Understanding physical mechanisms in gastric digestion to develop next generation of foods for healthful benefits

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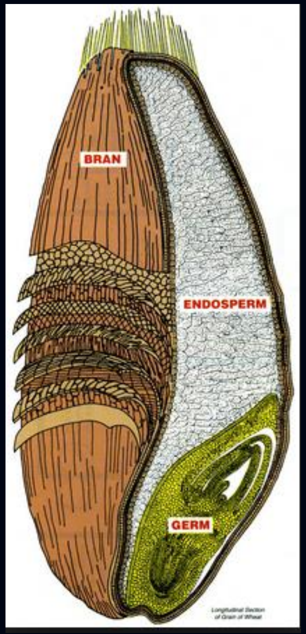
Food Chain
Farm to Fork

- Safety
- Quality
- Healthy
- Affordability
- Convenience
- Sustainability

- Food Microbiology
- Food Chemistry
- Sensory Science
- Nutrition
- Engineering

Food Chain -
Food Structure modifications



Grinding

Milling

Baking

Emulsifying

Separation processes

Drying

Crystallization

Cooking

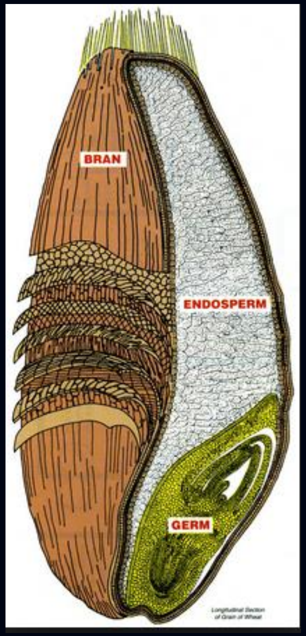
Concentration

Frying

http://cookingking.org/wp-content/uploads/2013/08/baguette-courte.jpg

http://pantryparatus.com/media/blog-images/Kernel_of_Wheat_free_use.jpg

Food Chain -
Food Structure modifications



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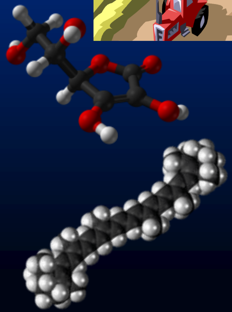
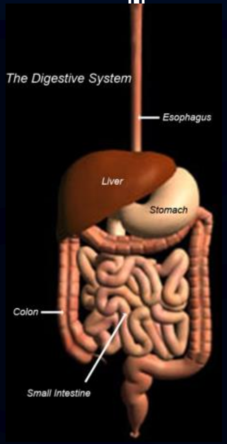
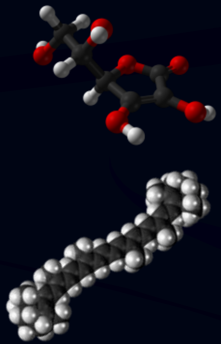
Food Chain -
Food Structure modifications

Molecules





Processes:
- Size reduction
- Fluid flow
- Mixing
- Mass transfer
- Diffusion
- Dissolution
- Erosion
- Fermentation



Molecules

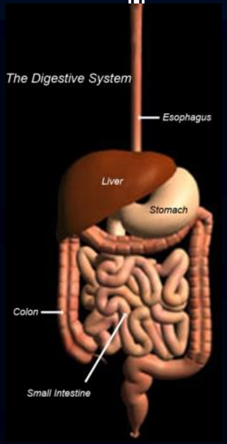
Gastrointestinal Tract --- the ultimate food processing factory!

https://upload.wikimedia.org/wikipedia/commons/c/ca/Ascorbic-acid-from-xtal-1997-3D-balls.png
By NEUROtiker - Own work, Public Domain, https://commons.wikimedia.org/w/index.php?curid=3962569

Food Chain -
Food Structure modifications



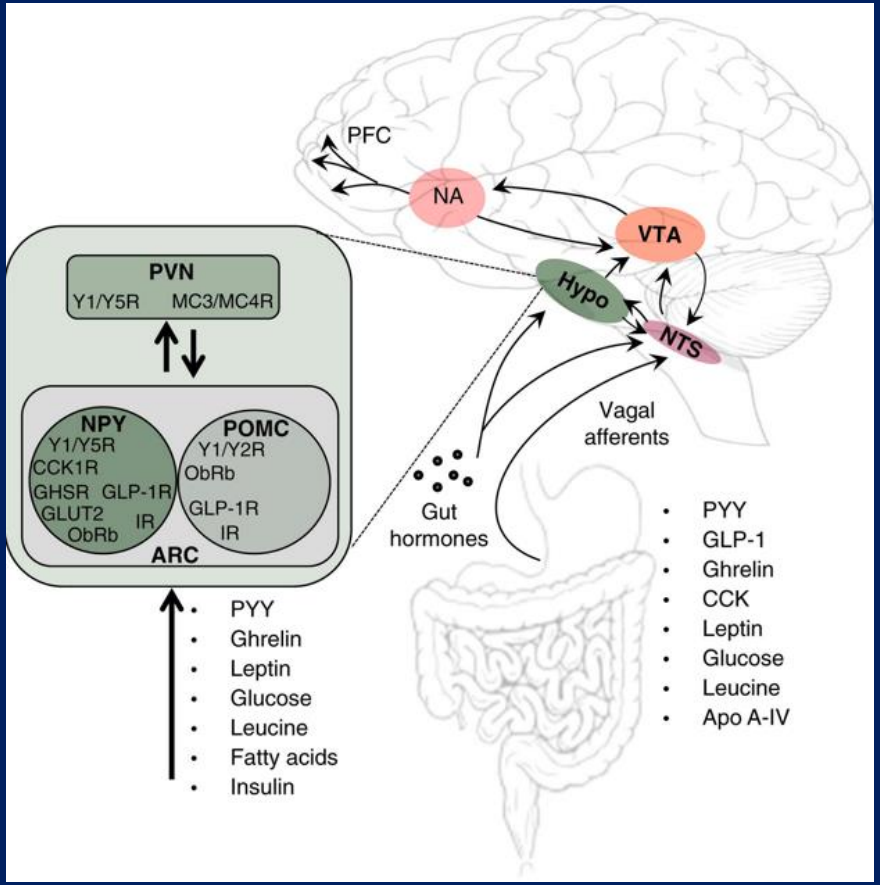
- Is there a link between physical and material properties of foods, and nutrient release from foods in the GI tract?

