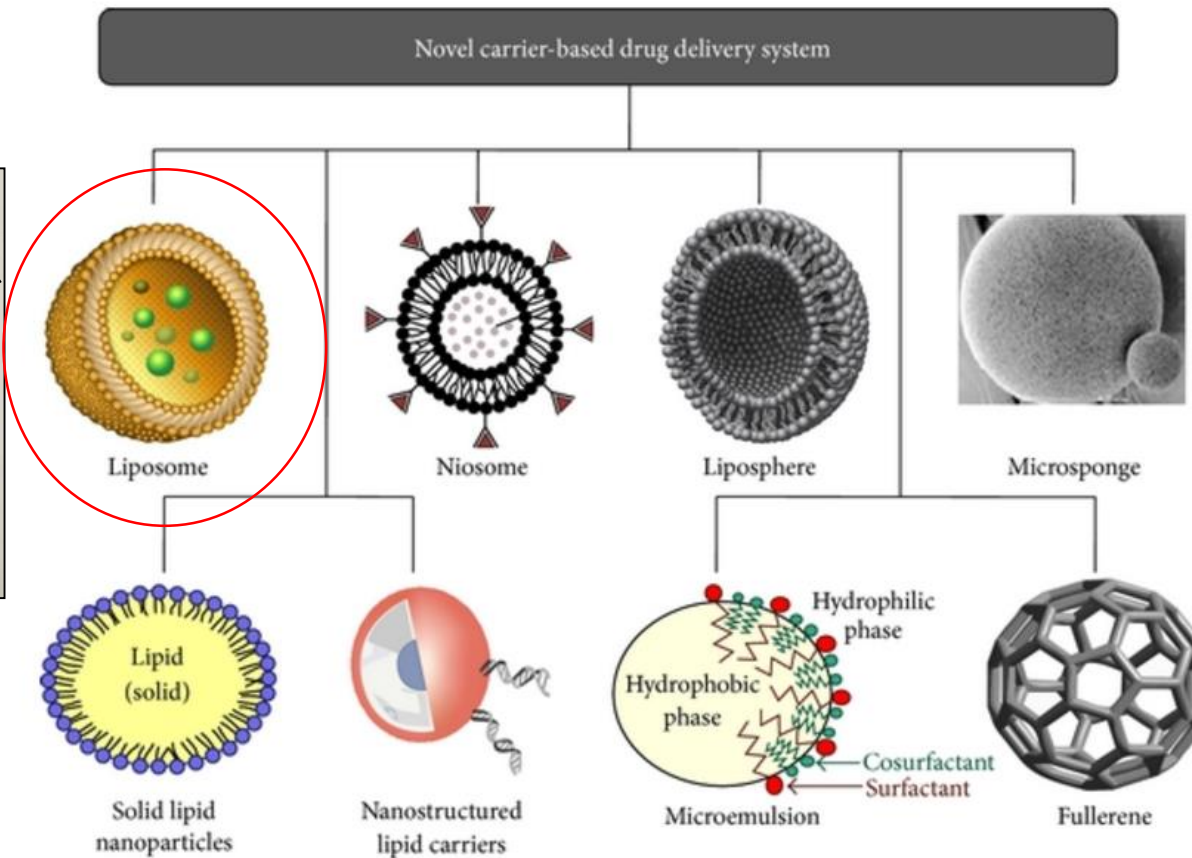




Drug delivery systems



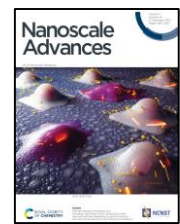
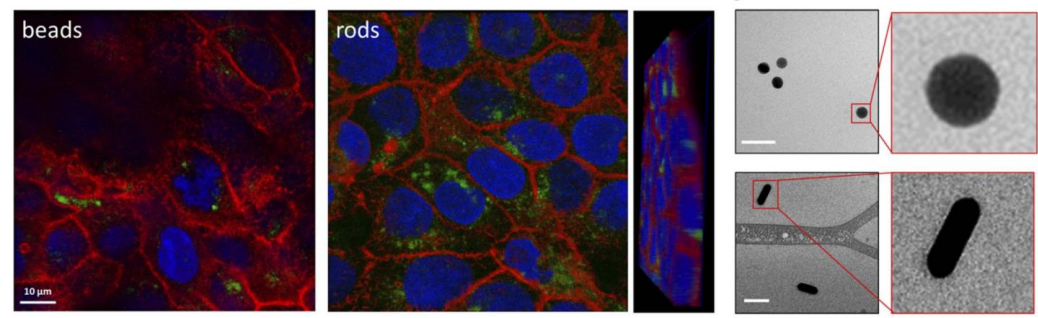
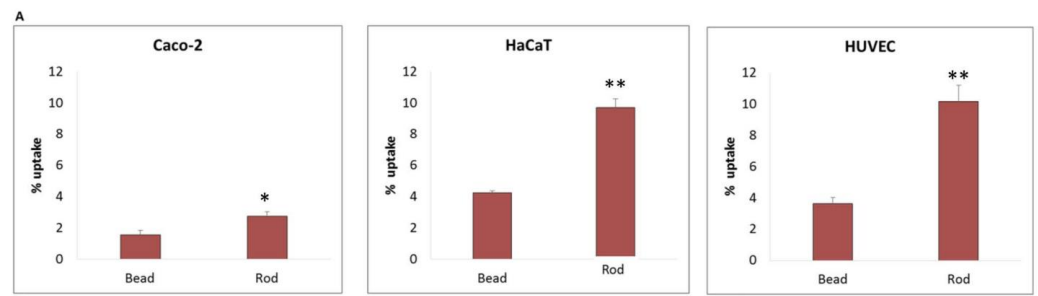
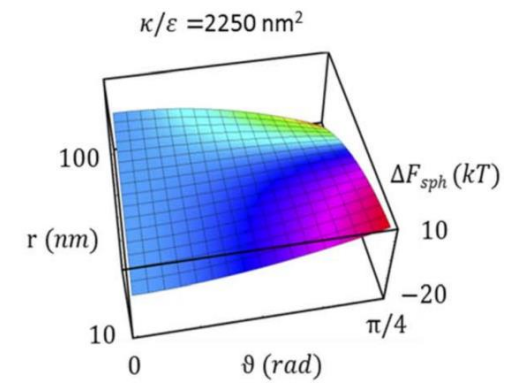
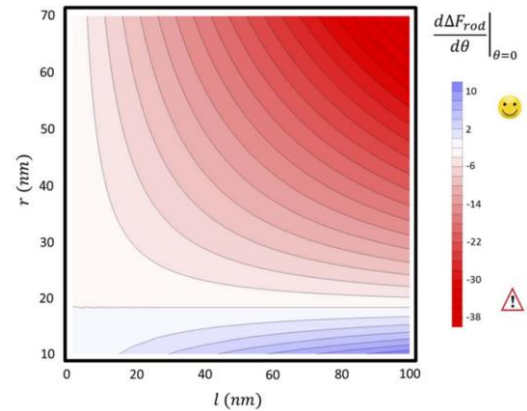
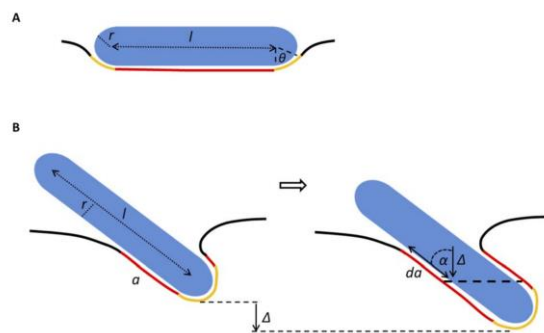
פרופ' יחזקאל ברנהולץ
פרופ' אלברטו גביזון





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Cytotoxicity



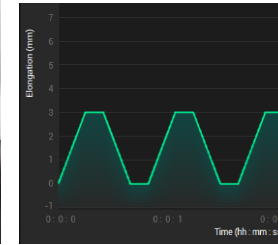
Brill-Karniely* et al., *Nanoscale Adv.* 2022



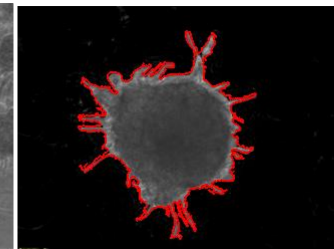
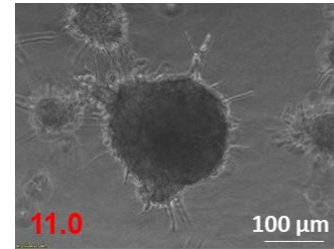
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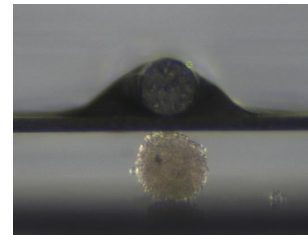
□ Why are biomechanical aspects important in the study of bovine mammary glands?



