‘Big’ Data, Gas and more: *technology development to transform the patient experience*

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CRS 2022 Annual Meeting & Expo

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

Advanced Delivery Science

Disclosures

	Equity/ Stock	Board/ Advisor	Consultant	Royalties	Grant
Lyndra	X	X		X	
Suono Bio	X	X		X	
Celero	X	X			
Vivtex	X	X		X	
Teal Bio	X	X		X	
Bilayer Therapeutics	X	X		X	
Syntis Bio	X	X		X	
Novo Nordisk			X		X
Moderna			X		
Exact Sciences				X	
Horizon				X	

All outside/industry relationships are reviewed by the Office for Interactions with Industry, Partners Healthcare

HOPE FUNDS for CANCER RESEARCH

Prostate Cancer Foundation
Curing Together.

POSTER #132

James Byrne

Leo Otterbein

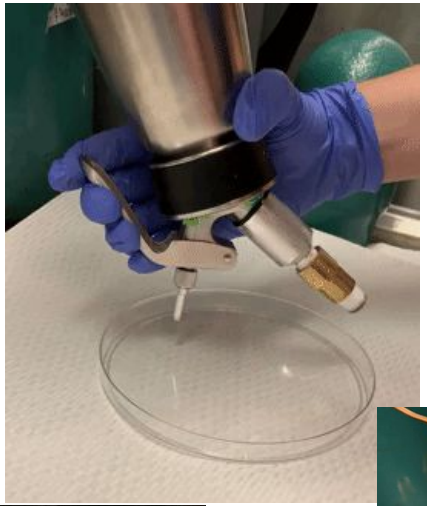
MOLECULAR GASTRONOMY-INSPIRED MATERIALS FOR THE TREATMENT OF INFLAMMATION

Gases are pharmacologic agents

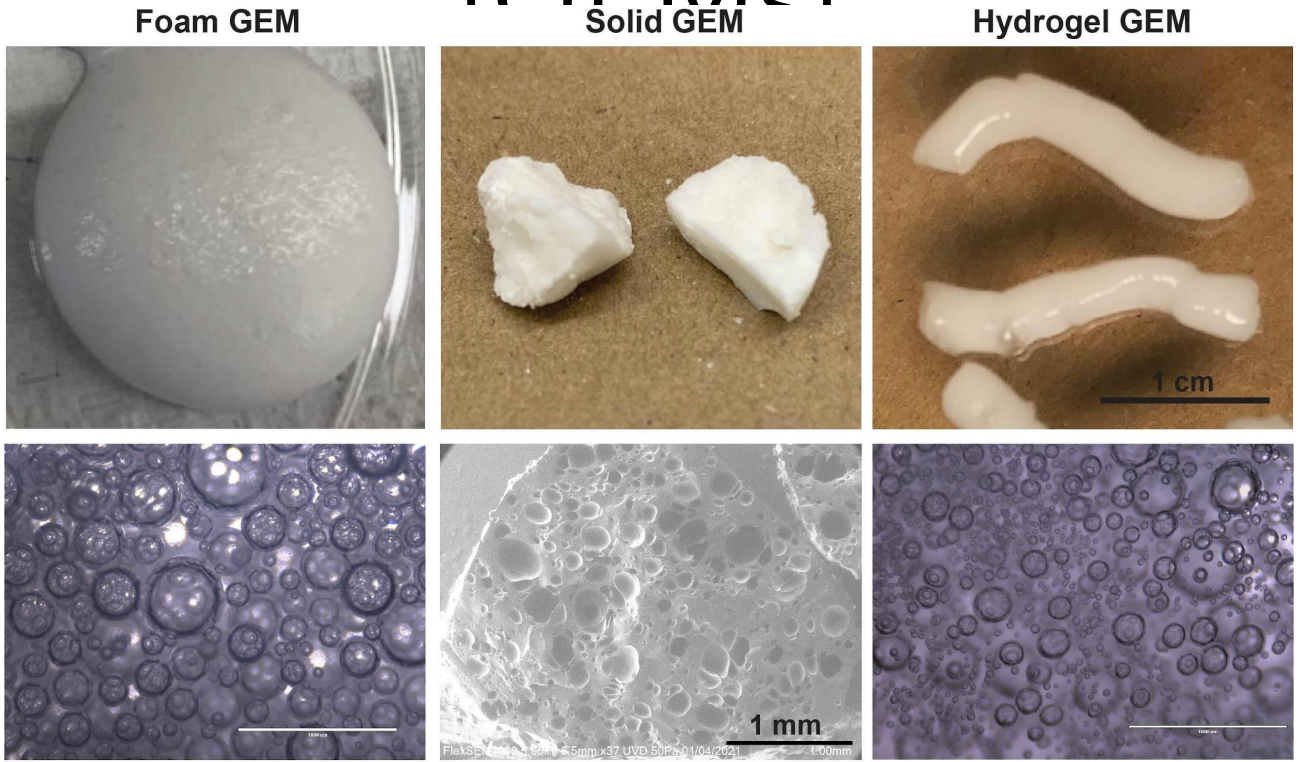
- Carbon monoxide
  >10 ongoing trials
- Nitric oxide
  >50 ongoing trials
- Oxygen
  >100 ongoing trials

NIH U.S. National Library of Medicine
ClinicalTrials.gov

Materials and Formulation Development



Gas-entrapped materials (GEMs)



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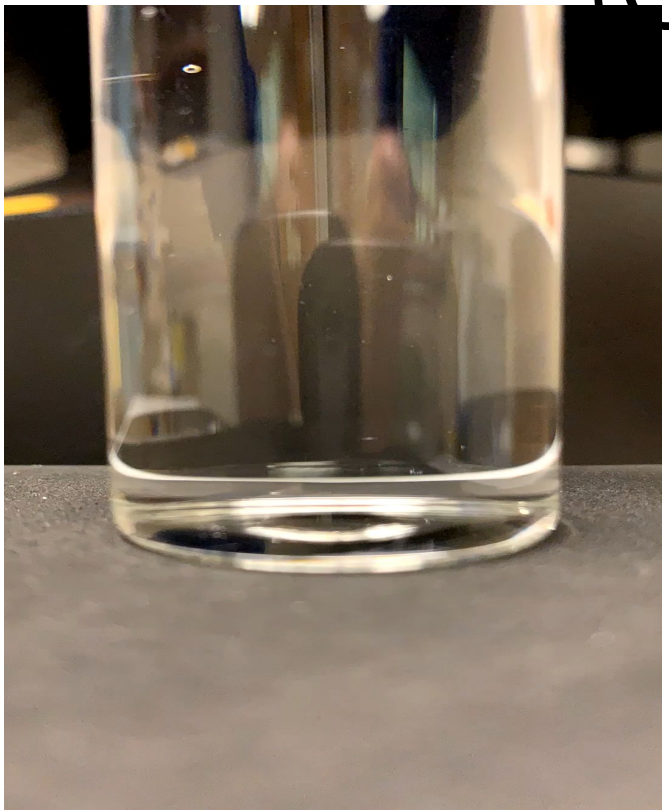

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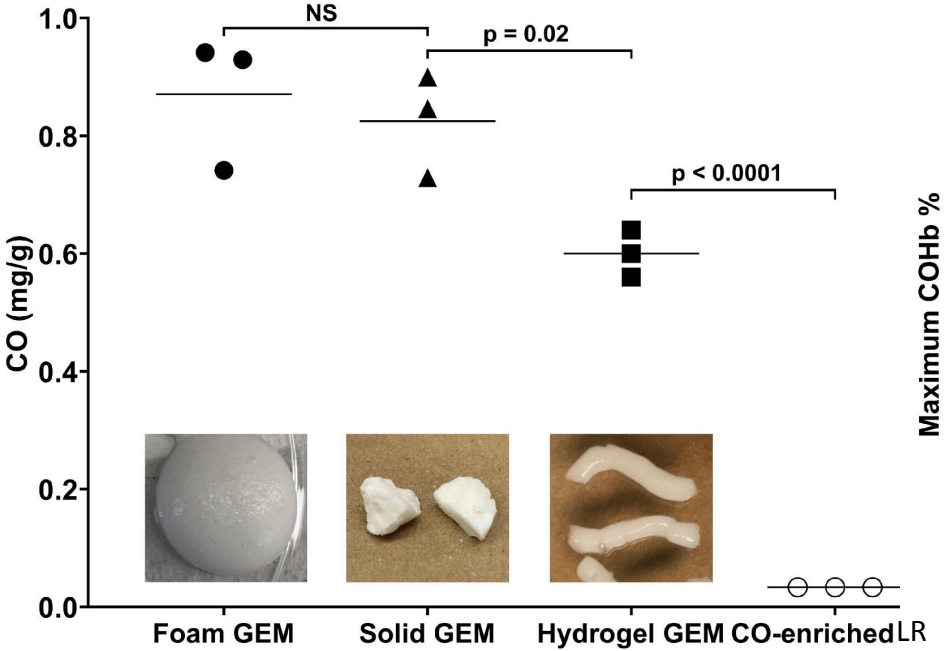
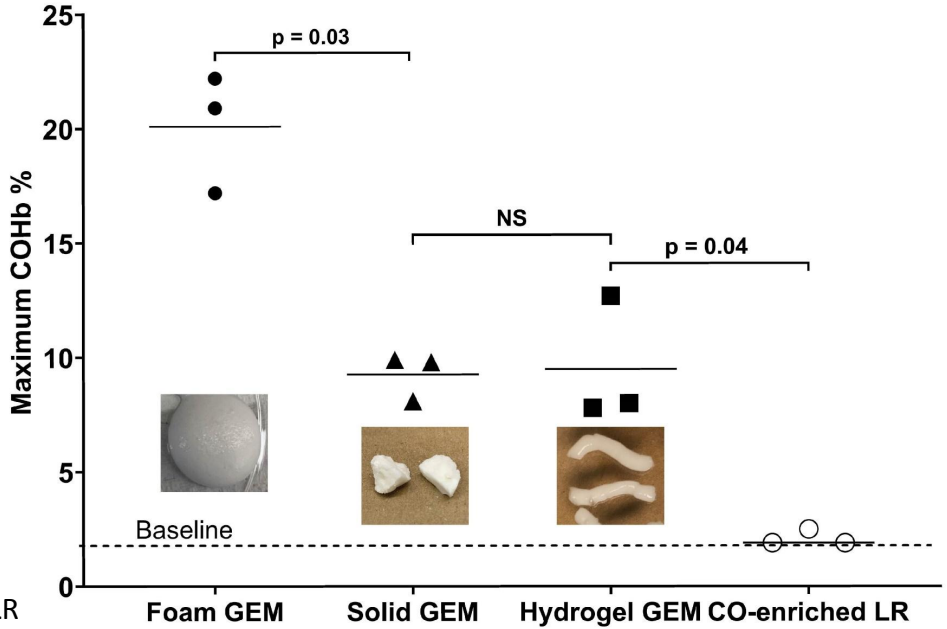
High loading of CO for therapeutically relevant carboxyhemoglobin levels