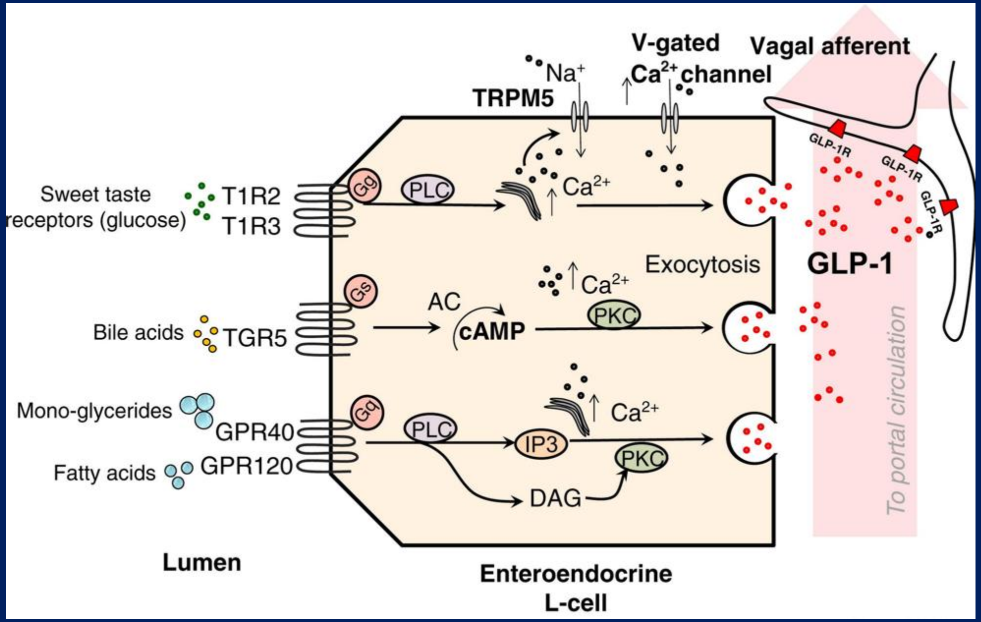




Role of Food Material Properties and Disintegration Kinetics in Gastric Digestion - USDA NRI 2008-

Brain – Gut Connections





Serrano,J.,Casanova-Martí,A.,Blay, A.T.,Terra,X., Pinent, M.,Ardevol,A. Trends in Food Science & Technology 68 (2017) 113-129
Chambers, A. P., Sandoval, D.a., & Seeley, R. J. (2013). Integration of satiety signals by the central nervous system. Current Biology: CB, 23(9)

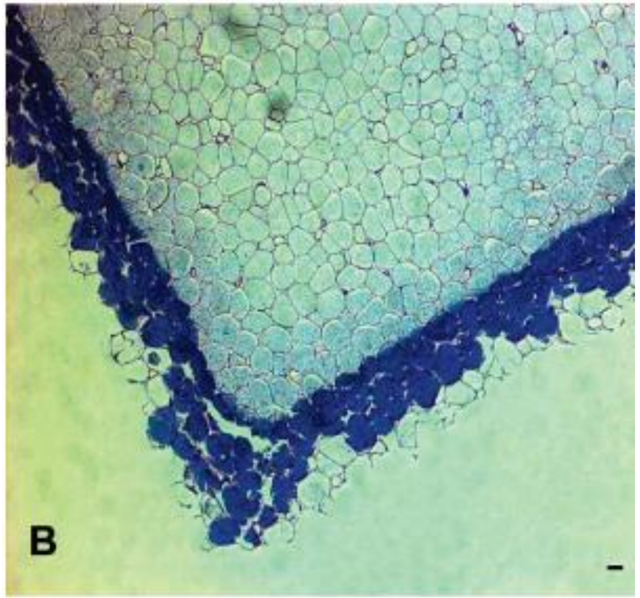
Food Matrix Structure and Nutrient Bioavailability

Nutrient	Food	Matrix state	Bio-availability	Reference
β-carotene	Carrot	Raw	19-34%	Van het Hof et al. (2000)
	Carrot	Carrot Juice	70% higher than raw	Castenmiller et al (1999)
α– tocopherol	Broccoli	Different cooking methods	480%-530% higher than raw	Bernhardt & Schlich (2005)
Lutein	Tomato	Tomato paste	22%-380% greater plasma response than fresh tomato	Van het Hof et al. (2000)

- Almonds are one of the richest sources of dietary vitamin E with benefits to reducing risk of CHD and certain cancers.
- Only about 45% of vitamin E was bioaccessible from powdered almonds.