□ Applicative biomechanical research



□ Present research and perspectives

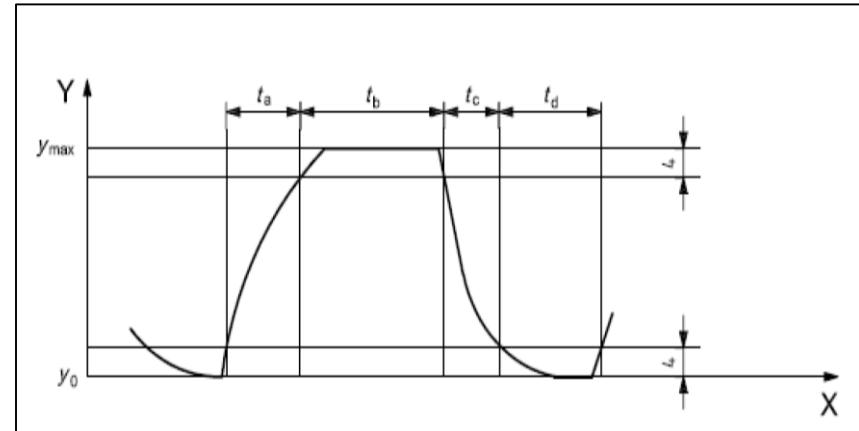




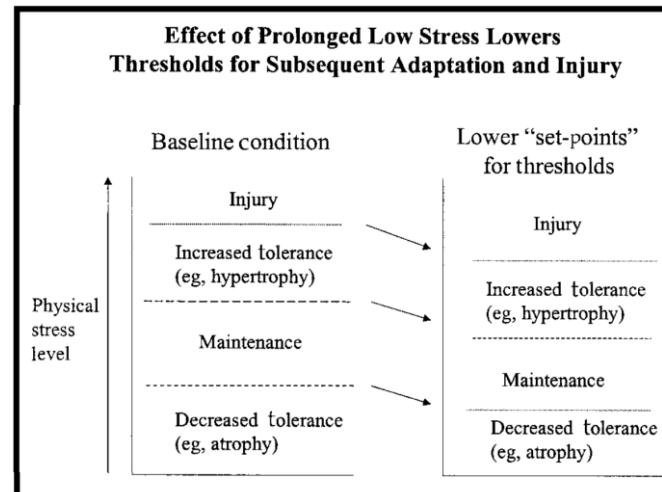
Vacuum forces during milking



From a tour guided by Prof. Uzi Moallem (Volcani Inst.)



Israel recommendation for milking apparatus, Israel Dairy Board 2007



Mueller et al., Physical Therapy . Volume 82 . Number 4 . April 2002

8.7 ואקום ביחידת החליבה:
 ההוראות למשתמש לחליבה יציין, לקצב זרימה מוגדר (כאשר לפחות אחד מהנתונים בטבלה מס. 1 נבחר):
 א. רמת הוואקום הממוצעת בבטנה ו \ או רמת הוואקום הממוצעת הרצויה בבטנה במשך שלב B ושלב D של הפעימה.
 ב. רמת הוואקום הנומינלית המקבילה בקו החלב. רמת ואקום הנומינלית תהיה מבוססת על מפל הוואקום הממוצע כפי שנמדד בסעיף 8.6 בפרק ג'.
 הערה: הן המחקר והן הנסיון בשדה מראים שרמת ואקום ממוצעת בבטנה בתחום שבין **32 kPa - 42 kPa** במשך שיא זרימת החלב בחליבה של פרות מבטיח כי רוב הפרות יחלבו במהירות, בעדינות והיטב. במקביל רמת

ההמלצות הישראליות למתקני חליבה, מאל"ה – מועצת החלב 2007



In vivo: Effects of pulsation ratio and rate

Effects of Pulsation Ratio, Pulsation Rate, and Teatcup Liner Design on Milking Rate and Milk Production

CRAIG V. THOMAS¹
University of California
Cooperative Extension
Fresno 93702

DONNA K. FORCE and DAVID H. BREMEL
Department of Animal Science
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TABLE 4. Least squares means by pulsation ratio.