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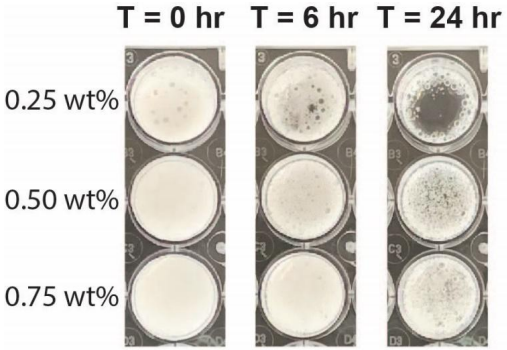
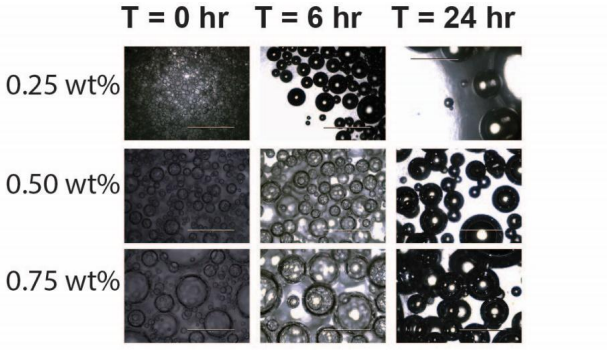
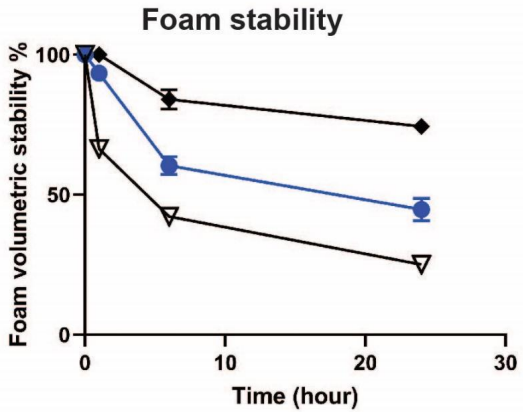
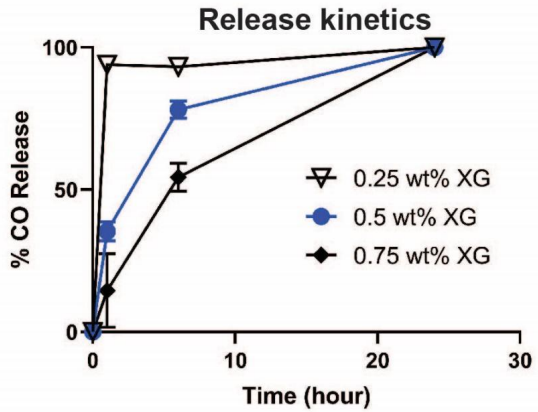
CO-entrapped foams enable tunable delivery of CO









XG=xanthan gum

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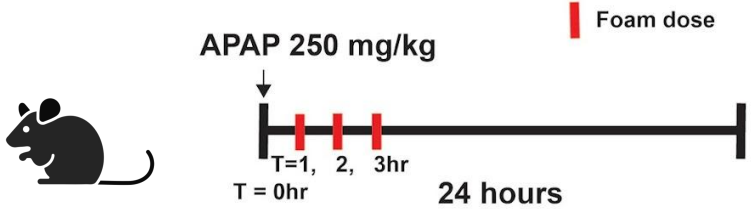
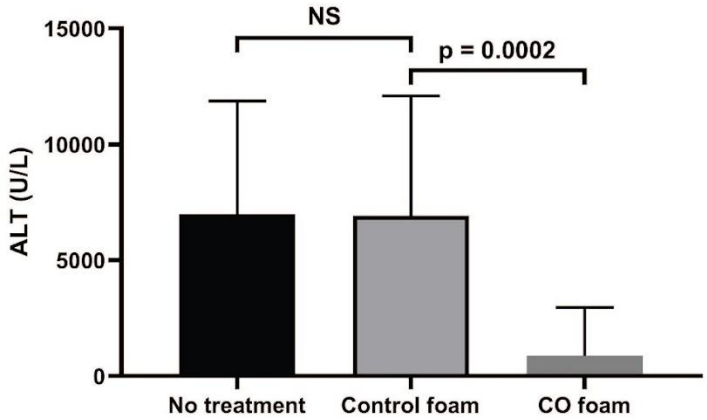
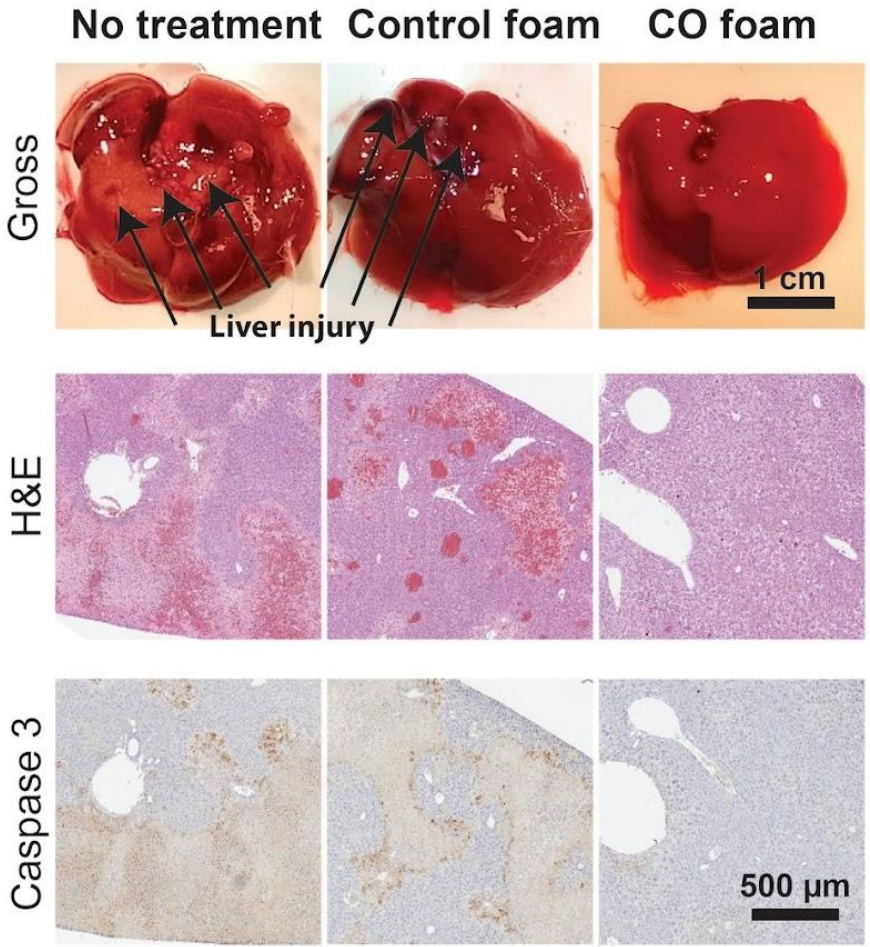
Acetaminophen Overdose Model