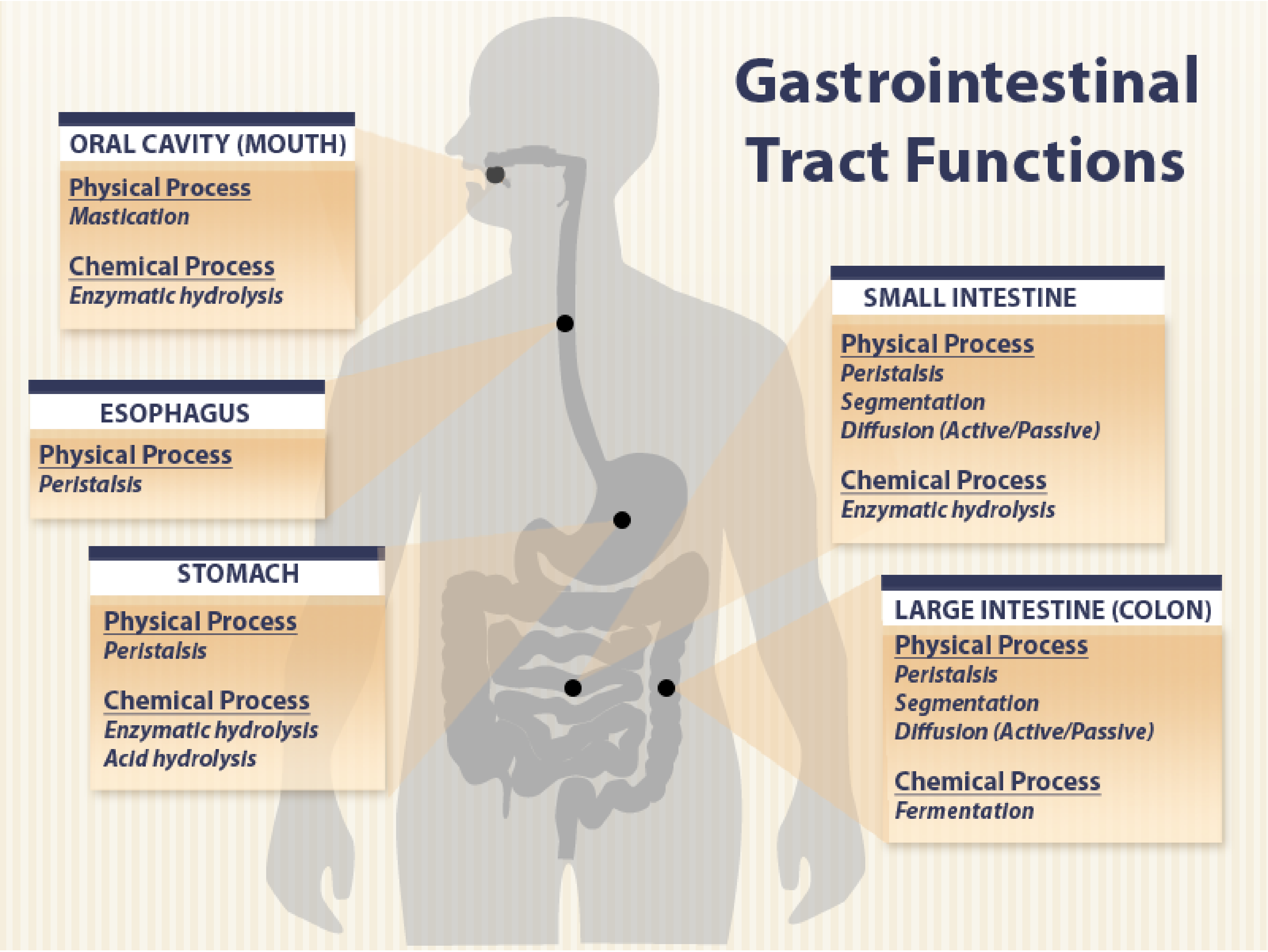
Bioaccessibility

Proportion of a nutrient that can be released from a complex food matrix and potentially available for absorption in GI tract

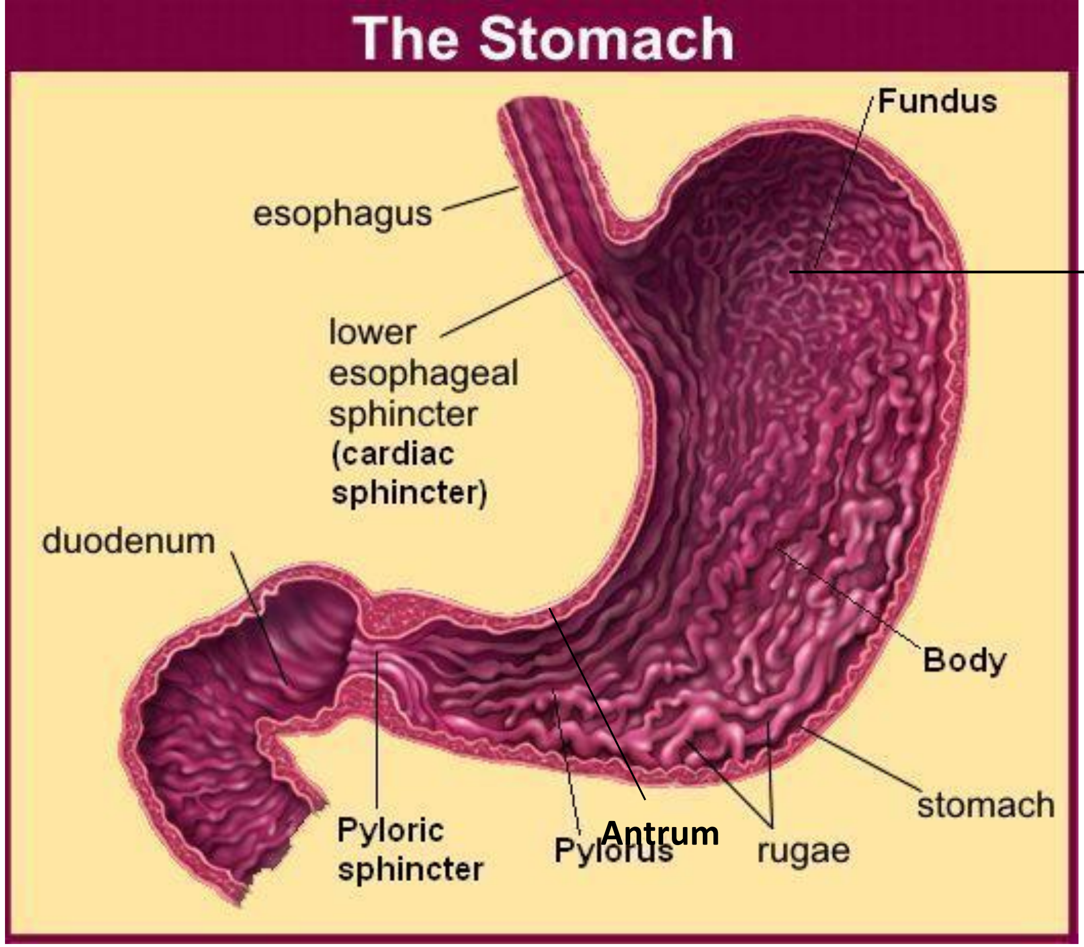


Samples obtained via ileostomy after 3.5 hr of digestion. Volunteers fed 2 mm cube raw almonds