Pulsation ratio	Fat %	Protein %	SCC (× 1000)	Total yield per milking (kg)	Machine-on time per milking (min)
50:50	3.96	3.43	108	12.1 ^a	8.44 ^a
60:40	3.97	3.39	112	12.6 ^{ab}	8.00 ^b
70:30	4.09	3.44	105	12.6 ^b	7.47 ^c
Average flow rate (kg/min)	Yield at 2 min (kg)	3.5% FCM per milking (%)	Fat yield (kg)		
50:50	1.5 ^a	4.5 ^a	38.7 ^a	48 ^a	13.0 ^a
60:40	1.6 ^b	5.2 ^b	42.2 ^b	49 ^{ab}	13.4 ^{ab}
70:30	1.7 ^c	5.6 ^c	45.5 ^c	52 ^b	13.8 ^b

^{a,b,c}Means with different superscripts differ ($P < .05$).

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Milk flow-controlled changes of pulsation ratio and pulsation rate affect milking characteristics in dairy cows

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Table 1. The milking machine settings and their changes when milked with milk flow-controlled b-phase

Milk flow rate, kg/min	Pulsation ratio	Pulsation rate, cycles/min	a-+b-phase, ms
0–2:0	60/40	55	655
2:0–2:5	63/37	53	713
2:5–3:0	65/35	51	765
3:0–3:5	68/32	48	850
3:5–4:0	70/30	45	933
4:0–4:5	73/27	43	1019
4:5–5:0	74/26	42	1057
5:0+	75/25	42	1071

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The effect of pulsation ratio on teat condition, milk somatic cell count and productivity in dairy cows in automatic milking

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Table 4. Milk yield, strip milk fat content and strip milk somatic cell count (SCC) in control (C) and treated (T) quarters after pulsation ratio treatments were applied, and p-values for the differences between pre- and post-treatment values. Values presented are mean ± se, n = 320

	Milk yield (kg per udder half)		Fat content (% per udder half)		SCC† (×1000 cells/ml per quarter)		P values‡		
	C	T	C	T	C	T	Milk yield	Fat content	SCC
60:40	5.3 ± 0.1	5.3 ± 0.1	9.4 ± 0.3	8.9 ± 0.3	4.90 ± 0.05 (79)	4.95 ± 0.05 (89)	0.21	0.17	0.13
70:30	5.3 ± 0.1	5.3 ± 0.1	9.1 ± 0.3	9.0 ± 0.3	5.04 ± 0.05 (110)	4.96 ± 0.05 (91)	0.54	0.86	0.69
75:25	5.6 ± 0.1	5.8 ± 0.1	8.7 ± 0.2	9.0 ± 0.2	5.12 ± 0.05 (132)	5.16 ± 0.05 (144)	0.54	0.40	0.54

†Somatic cell count, Log₁₀ values with antilog values within brackets

‡Statistical significance of the difference between quarters compared with pre-treatment

Relationship of Pulsation Rate, Pulsation Ratio, and Vacuum Decrease Time to Milking Performance¹

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TABLE 2. Effect of static pulsation ratio on milking.

Variable	n ¹	Ratio				SE
		40:60	50:50	60:40	70:30	
Time to reach peak rate, min	48	2.03 ^a	1.79 ^{ab}	1.60 ^{ab}	1.26 ^b	.146
Peak rate, kg/min	48	.61 ^a	.69 ^b	.78 ^c	.85 ^d	.015
Average rate, kg/min	48	.48 ^a	.55 ^b	.61 ^c	.66 ^d	.011
Machine time, min	48	5.08 ^a	4.41 ^b	4.02 ^c	3.64 ^d	.084
Machine yield, kg	48	2.28	2.28	2.26	2.24	.011
Stripping yield, kg	48	.04 ^a	.05 ^a	.05 ^a	.07 ^b	.004
Total yield, kg	48	2.31	2.32	2.31	2.31	.011
Fat percent of total yield	48	4.10	4.15	4.12	4.13	.017

^{a,b,c,d}Means with different superscripts differ by Honestly Significant Difference ($P < .05$).

¹Number of observations in each mean.