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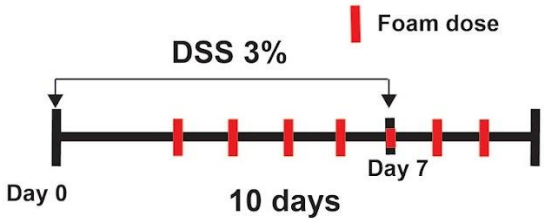
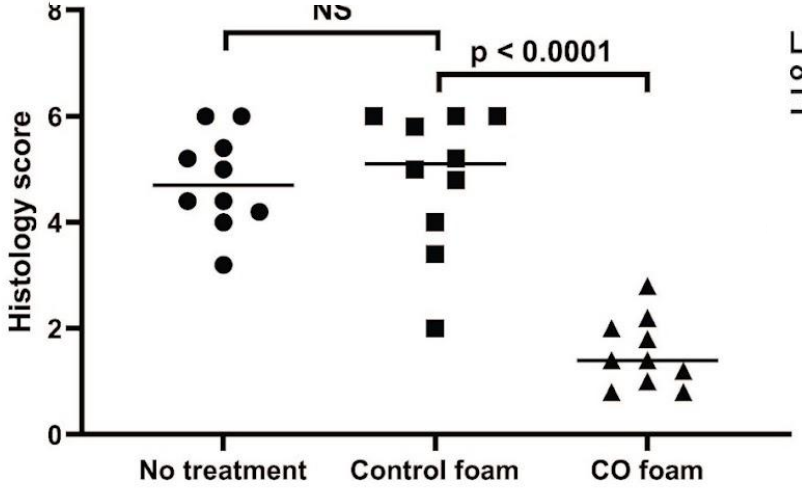
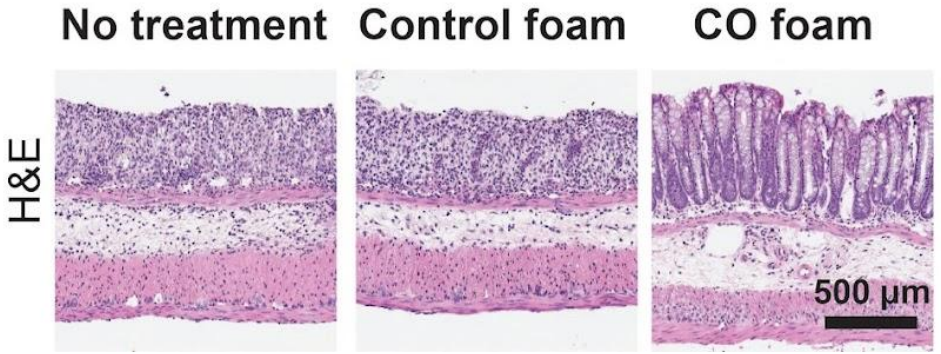
DSS Colitis Model







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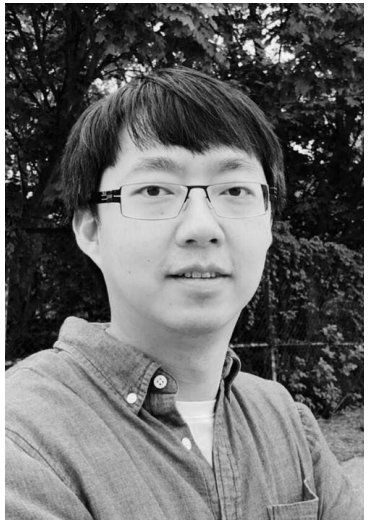
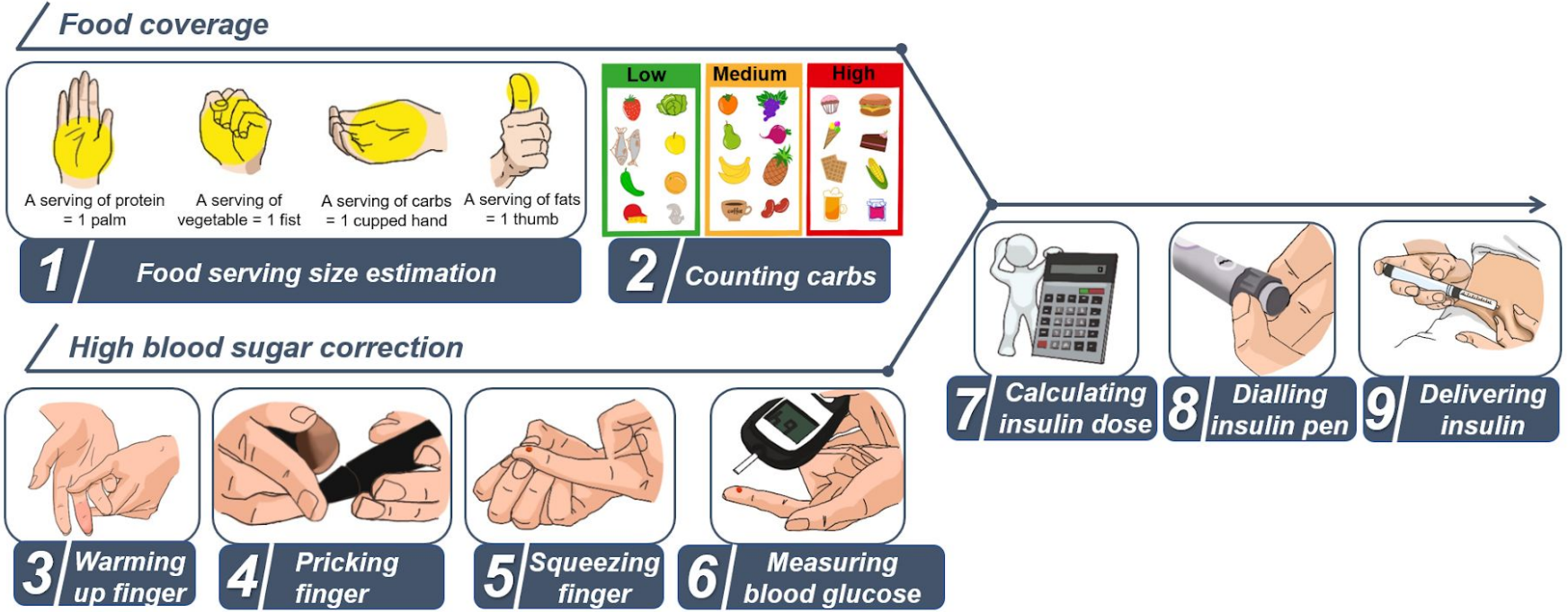


Hen-wei Huang

Siheng Sean You

ALL-IN-ONE NEEDLE: INTEGRATED SYSTEMS FOR GLYCEMIC CONTROL

Pre-prandial (Pre-meal) Dosing of Insulin

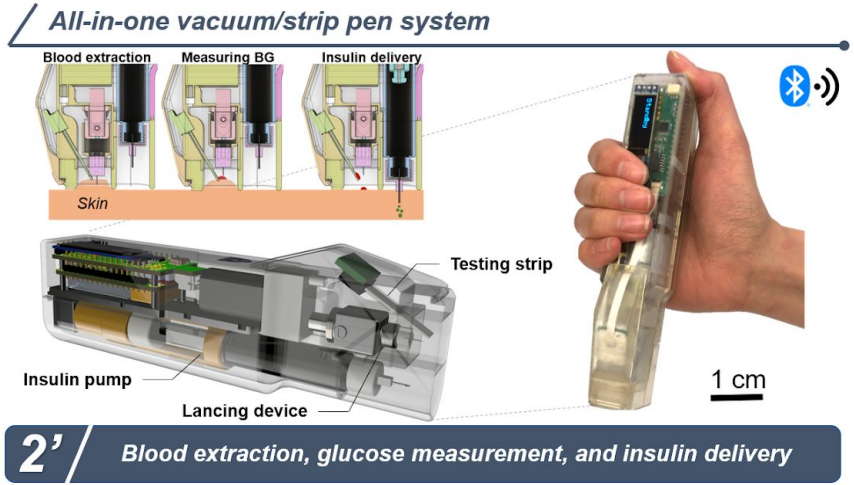


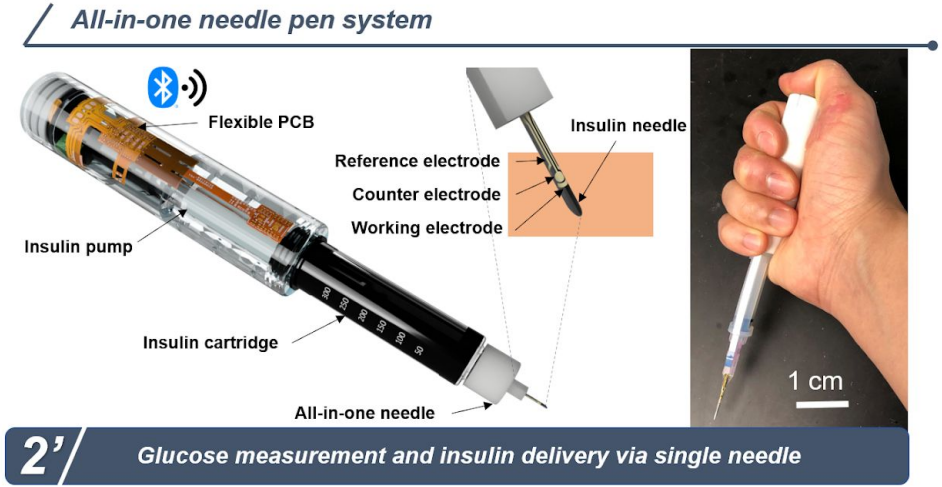
H. Huang*, S. You*, L. Di Tizio*, C. Li* *et al*, JCR 2022

