

Supplementary information

Mucosa-interfacing electronics

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SUPPLEMENTARY INFORMATION

Mucosa-Interfacing Electronics

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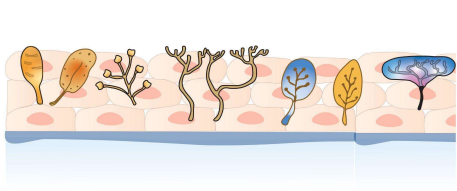
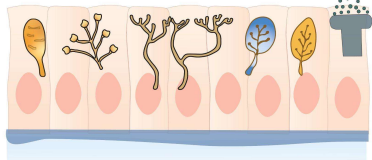
Table S1: Detailed comparisons between skin and mucosa regarding structures, dynamics, and chemical/biological environments.

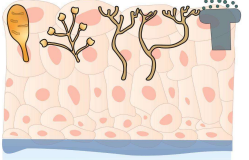
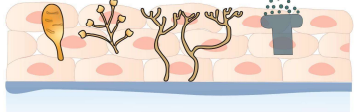
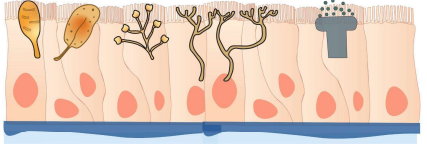
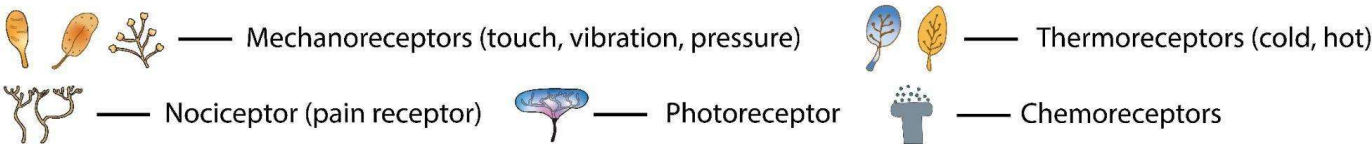





Properties	Skin	Mucosa
Surface area	2 m ² ¹	Digestive Tract: 32 m ² ² Respiratory Tract: <i>lungs:</i> 35m ² (deep expiration); 100 m ² ³ (deep inspiration) Female Reproductive Tract: <i>uterus:</i> 0.048 – 0.065 m ² Urinary Tract: <i>bladder:</i> 0.02-0.03 m ² ⁴
Thickness	0.5-4 mm ⁵	Digestive Tract: <i>esophagus:</i> 1.9-5.7 mm; <i>stomach:</i> 3-6 mm; <i>small intestines:</i> 0.9-1.6 mm; <i>colon:</i> 1.1-2.1 mm ^{6,7} Respiratory Tract: <i>lungs:</i> 1.5-9 mm ⁸ ; <i>bronchi:</i> 1.2-1.4 mm ⁹ Female Reproductive Tract: <i>uterus:</i> 2-16 mm ¹⁰ Urinary Tract: <i>bladder:</i> 2-4 mm ¹¹
Elastic modulus	<i>Stratum Corneum:</i> 75 – 300 MPa (dry), 10 – 50 MPa (wet) ^{12,13}	Digestive tract: <i>esophagus:</i> ~1.2 MPa; <i>stomach:</i> 0.5-0.7 MPa; <i>small intestines:</i> ~0.9 MPa; <i>colon:</i> ~0.9 MPa ¹⁴ Respiratory Tract: <i>respiratory duct:</i> 0.06-0.4 MPa ^{15,16} ; <i>bronchi:</i> 0.0007-0.025 MPa ¹⁷ Female Reproductive Tract: <i>vaginal mucosa (premenopausal):</i> 11.5MPa; <i>vaginal mucosa (postmenopausal):</i> 14.35MPa; <i>uterus:</i> 0.5-2MPa ^{18,19} Urinary Tract: <i>bladder mucosa:</i> 0.087-0.18 MPa; <i>bladder detrusor muscle:</i> 0.007-0.012 MPa; <i>adventitia:</i> 0.009-0.022 MPa ²⁰
Elongation (Strain) at break	40-180% ²¹	Digestive Tract: <i>esophagus:</i> 140%; <i>stomach:</i> 190%; <i>small intestine:</i> 140%; <i>colon:</i> 180% ^{14,22} Respiratory Tract: <i>lungs:</i> 150-200% ²³ Female Reproductive Tract: <i>normal cervix:</i> 5-10%; <i>short cervix:</i> 4-6% ¹⁹ Urinary Tract: <i>bladder:</i> ~300% ²⁴
Cellular turnover rate	~27 days ²⁵	Digestive Tract: <i>esophagus:</i> 5-8 days ^{26,27} ; <i>stomach:</i> 4-20 days ²⁸ ; <i>small intestines:</i> 4-5 days; <i>colon:</i> 4 days ^{29,30} Respiratory Tract: <i>lungs:</i> 0.3% cells at any time ³¹ ; <i>bronchi:</i> ~150 days ²⁸ Female Reproductive Tract: <i>cervix:</i> 5.7 days ³² Urinary Tract: <i>urothelium cells:</i> 3-6 months ³³ ; <i>bladder:</i> ~200 days ³⁴
Mode of motion	Stretching, folding, and compression due to body motion	Digestive Tract: peristalsis (<i>stomach:</i> 0.05 Hz, <i>small intestines:</i> 0.15-0.2 Hz, <i>colon:</i> 0.01-0.04 Hz (long-duration), 0.05-0.2 Hz (short-duration) ³⁵) Respiratory Tract: respiration (0.2–0.34 Hz) ³⁶