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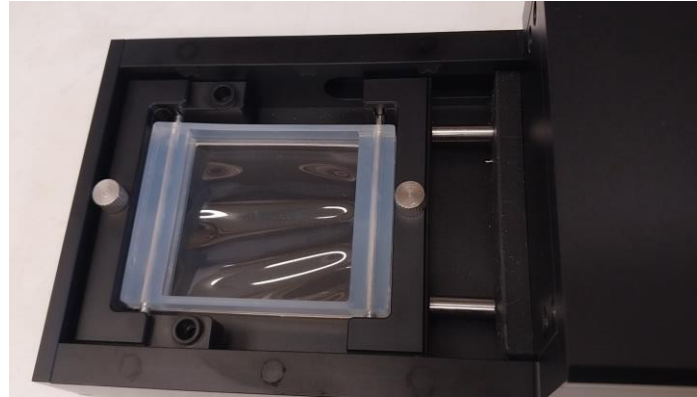
An *in vitro* model of stretching pulses during milking



Guy Dabby



Relaxed



CytoStretcher (CuriBio)



After stretching cycles



L1 bovine mammary epithelial cells generously provided by Prof. Itamar Barash (Volcani Inst.):
German and Barash, *In Vitro Cell Dev Biol – Animal* 2002



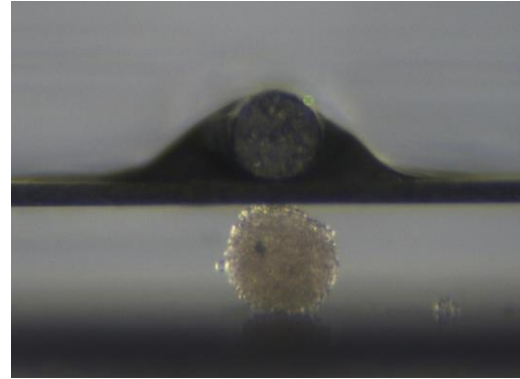
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Acute compression of bovine MEC spheres

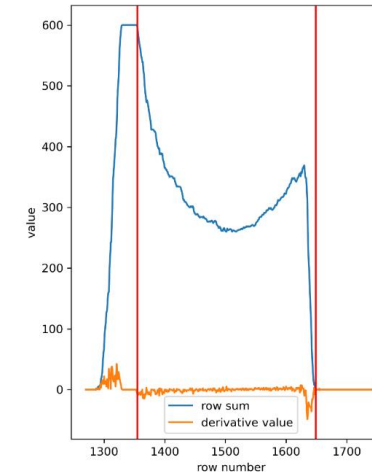
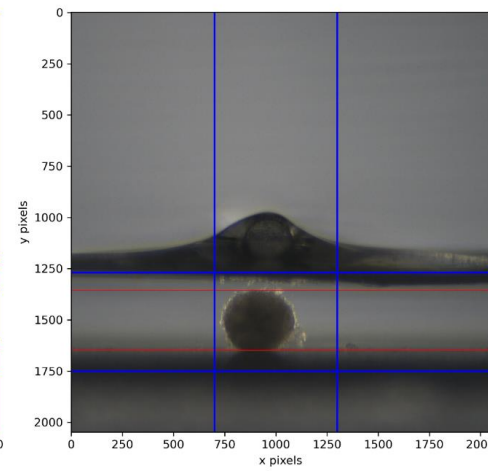
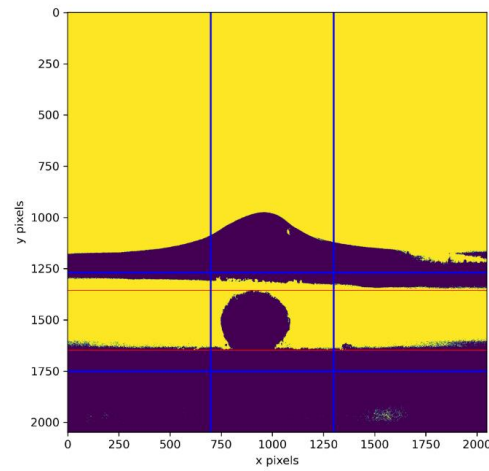
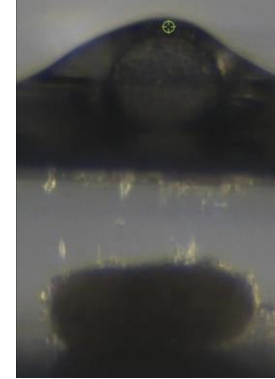