Automating carbohydrate counting

H. Huang*, S. You*, L. Di Tizio*, C. Li* *et al*, JCR 2022

All-in-one pens: glucose sensing and dosing





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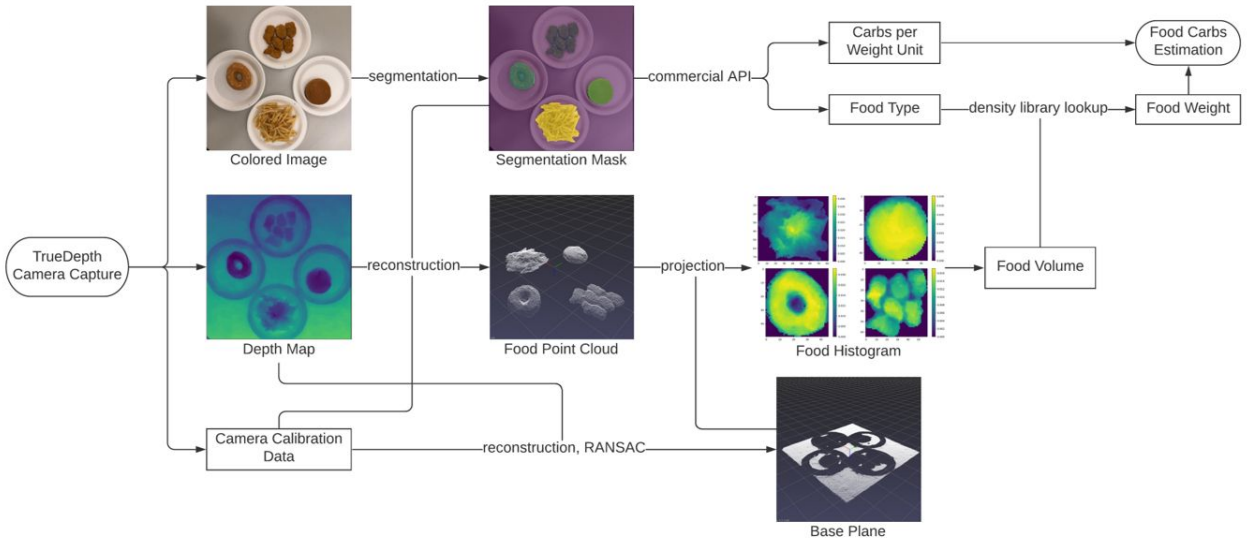
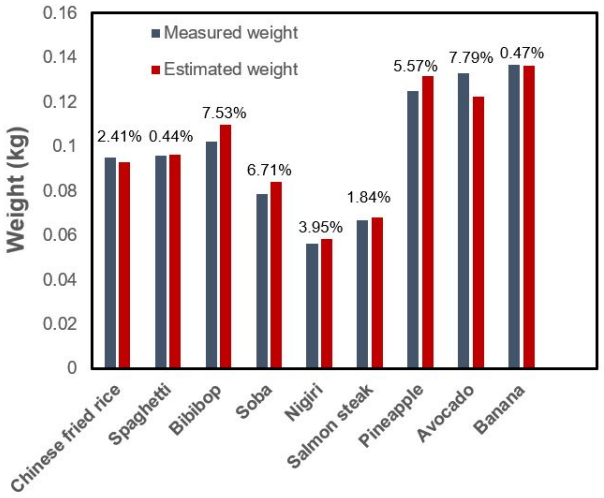
App-based mass quantitation





H. Huang*, S. You*, L. Di Tizio*, C. Li* *et al*, JCR 2022

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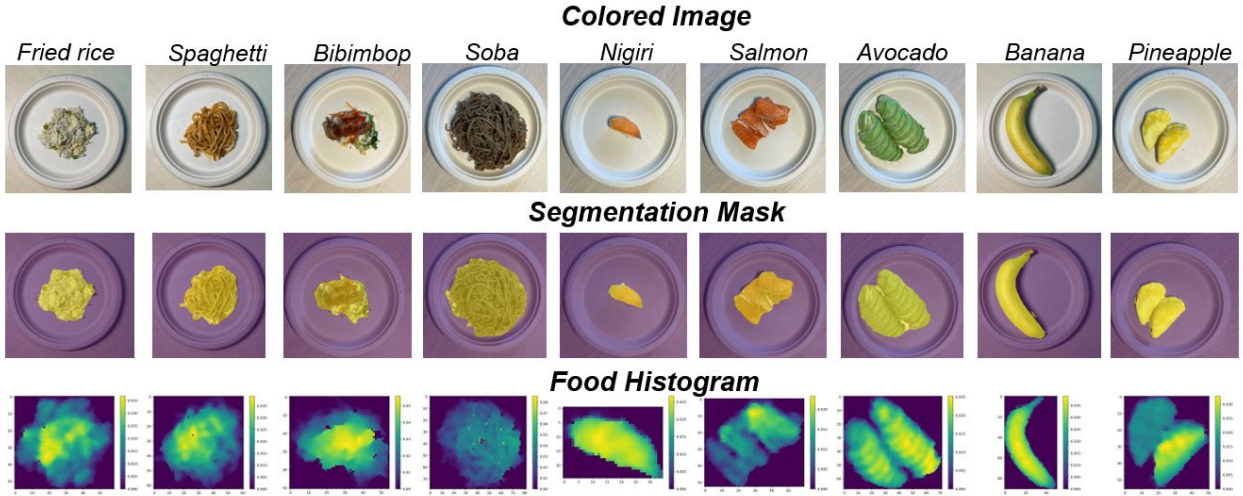

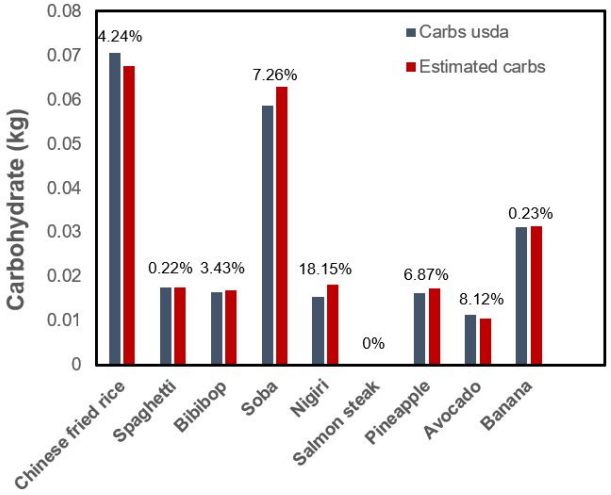

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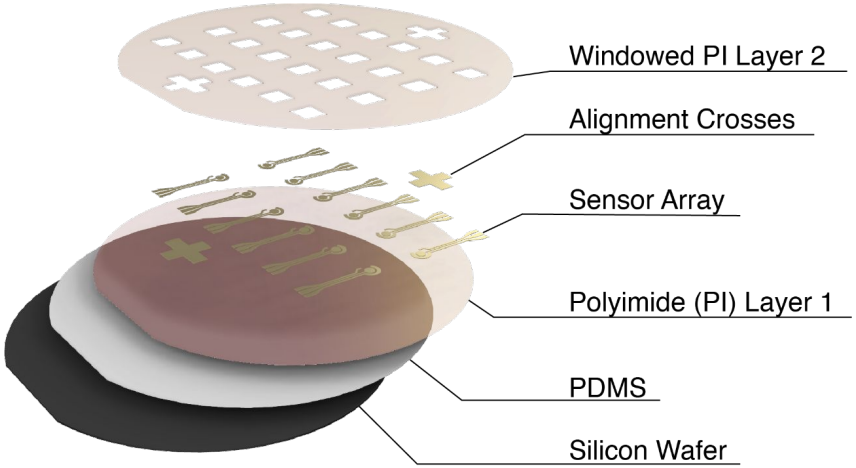
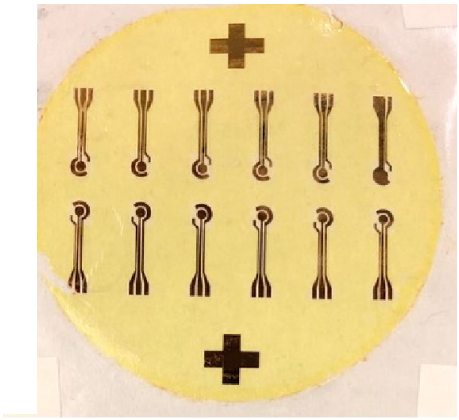
Results: Fabrication of electrodes on needle



Flexible electrode film fabricated on silicon wafer

Film is peeled off of silicon wafer using water soluble tape



Total thickness < 10 um

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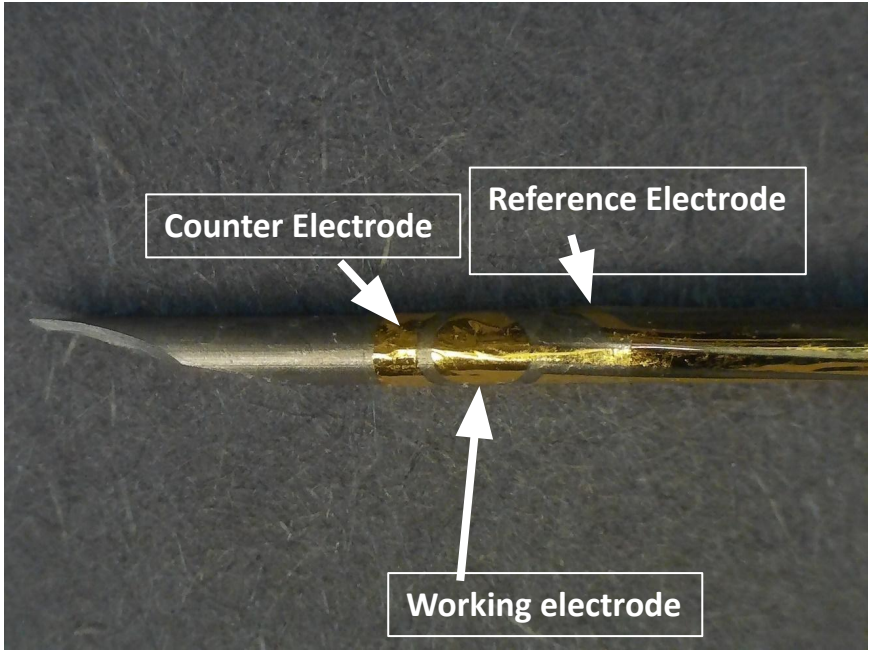
Results: Transfer of Electrodes onto needle



Example of electrodes transferred onto 18 g needle

All in one needle with FFC Connector

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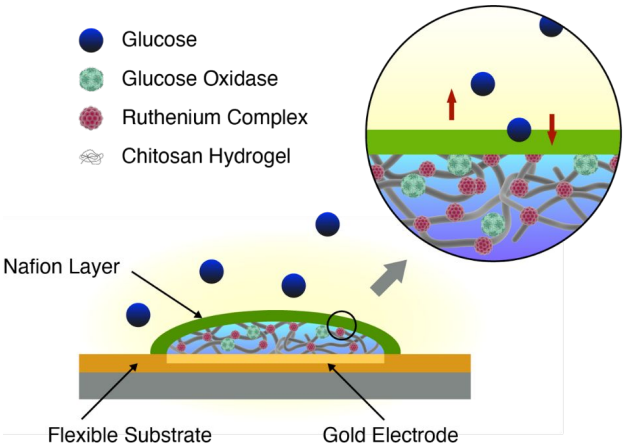
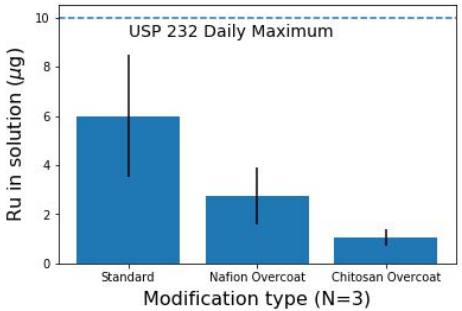
Result: electrode modification for glucose sensing

- Chitosan hydrogel with Glucose Oxidase
- Glutaraldehyde crosslinker
- Hexaammineruthenium (III) chloride mediator
- Encapsulation of mediator and enzyme with Nafion



Drop cast on working electrode surface



Ru leaching testing indicates amount used is below USP 232 recommended levels.