		<p>Female Reproductive Tract: uterine contraction (0.02-0.08 Hz)³⁷</p> <p>Urinary Tract: bladder emptying (4-5 times per day)</p>
Mean temperature	<p>At rest: 28.1 - 34.7 °C</p> <p>In cold conditions: 19.4 - 30.3 °C</p> <p>During exercise: 38.2- 40.1 °C</p>	<p>Digestive Tract: between 36.5-37.5 °C with small variations^{38,39}</p> <p>Respiratory Tract: <i>upper trachea:</i> 29.2-32°C; <i>subsegmental bronchi:</i> 33.9-35.5 °C. In cold conditions: <i>upper trachea:</i> ~20.5 °C; <i>subsegmental bronchi:</i> 31.6 °C⁴⁰</p> <p>Female Reproductive Tract: temperature slightly increased (by 0.3-0.5 °C) after ovulation⁴¹</p> <p>Urinary Tract: Bladder: 36.0-38.3°C^{42,43}</p>
Secretion pH	4-6 ⁴⁴	<p>Digestive Tract: <i>esophagus:</i> 5-7; <i>stomach:</i> 1.0-2.5; <i>small intestines:</i> 6.1-7.1; <i>colon:</i> 7.1-7.5⁴⁵</p> <p>Respiratory Tract: 7.38-7.42^{46,47}</p> <p>Female Reproductive Tract: <i>endocervix:</i> 6.5-7.5; <i>vagina:</i> 3.4-7.4⁴⁸</p> <p>Urinary Tract: 4.6-8.0⁴⁹</p>
Secretion Rate	Sweat rate is in general low, but can be up to 2-4 L/hour during exercise ⁵⁰	<p>Digestive Tract: <i>stomach:</i> 1.2-1.5 L/day⁵¹; <i>small intestines:</i> 0.5L /day from liver, 1.5 L/day from pancreas⁵²; <i>colon:</i> 1.5-2 L/day⁵¹</p> <p>Respiratory Tract: 2L/day⁵³</p> <p>Female Reproductive Tract: 2-5 mL/day⁵⁴</p> <p>Urinary Tract: 0.8-2 L/day⁵⁵</p>
Secretion Composition	Ammonia, urea, mineral salts, sugar ⁵⁶	<p>Digestive Tract: <i>stomach:</i> hydrochloric acid, electrolytes, mucin, pepsin, and protein^{57,58}; <i>small intestines:</i> mucin, digestive enzymes, hormones, electrolytes⁵¹; <i>colon:</i> electrolytes, mucin, niacin, vitamins⁵¹</p> <p>Respiratory Tract: water, carbohydrates, lipids, mucin, proteins^{53,59}</p> <p>Female Reproductive Tract: vaginal discharge⁵⁴</p> <p>Urinary Tract: urine⁶⁰</p>
Microbes	Density: 10 ⁴ to 10 ⁶ /cm ² ⁶¹ (bacteria, fungi, viruses)	<p>Digestive Tract: density of bacteria: 10/gram (stomach), 10³/gram (duodenum), 10⁴/gram (jejunum), 10⁷/gram (ileum), 10¹²/gram (colon)⁶²; play crucial roles in maintaining homeostasis and protecting against pathogens, and have shown ties with inflammatory diseases⁶³ and neurological disorders⁶⁴</p> <p>Respiratory Tract: low density (10²-10³/ml) and function as gatekeepers to respiratory health⁶⁵</p> <p>Female Reproductive Tract: exist in abundance (10⁸/ml) and influence maternal and fetal immune systems⁶⁶</p>