Nir Zaharoni

Acute compression



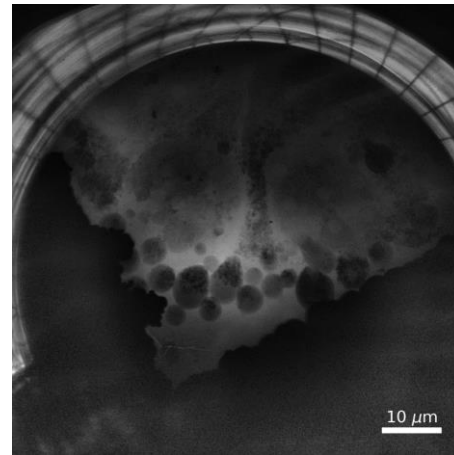
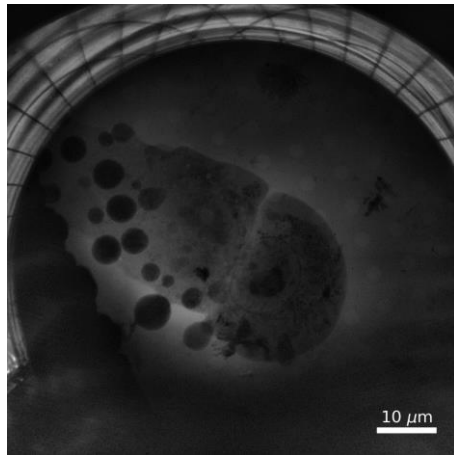
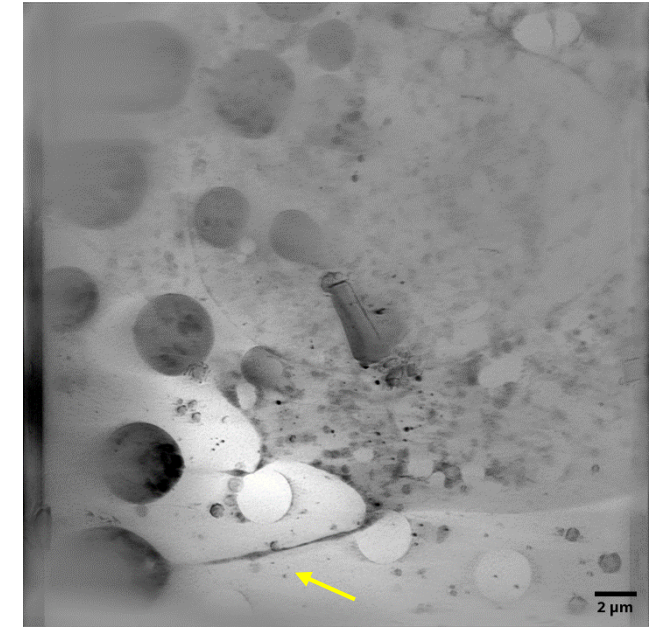
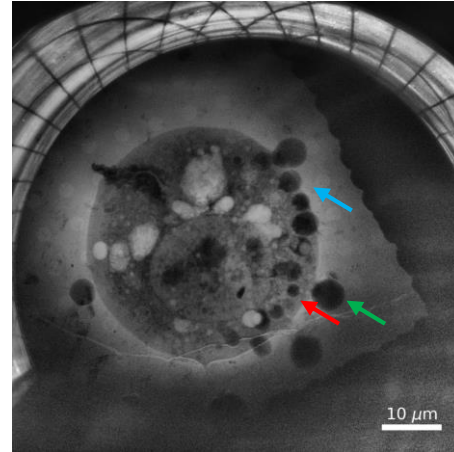
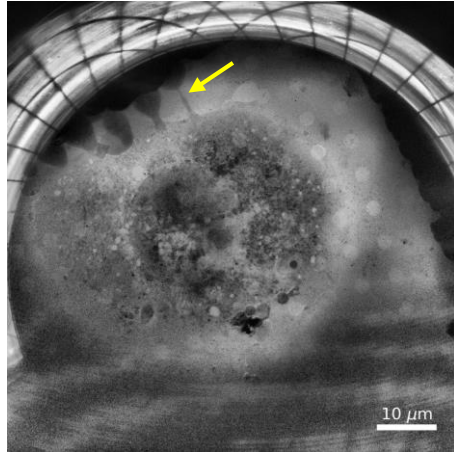
Partial recovery