Mandalari et al. (2008) J Ag Food Chem



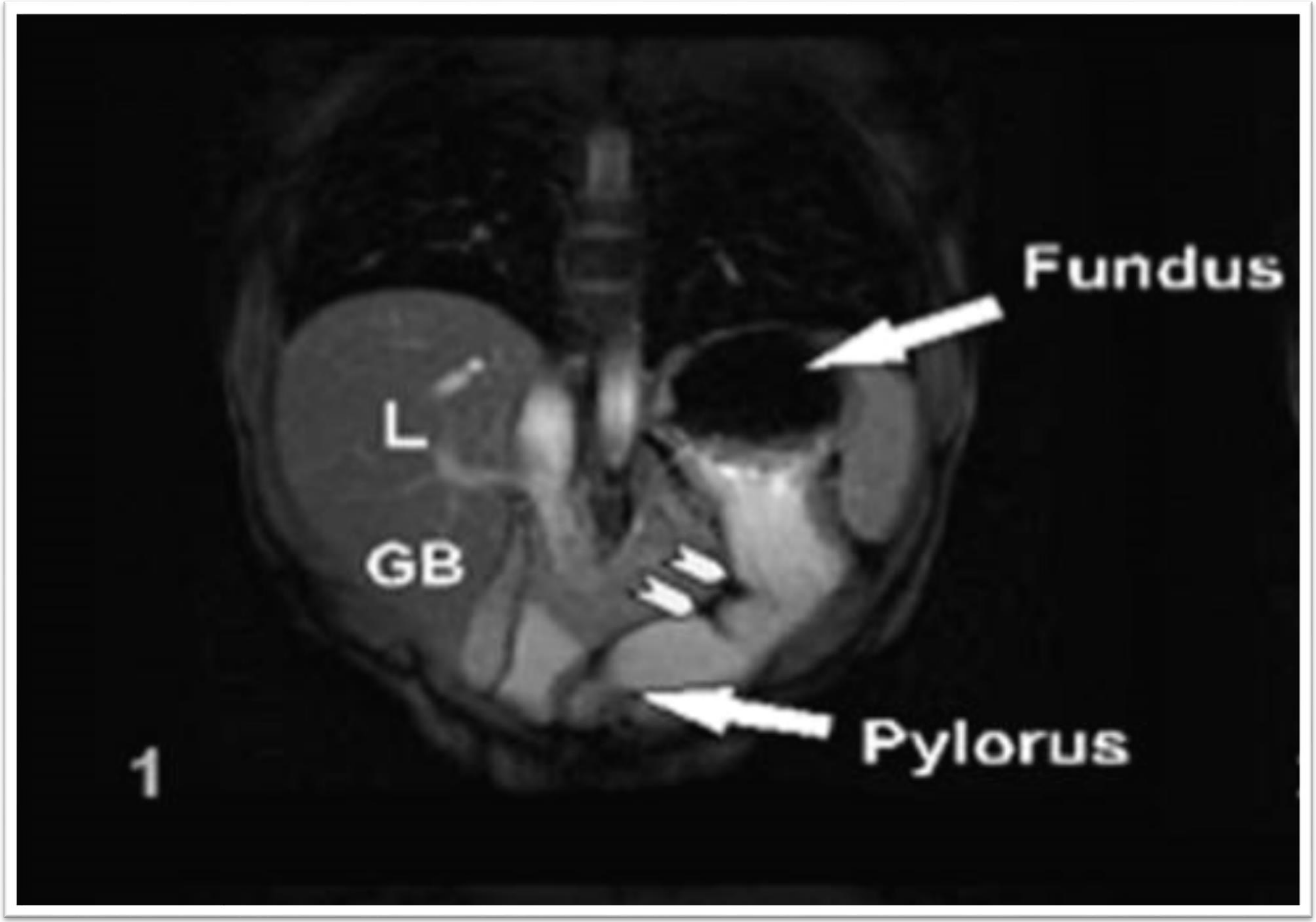
Gastrointestinal Tract Functions
ORAL CAVITY (MOUTH)
Physical Process
Mastication
Chemical Process
Enzymatic hydrolysis
ESOPHAGUS
Physical Process
Peristalsis
STOMACH
Physical Process
Peristalsis
Chemical Process
Enzymatic hydrolysis
Acid hydrolysis
SMALL INTESTINE
Physical Process
Peristalsis
Segmentation
Diffusion (Active/Passive)
Chemical Process
Enzymatic hydrolysis
LARGE INTESTINE (COLON)
Physical Process
Peristalsis
Segmentation
Diffusion (Active/Passive)
Chemical Process
Fermentation