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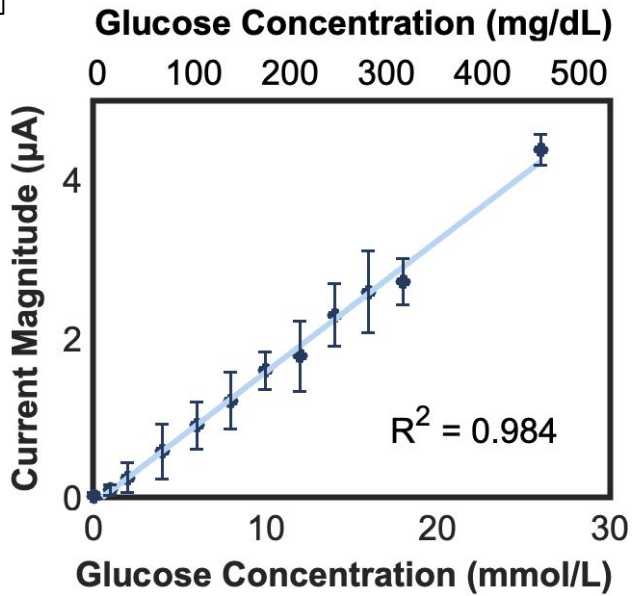
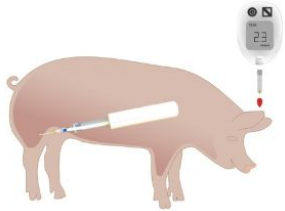
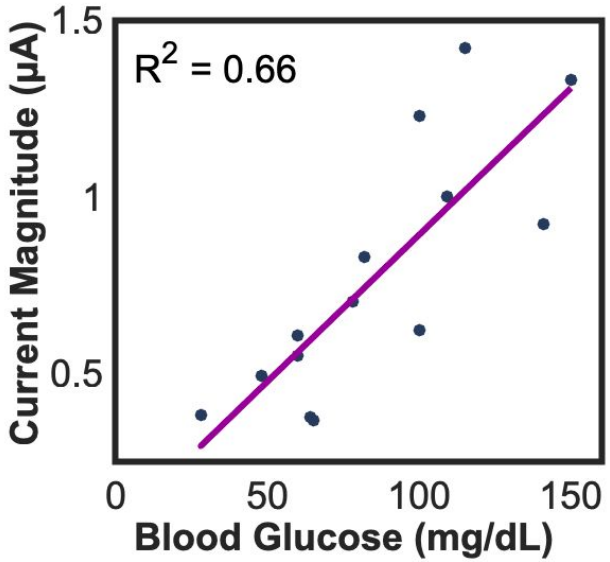
Result: In vitro and In vivo performance

In vitro





In vivo



In-vitro characterization of our sensor indicates we have linear response in current vs glucose concentration up to 26 mmol/L

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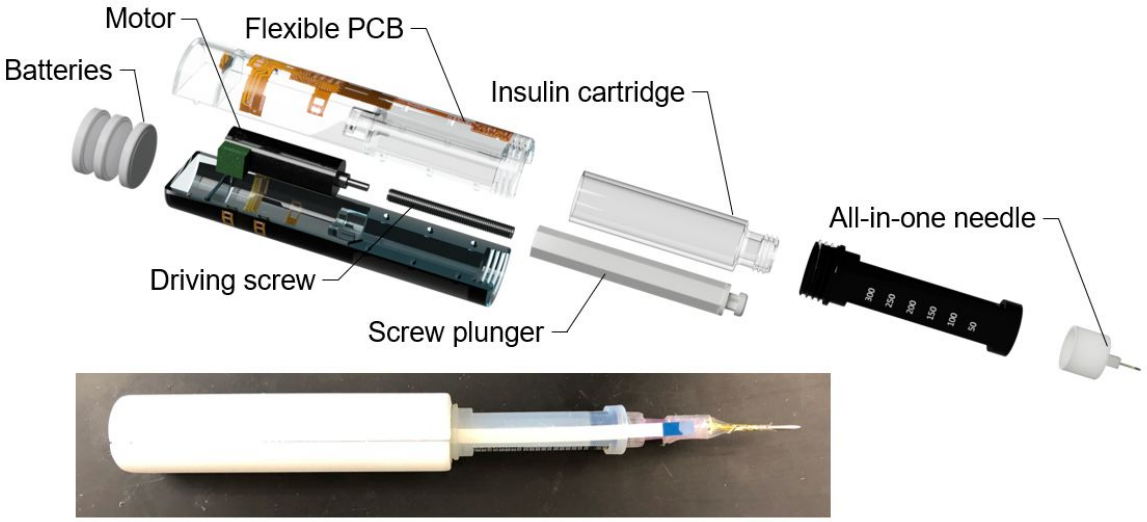
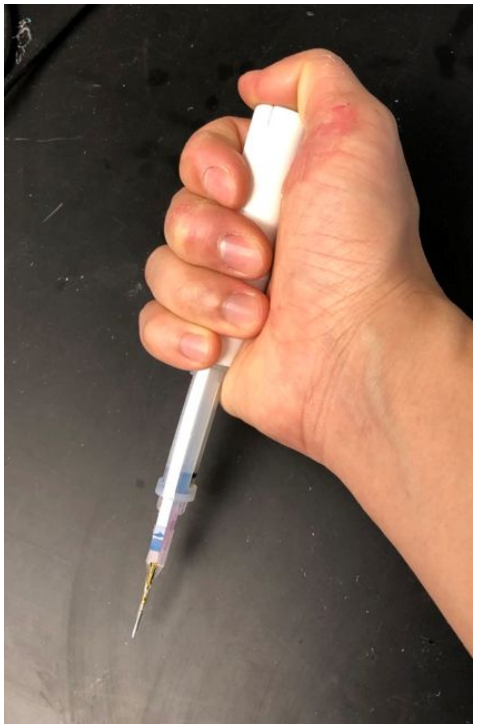
Integrated all-in-one device





BILL & MELINDA GATES foundation

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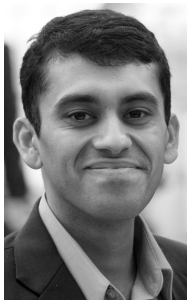
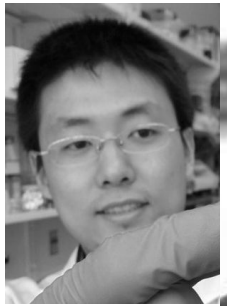
LYNDRA THERAPEUTICS


Ameya Kirtane


Andrew Bellinger


Shiyi Zhang


Phillip Welkfhoff


Hannah Slater

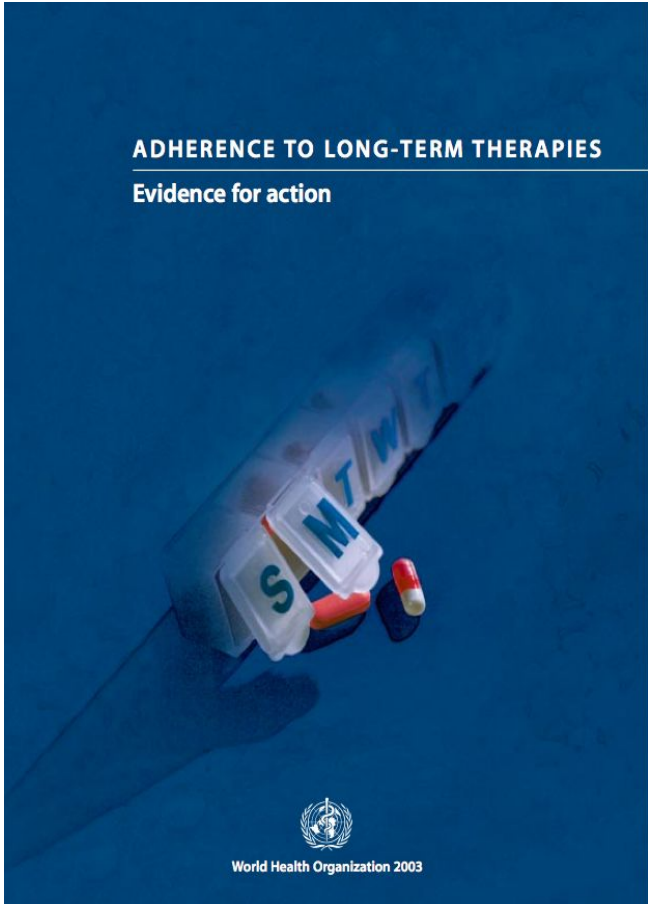

Alison Hill


Robert Langer

SOLUTIONS TO THE MEDICATION NON-COMPLIANCE CHALLENGE

"Drugs don't work if people don't take them."