		Urinary Tract: typical density: 10^3 - 10^5 /ml; show correlations with many urinary conditions (e.g. kidney stone diseases, acute&chronic kidney injury, urinary tract infections) ⁶⁷
Gas	Atmospheric air	Digestive Tract: (in addition to atmospheric air) carbon dioxide, hydrogen, methane, and hydrogen sulfide ⁶⁸ Urinary Tract: high concentration of carbon dioxide in patients with diabetes ⁶⁹ Female Reproductive Tract: increased carbon monoxide during pregnancy ⁷⁰

Table S2: Detailed comparisons between skin and mucosa regarding epithelial types and sensing functions.

Anatomic Sites	Schematic of Surface Epithelium and Receptor Types	Main Functions of Epithelium	Main Sensory Receptor Types and Inputs	Functional Outcomes
Skin	 <p>Stratified squamous epithelium</p>	Protection against mechanical abrasions, microorganisms, and water loss	<ul style="list-style-type: none"> •Mechanoreceptors: pressure, skin stretch and deformation, vibration ⁷¹ •Nociceptors: mechanical injury, extreme temperatures, reactive chemical species ⁷² •Thermoreceptors: external temperature ⁷³ •Photoreceptors: UV radiation ⁷⁴ 	<ul style="list-style-type: none"> •Sensations of touch, pain, temperature, position, texture •Regulation of blood flow, sweating, melanin production ⁷⁴, immune responses ⁷²
Gastrointestinal mucosa	 <p>Simple columnar epithelium</p>	Secretion and absorption; transport substance in a specific direction; protection against acid and bacteria	<ul style="list-style-type: none"> •Mechanoreceptors: stretching •Nociceptors: toxins, bacteria, inflammation ⁷⁵ •Chemoreceptors: nutrients, endocrine mediators, immune mediators ⁷⁶, acids ⁷⁷, gasses ⁷⁷ •Thermoreceptors: heating and cooling ⁷⁸ 	<ul style="list-style-type: none"> •Regulation of digestion, peristalsis, blood flow, fluid transport, and gut homeostasis ⁷⁶ •Sensations of taste (sweet, salty, sour, umami, bitter), satiety, nausea, pressure, and pain ⁷⁶

Urinary mucosa	 <p>Transitional epithelium</p>	Allowing the urinary organs to significantly stretch and expand	<ul style="list-style-type: none"> •Mechanoreceptors: bladder stretching⁷⁹ •Nociceptors: acid⁸⁰, inflammatory mediators •Chemoreceptors: toxins, bacteria, detection mediated by taste (e.g. bitter, umami) taste receptors⁸¹ 	<ul style="list-style-type: none"> •Regulation of bladder voiding⁷⁹ •Sensations of bladder filling, pain, urgency, and micturition⁸²
Reproductive mucosa	 <p>Stratified squamous epithelium</p>	Protection against mechanical abrasions, microorganisms, and water loss	<ul style="list-style-type: none"> •Mechanoreceptors: uterine stretching, pressure⁸³ •Nociceptors: distension, injury, inflammation⁸⁴ •Chemoreceptors: reproductive hormones⁸⁵ 	<ul style="list-style-type: none"> •Regulation of fertility, menstruation, pregnancy, and childbirth⁸⁵ •Regulation of uterine distension and contractions, and cervical mucosa properties including cervical ripening⁸⁵ •Sensations of pain⁸⁴
Respiratory mucosa	 <p>Pseudostratified columnar epithelium</p>	Secretion and absorption; protection against foreign particles; transport of mucus	<ul style="list-style-type: none"> •Mechanoreceptors: lung inflation, bronchospasm, touch⁸⁶ •Nociceptors: irritants⁸⁷, carbon dioxide⁸⁸ •Chemoreceptors: water and acid⁸⁹, ATP⁸⁶ 	<ul style="list-style-type: none"> •Regulation of reflexes including cough, gagging, and sneezing⁸⁶ as well as mucus production and blood flow⁸⁷ •Sensations of urge to cough and taste⁸⁹
 <p>  — Mechanoreceptors (touch, vibration, pressure)  — Thermoreceptors (cold, hot) </p> <p>  — Nociceptor (pain receptor)  — Photoreceptor  — Chemoreceptors </p>				