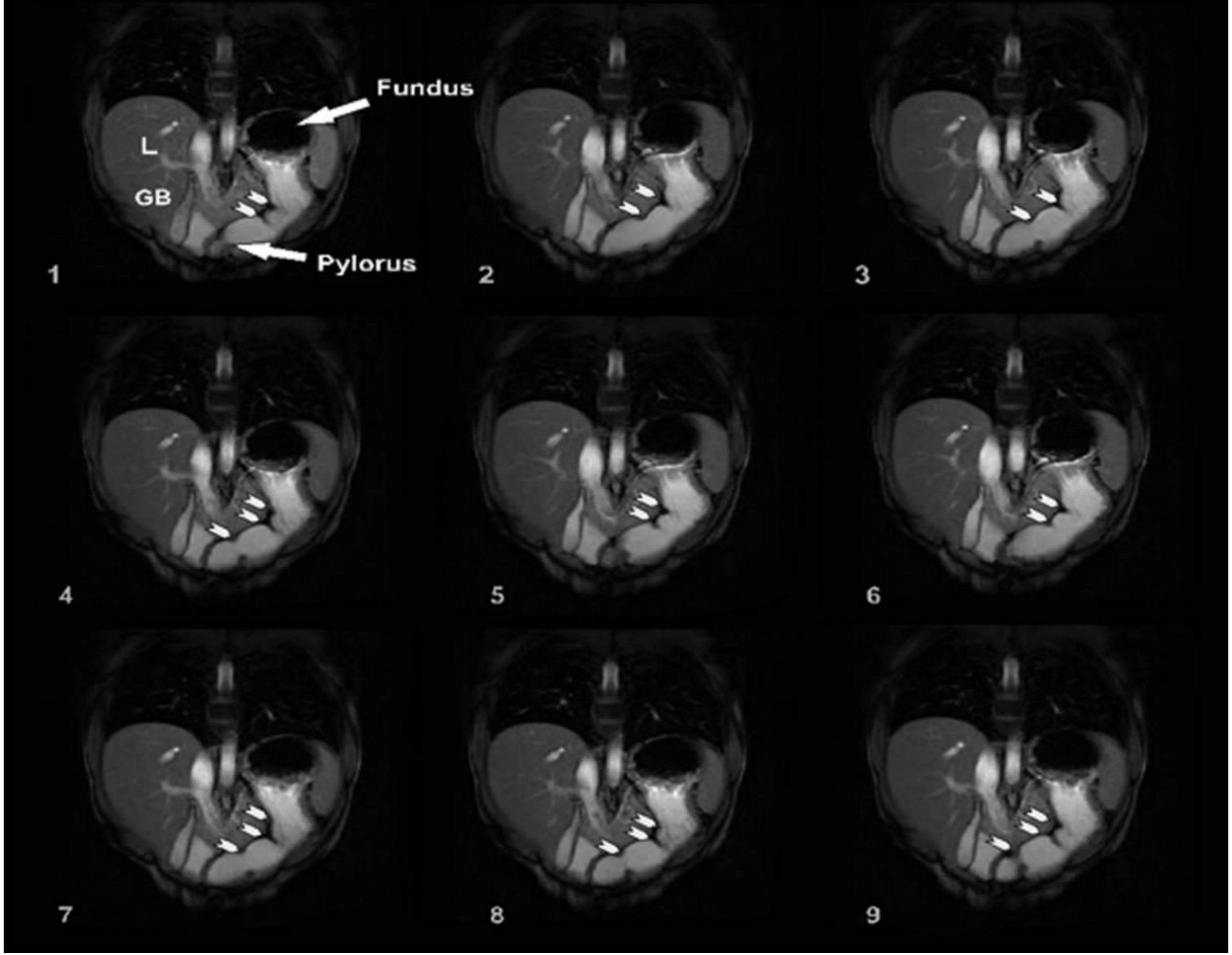


- Fundus: begins digestion of proteins and mixes together stomach contents.
- Body: digests proteins and blends materials in stomach and reduced to a paste
- Antrum: Breaks down large food material into small particles

- Pyloric sphincter: a specialized valve that selectively empties the small particles and retains the large

https://img.webmd.com/dtmcms/live/webmd/consumer_assets/site_images/articles/image_article_collections/anatomy_pages/stomach_72.jpg?resize=646px:*&output-quality=100

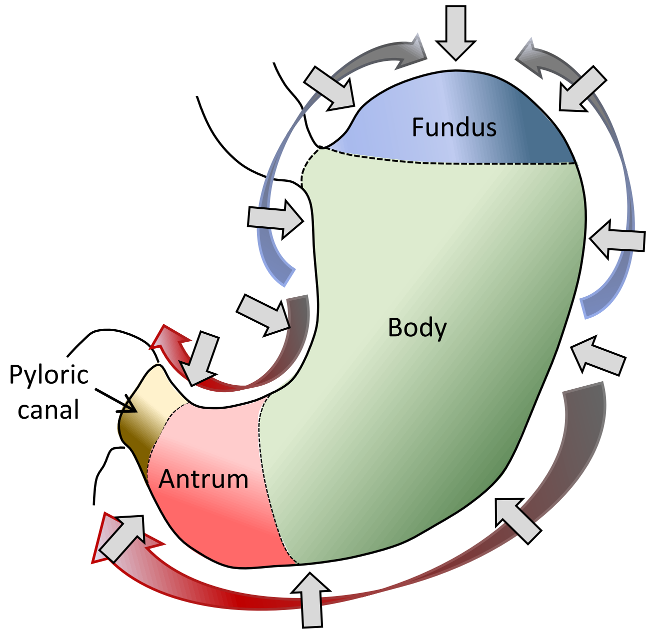

Fundus
L
GB
Pylorus
1



Dynamic MRI image series showing propagating antral contraction waves (small arrows) displayed in time intervals of 10 s. (Schwizer and others 2006)

Gastric Motility

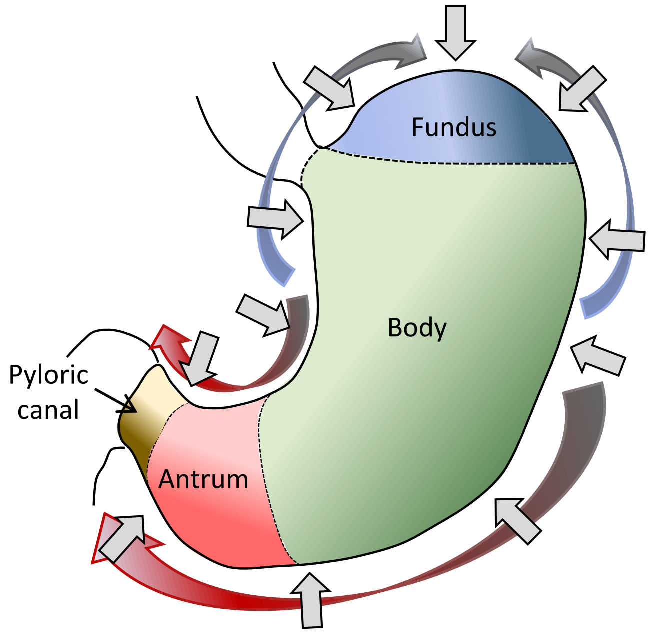
- The motility of the stomach wall can be characterized by three types of muscle contractions.
  - Slow and weak contractions that originate and develop in the upper part of the stomach.
  - A series of regular-peristaltic contraction waves (ACWs) that originate in the middle of the stomach, and propagate towards the pylorus.
  - A tonic contraction of the entire gastric wall that allows the stomach to accommodate itself to varying volumes.