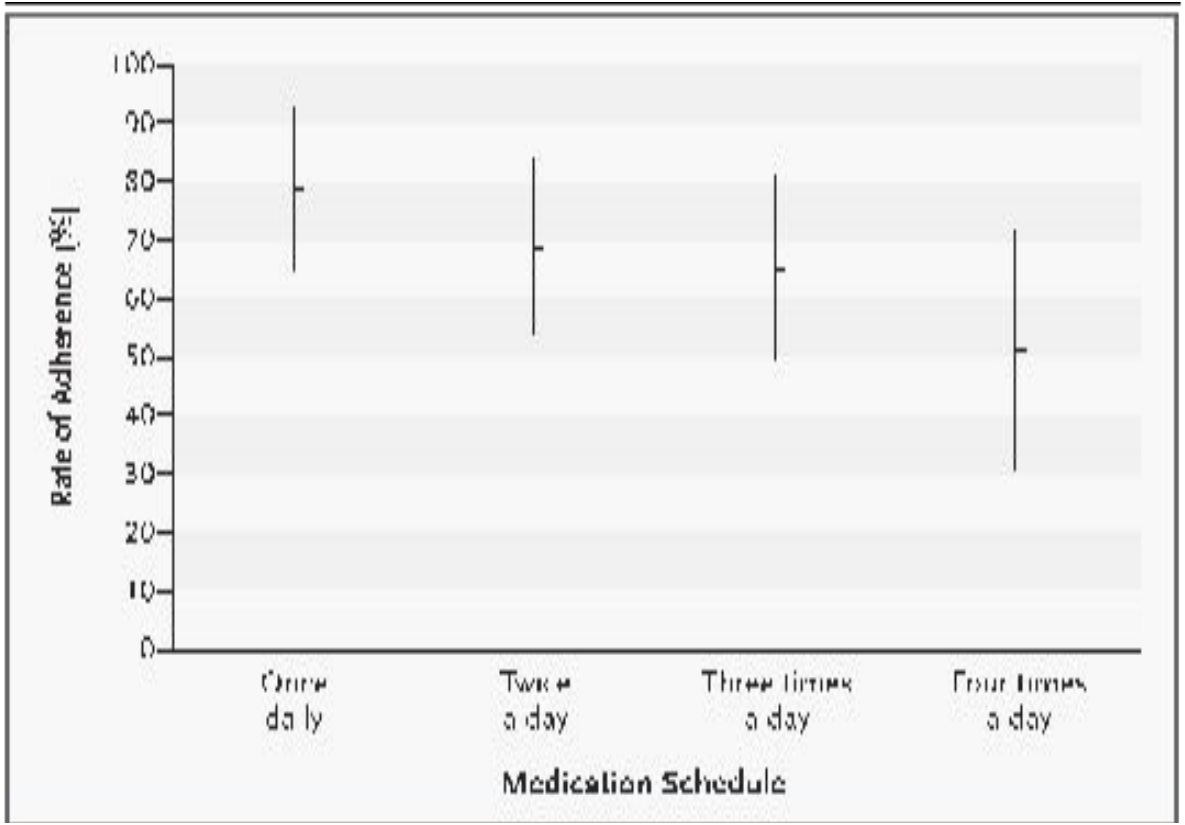
-C. Everett Koop, MD
Surgeon General



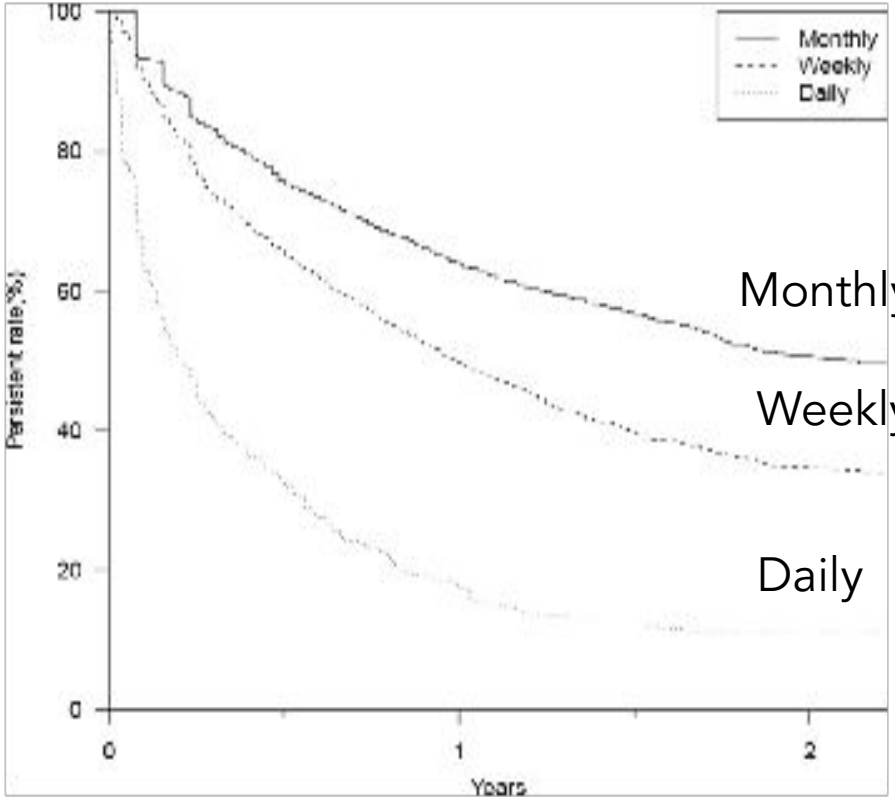
Poor adherence to treatment of chronic diseases is a worldwide problem of striking magnitude.
Adherence to long-term therapy in developed countries ~50%, in developing countries is even lower.

The impact of poor adherence grows as the burden of chronic disease grows worldwide. Noncommunicable disease, mental disorders, HIV/AIDS and TB together represented 54% of the burden of all disease worldwide
in 2001 and will >65% in 2020. The poor are disproportionately affected.

"Increasing the effectiveness of adherence interventions
may have a far greater impact on the health of the



Claxton et al Clin Ther 2001; Osterberg et al NEJM 2005



No. at risk

Monthly	4,938	2,859	1,240	211	107
Weekly	4,402	2,414	1,345	714	170
Daily	496	116	45	26	5

Monthly

Weekly

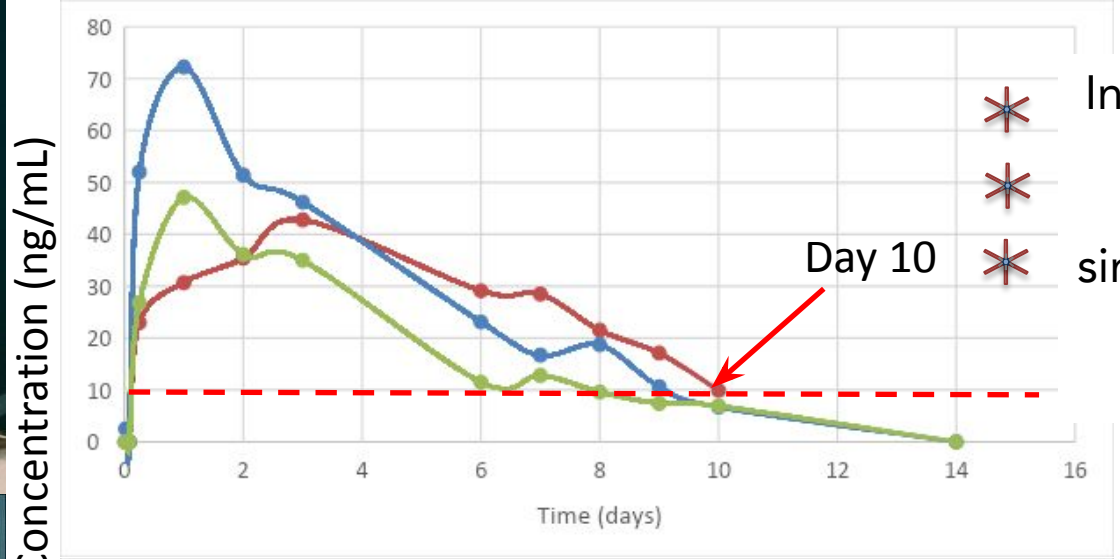
Daily

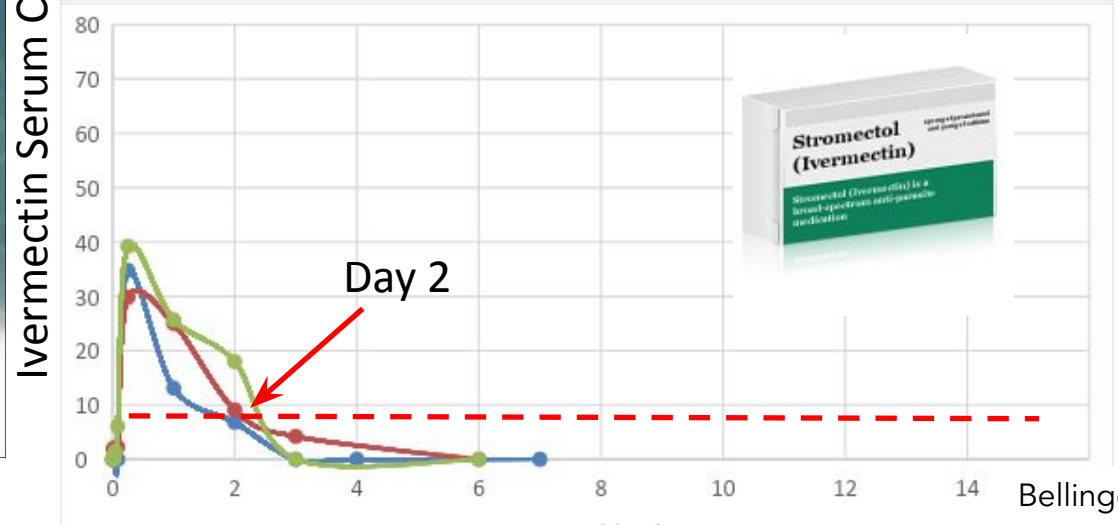
Persistence of Bisphosphonate use - daily, weekly and monthly dosing