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Competing interests:

Complete details of all relationships for profit and not for profit for G.T. can be found in the table below and at the following link:

<https://www.dropbox.com/sh/szi7vnr4a2ajb56/AABs5N5i0q9AfT1IqIJAE-T5a?dl=0>.

Disclosures - Carlo Giovanni Traverso - encompassing all professional not-for-profit and for profit relationships

Date: June 8, 2022

Please note that I make every effort to maintain this document up to date and as part of the disclosure process governed by the Sunshine Act further details can be found at:
<https://openpaymentsdata.cms.gov/physician/431893>

Employment and Professional Affiliations

	Position(s)	Years
Trinity College, University of Cambridge	Undergraduate student (1995-1998), Junior Research Fellow / Title A (2002-2007), Medical Student (2002-2006)	1995-1998, 2002-2007
Hospital for Sick Children, University of Toronto	Research Assistant (1997-1999)	1997-1999
Johns Hopkins University	PhD graduate student (1998-2002), Post-doctoral fellow (2002-2003)	1998-2003
Harvard Medical School	Fellow (2007-2014), Instructor (2014-2017), Assistant Professor, part time (2017-present)	2007-present
Brigham and Women's Hospital	Internal Medicine Resident (2007-2009), Attending Physician (2016-present)	2007-2009, 2016-present
Massachusetts Institute of Technology	Research Affiliate (2009-2018), Visiting Scientist (2018-present), Assistant Professor (2019-present)	2009-present
Massachusetts General Hospital	Gastroenterology Fellow (2009-2014), Attending Physician (2014-2015)	2009-2015

For Profit

	Equity/Stock	Board/Advisor	Consultant	Royalties	Gifts	Grants/ Scholarship	Years
Exact Sciences				x			2002-2014
Horizon				x			2014-2016
Pavoda	x	x	x				2015
Entrega, Inc			x				2015
CBSET			x				2015
Avaxia			x				2015-present
Lyndra	x	x		x			2015-present
Novo Nordisk			x			x	2015-2016
SNS Nano			x				2015-2017
Hoffman la Roche						x	2016
Janssen							2016
Egalet		x	x				2016
Janssen			x				2016
BMS					x		2016-2018
Synlogic			x				2016-2018
Freonome						x	2017-present
Suono Bio	x	x		x			2018
Merck			x				2018-2019
Verily			x				2018-present
Eagle Pharmaceuticals, Inc			x				2018-present
Vivtex	x	x		x			2018-present
Celero Systems	x	x		x			2020-present
Bilayer Therapeutics, Inc	x	x		x			2020-present
Teal Bio, Inc	x	x		x			2020-2021
Oracle						x	2020
Wired Consulting			x				2021
Avadel Pharmaceuticals			x				2022
Moderna			x				2022-present
Syntis Bio	x	x	x				

Not for Profit

	Equity/Stock	Board/Advisor	Consultant	Royalties	Gifts	Grants/ Scholarship	Years
Draper Laboratory						x	2012, 2019-2020
MIT Lincoln Laboratory						x	2018-present
NIH/NIBIB						x	2015-2016
Kenneth Rainin		x					2013-present
Bill and Melinda Gates Foundation						x	2018-present
NIH/NCI						x	2002-present
Johns Hopkins University / Technology Transfer Office				x			2015-present
Massachusetts Institute of Technology / Technology Licensing Office				x			2018-present
Mass General Brigham Innovation / Technology Licensing				x			1995-1998
Cambridge Commonwealth and Overseas Trusts, Univ. of Cambridge						x	2003-2006
Foulkes Foundation			x				2019-2022
Trinity College, University of Cambridge						x	2020-present
The Leona M. and Harry B. Helmsley Charitable Trust						x	2021-present
Karl van Tassel (1925) Career Development Professorship, MIT						x	
Defense Advanced Research Projects Agency						x	