Gastric Motility

- Despite recent advances in imaging technologies, the motility pattern of the gastric wall is still poorly characterized.

- The dynamics of ACWs is the only motor activity experimentally characterized.
  - By using MRI techniques, the motility of ACWs was tracked during 20 minutes after the ingestion of 500ml of a 10% glucose solution (Pal et al., 2007).

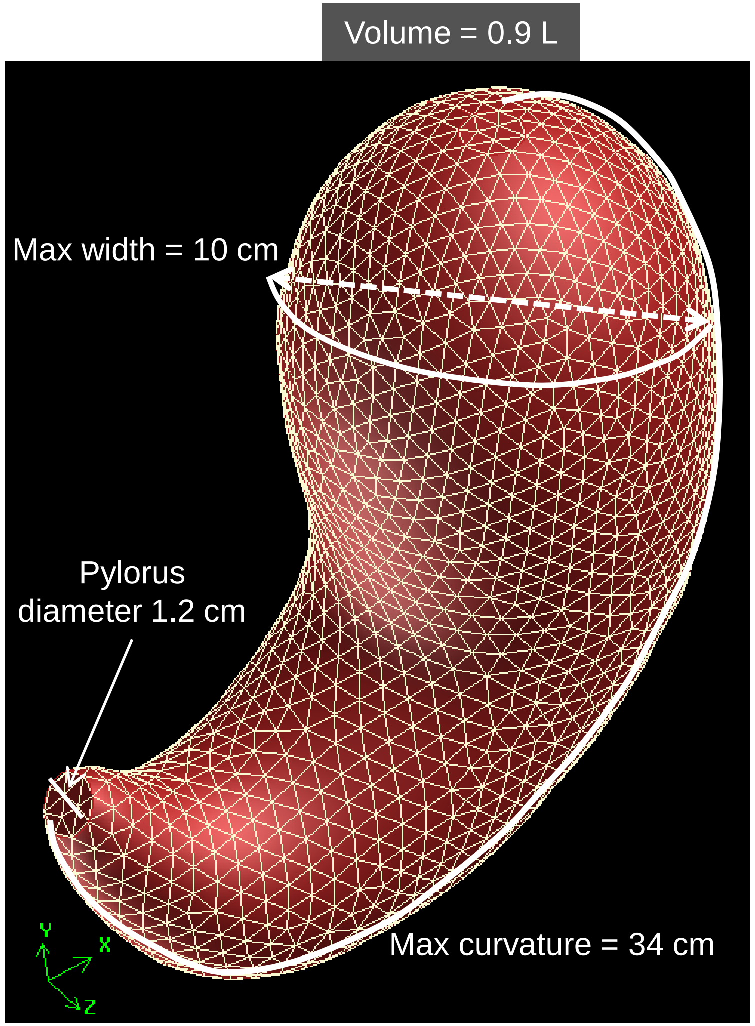


- From an engineering perspective, the human stomach is a receptacle, a grinder, a mixer and a pump that controls the digestion process.
- Consider stomach to be a flexible wall reactor, with peristaltic wall motility.

Develop a realistic computer-aided model of the human stomach and study flow characteristics and solid disintegration

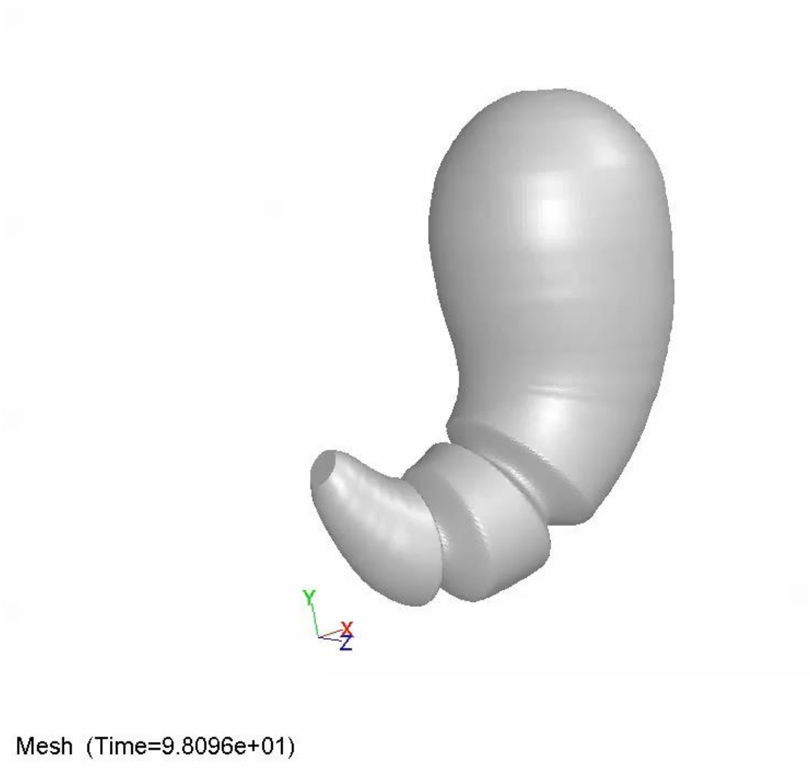
3D Model—Average-Sized human Stomach

- <u>Average dimensions</u>*
  - Greater curvature ≈ 31 cm long.
  - 15 cm wide (at its widest point).
  - Pylorus' diameter is ≈ 1 cm.
  - Stomach's capacity is about 0.94 L.