Kishimoto et al Arch Osteop 2015

The Economist, In for the long haul, Sept 5, 2015

Endoscopic video – day 35 post-deployment



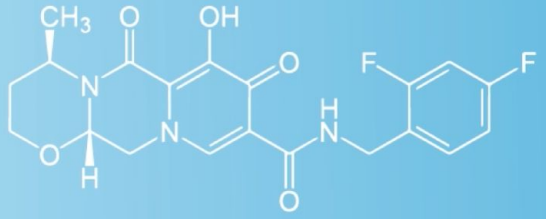


In vivo Evaluation of Ivermectin Loaded Stars – single administration of Stars vs single dose

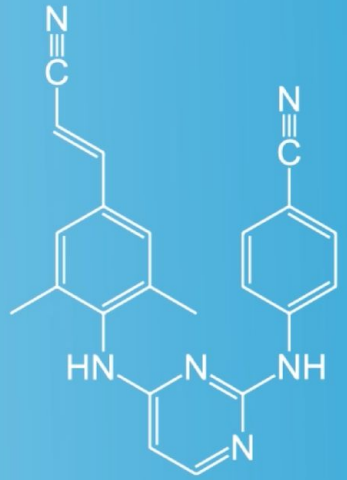
8ng/ml=> mosquitoes Biting will have mean annual lifespan of 1.7 days

Bellinger et al. Science Tr Med 2016

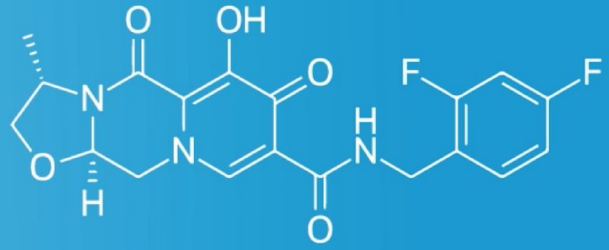
dolutegravir



rilpivirine

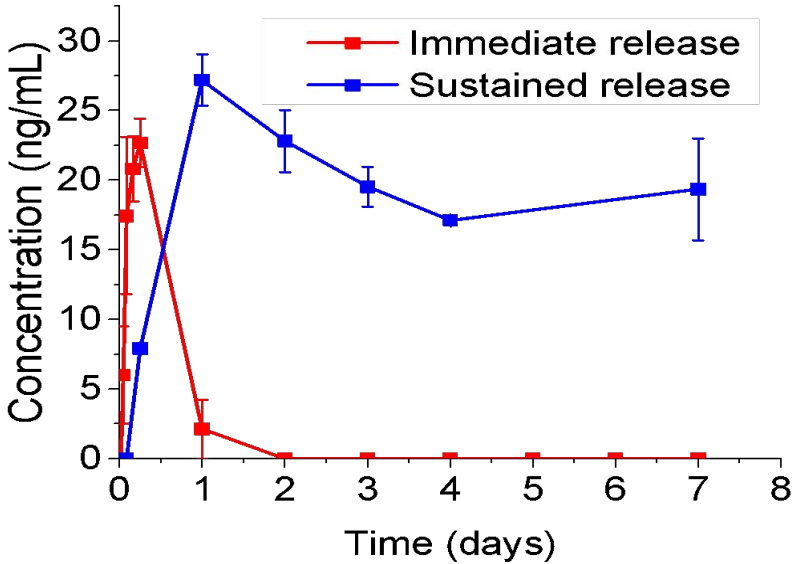


cabotegravir



Kirtane, Abouzid, et al. Nat Comm 2018

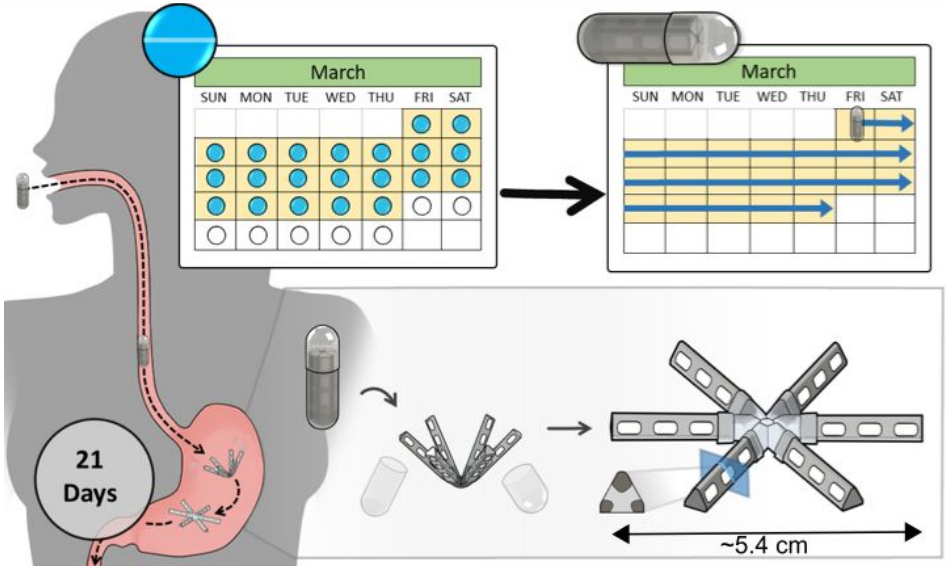
Sustained delivery of antiretrovirals – Rilpivirine

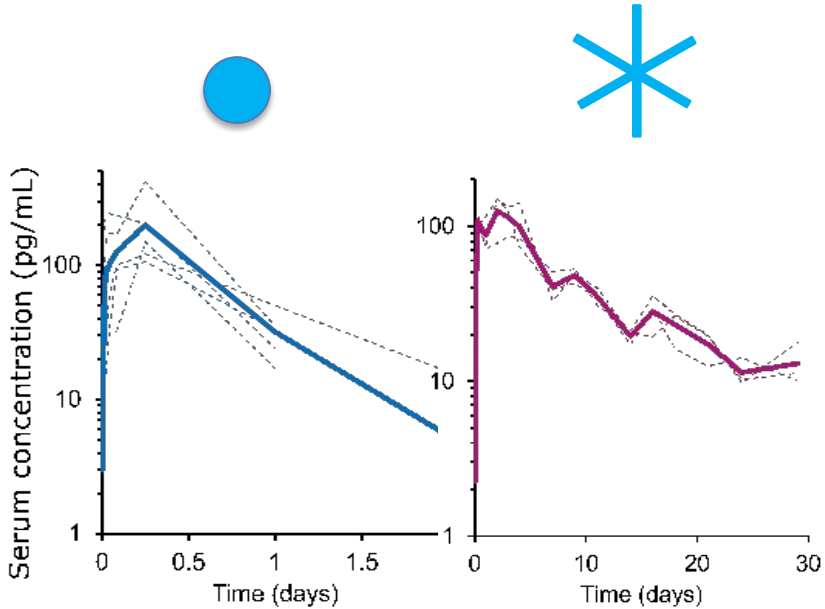


Rilpivirine was dosed to pigs either as an immediate release or sustained release formulation. Plasma concentrations of the drug were assessed using LC-MS/MS. Data is represented as mean ± S.E.M., n=3 animals/group.

Kirtane, Abouzid, et al. Nat Comm 2018

Once a month oral contraception

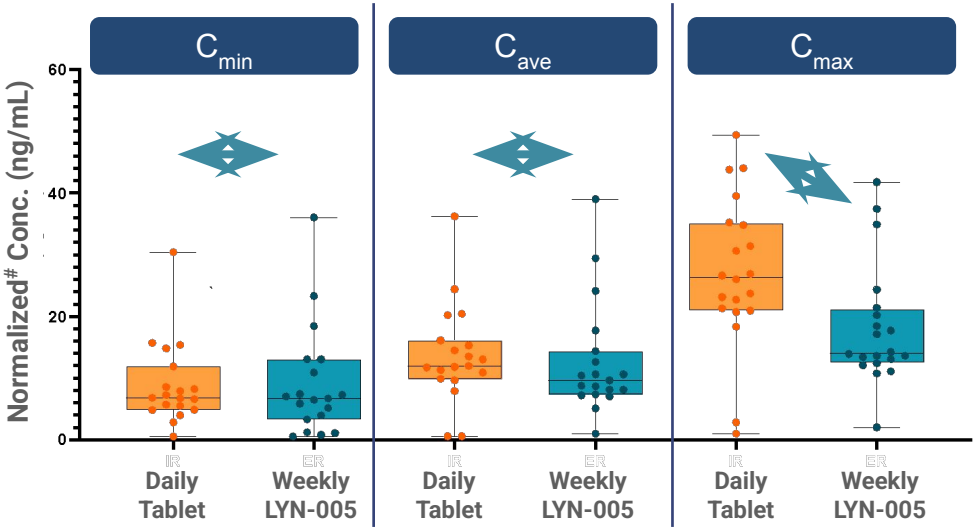




But what is next?