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Milk fat globules secreted by bovine MECs: cryo soft X-ray tomography



Prof. Michael Elbaum
Weizmann Institute of Science

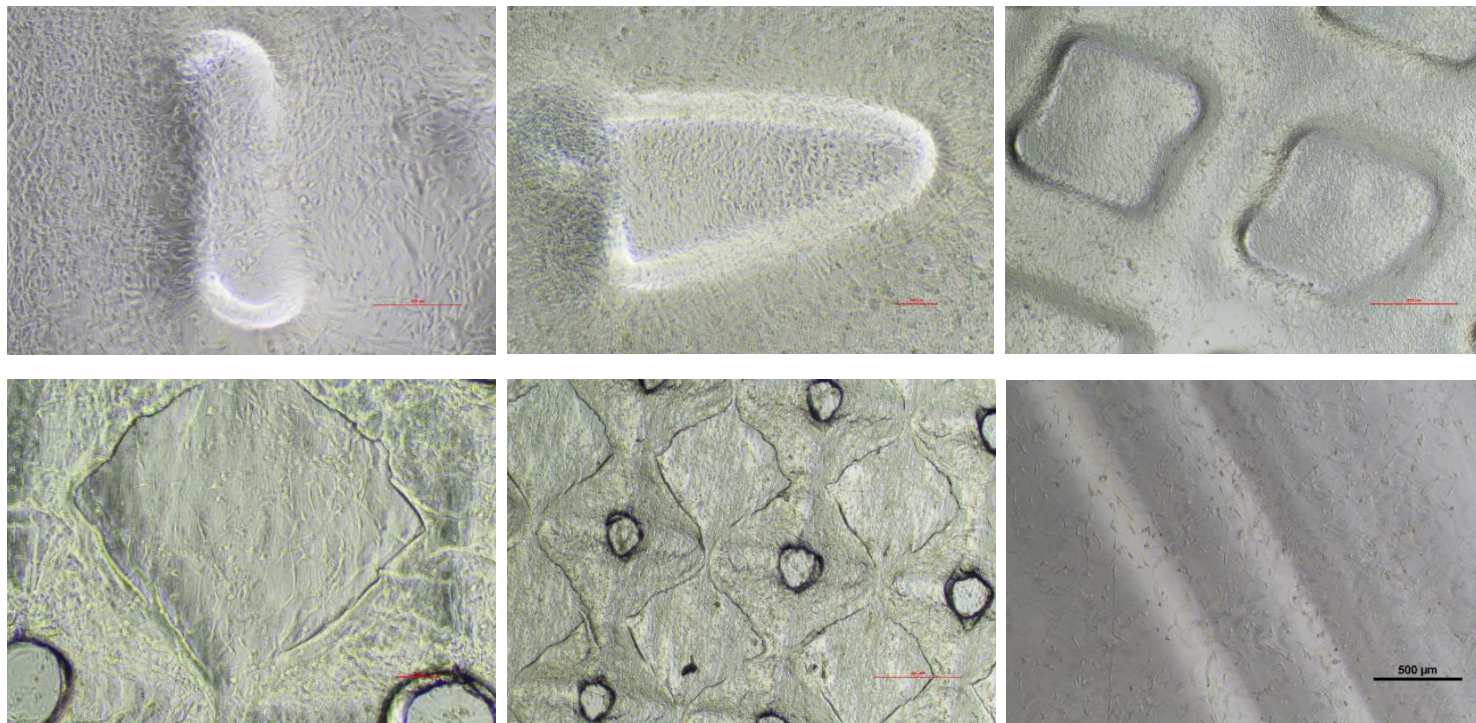


Dr. Sergey Kapishnikov
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Culture topography



State of Israel
Ministry of Agriculture
Food Security &
Chief Scientist Office



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משרד החקלאות
וביטחון המזון
לשכת המדען הראשי



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Summary

- Holistic approach that involves mechanical aspects can make significant contribution to udder research.
- In other fields such research is at the forefront of various application developments.

Thanks you



משרד החדשנות,
המדע והטכנולוגיה
Ministry of Innovation, Science & Technology



State of Israel
Ministry of Agriculture
Food Security &
Chief Scientist Office

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