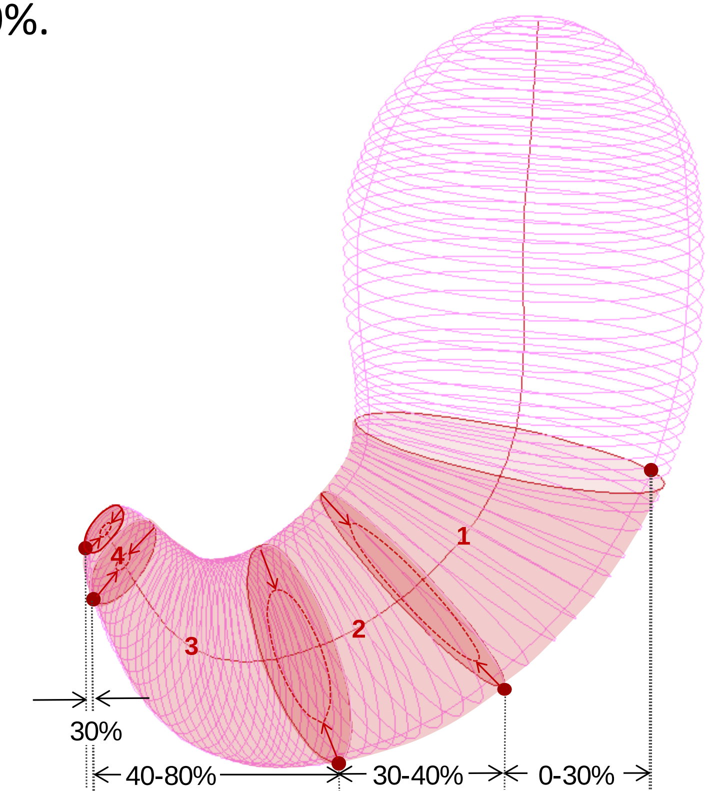
* Keet, 1993; Schulze, 2006.

Gastric Motility during Digestion



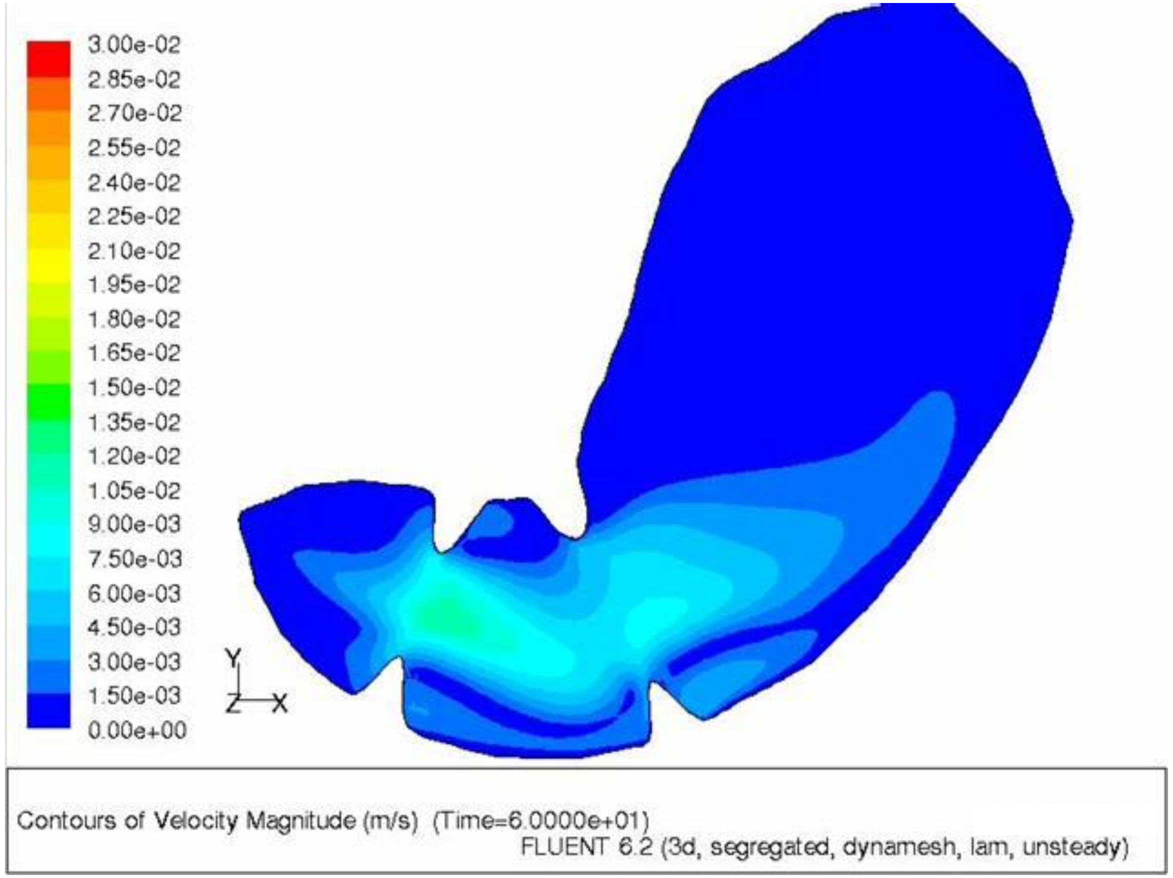
ACW dynamics:

- Initiated every 20s at 15cm from the pylorus.
- Relative occlusion of ACWs: from 0 to 80%.



Fluid Flow in the Stomach

- The strongest fluid motions were predicted within the lower part of the stomach model.
- The rheological properties of gastric contents has a significant effect on the behavior of the antropyloric flow.



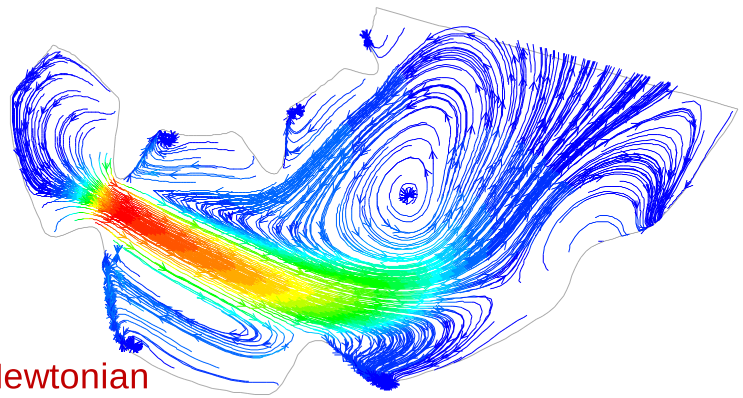
RHEOLOGICAL PROPERTIES OF GASTRIC CONTENTS

- Fluid-dynamics of three different liquid meals were investigated.