Kirtane, Hua, et al. *Science Translational Medicine (2019)*

Phase 2 Study Demonstrated **Target PK Achievable** for Oral Weekly Product



Richard Scranton

Jess Ballinger

Patricia Hurter

Oral weekly risperidone shows comparable Cmin and Cave & desirable reduction in Cmax

Disclosure: G. Traverso is a co-founder, BOD member and has a financial interest in Lyndra

2mg and 4mg daily equivalents normalized to 2mg dose

2021

Massachusetts Institute of Technology

HARVARD MEDICAL SCHOOL

BWH BRIGHAM AND WOMEN'S HOSPITAL

MITMECHE

James Byrne

POSTER #132

Thank you!

Vivian Feig

POSTER #454

Giovanni Traverso

cgt20@mit.edu, ctraverso@partners.org

BILL & MELINDA GATES foundation

NATIONAL INSTITUTES OF HEALTH

novo nordisk

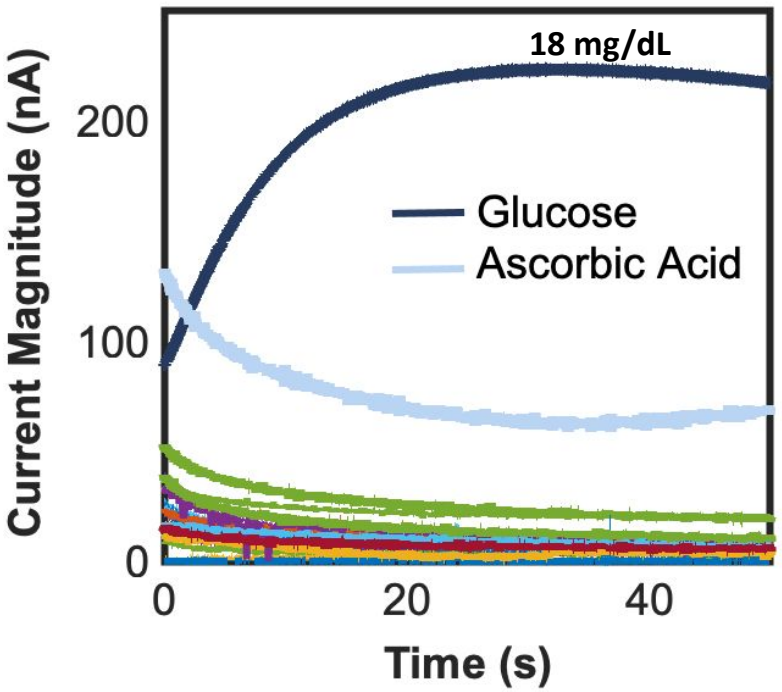
THE LEONA M. AND HARRY B. HELMSLEY CHARITABLE TRUST

DARPA

Karl Van Tassel (1925) Career Development Professorship

EXTRAS

Results: Cross-Sensitivity Testing



Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use

Guidance for Industry and Food and Drug Administration Staff

Document issued on: September 29, 2020.
The draft of this document was issued on November 30, 2018.

- Tested interferences at concentrations recommended by **FDA-2013-D-1446**
- Only interferent is ascorbic acid, at a 8x physiological concentration which is

Current magnitude (nA) of interferents and Glucose			
Glucose (18mg/dL)	**220.94 ± 12.68**	Ibuprofen	1.76 ± 0.84
Acetaminophen	9.27 ± 1.31	L-Dopa	8.94 ± 0.87
Ascorbic Acid	81.94 ± 1.26	Mannitol	4.55 ± 0.99
Bilirubin (conjugated)	13.85 ± 0.39	Mannose	2.55 ± 0.96
Bilirubin (unconjugated)	8.98 ± 0.94	Methyldopa	32.61 ± 1.07
Cholesterol	9.51 ± 0.81	Salicylic Acid	11.62 ± 1.14
Creatinine	6.14 ± 0.80	Sodium	5.77 ± 0.97
Dopamine	2.73 ± 0.55	Sorbital	10.19 ± 0.83
EDTA	11.32 ± 0.95	Tolazimide	13.39 ± 1.12
Galactose	5.14 ± 0.99	Tolbutamide	3.02 ± 0.75
Gentisic Acid	6.67 ± 0.89	Triglycerides	5.66 ± 0.97
Reduced Glutathione	6.70 ± 0.63	Uric Acid	5.97 ± 0.64
Hemoglobin	6.56 ± 0.91	Xylitol	7.75 ± 0.81
Heparin	4.04 ± 0.88	Xylose	6.82 ± 0.56

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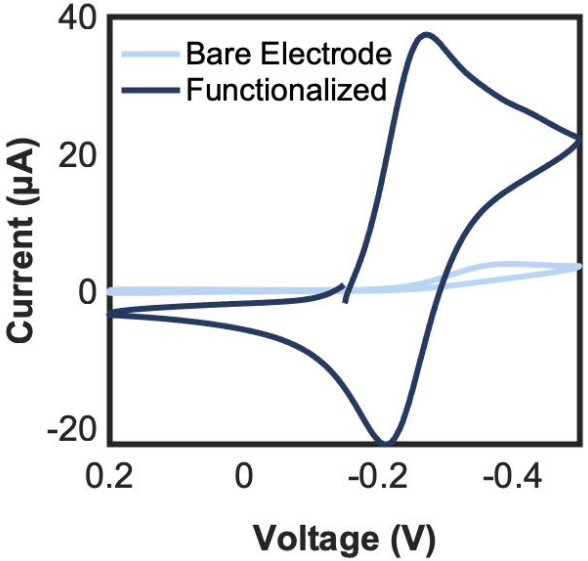
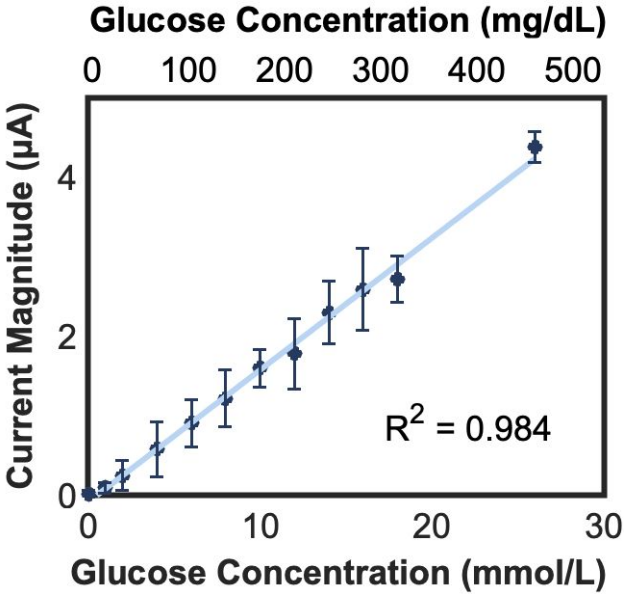
Result: Electrode surface modification



Cyclic voltammetry confirms that our working electrode is electrochemically active.



In-vitro characterization of our sensor indicates we have linear response in current vs glucose concentration up to 26 mmol/L

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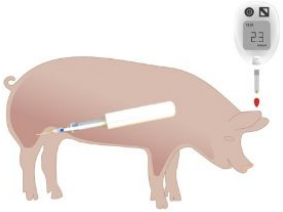
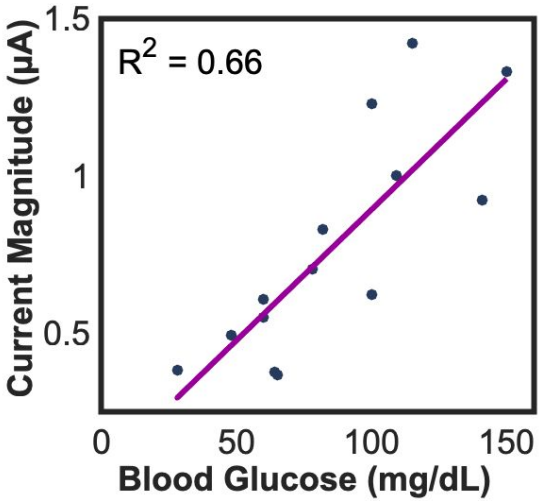
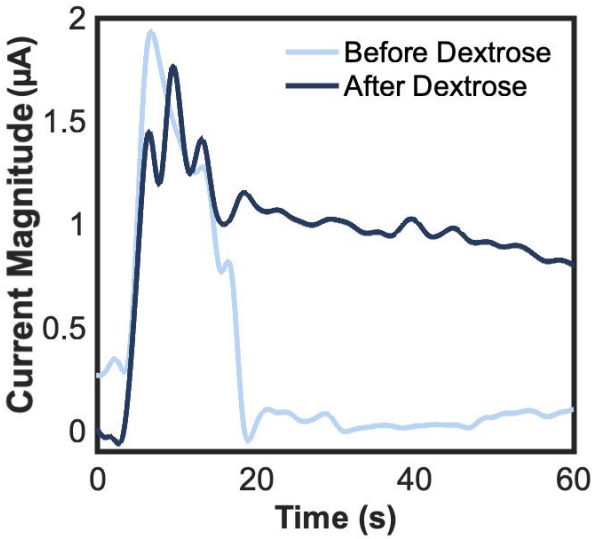
Results: In-vivo measurements





Measurement before and 5 mins following dextrose delivery via femoral catheter.



- All-in-one needle sensor measurements corresponds to blood glucose measurements
- It is possible that distribution can be reduced from calibration to the animal, and optimization of insertion location
- There could also be differences in interstitial fluid glucose vs blood glucose that should be investigated in future