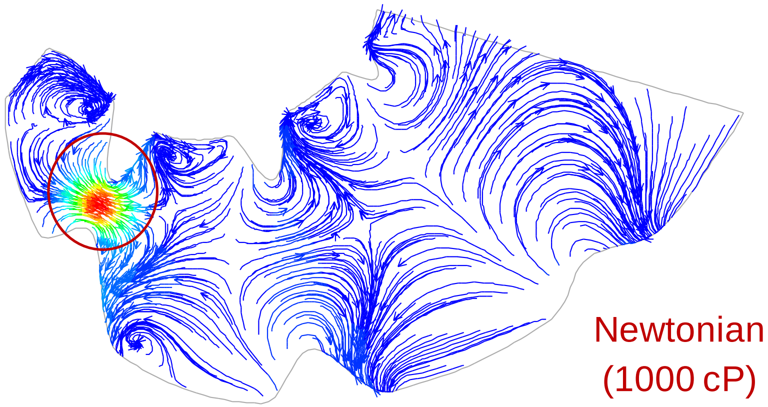
  - Newtonian fluid ($\tau = \mu\ \gamma$).
    - Water: μ =1 cP.
  - Newtonian fluid ($\tau = \mu\ \gamma$).
    - Honey: μ =1000 cP.
  - Non-Newtonian (τ = K γn).
    - Tomato juice (5.8 %):
      K = 0.223 Pa.s^n
      n = 0.59.

ANTROPYLORIC FLOW MOTION

- Effect of viscosity on the formation of the retropulsive jet-like structure.

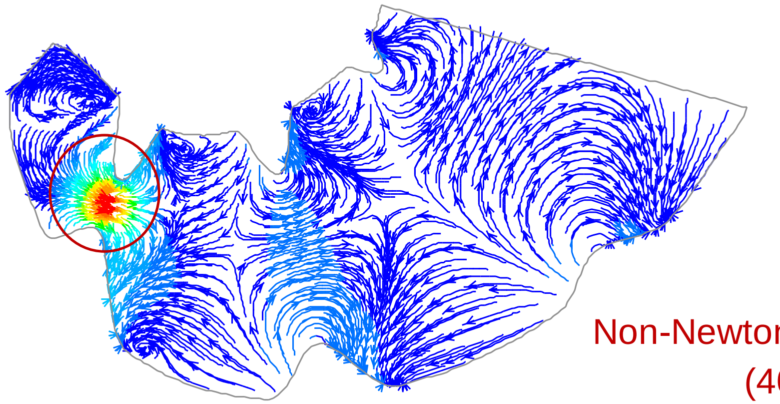


Newtonian
(1 cP)



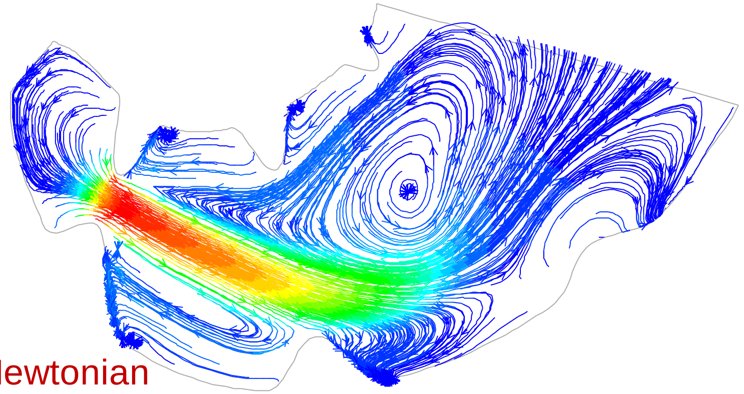
Newtonian
(1000 cP)

- No retropulsive jet-like structure developed.
- Higher and more localized retropulsive velocities were predicted at the peak of the ACW.

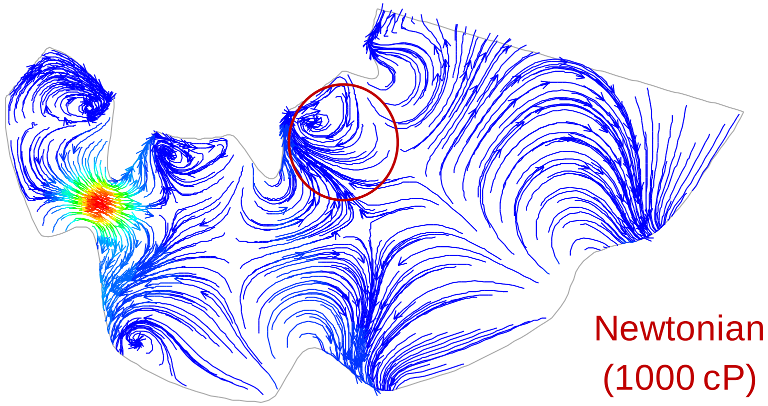


Non-Newtonian-shear thinning
(40-570 cP)

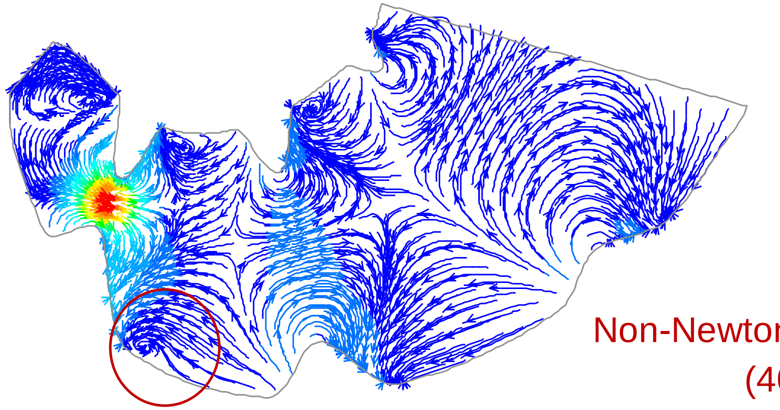
- Effect of viscosity on the formation of eddy structures.



Newtonian
(1 cP)

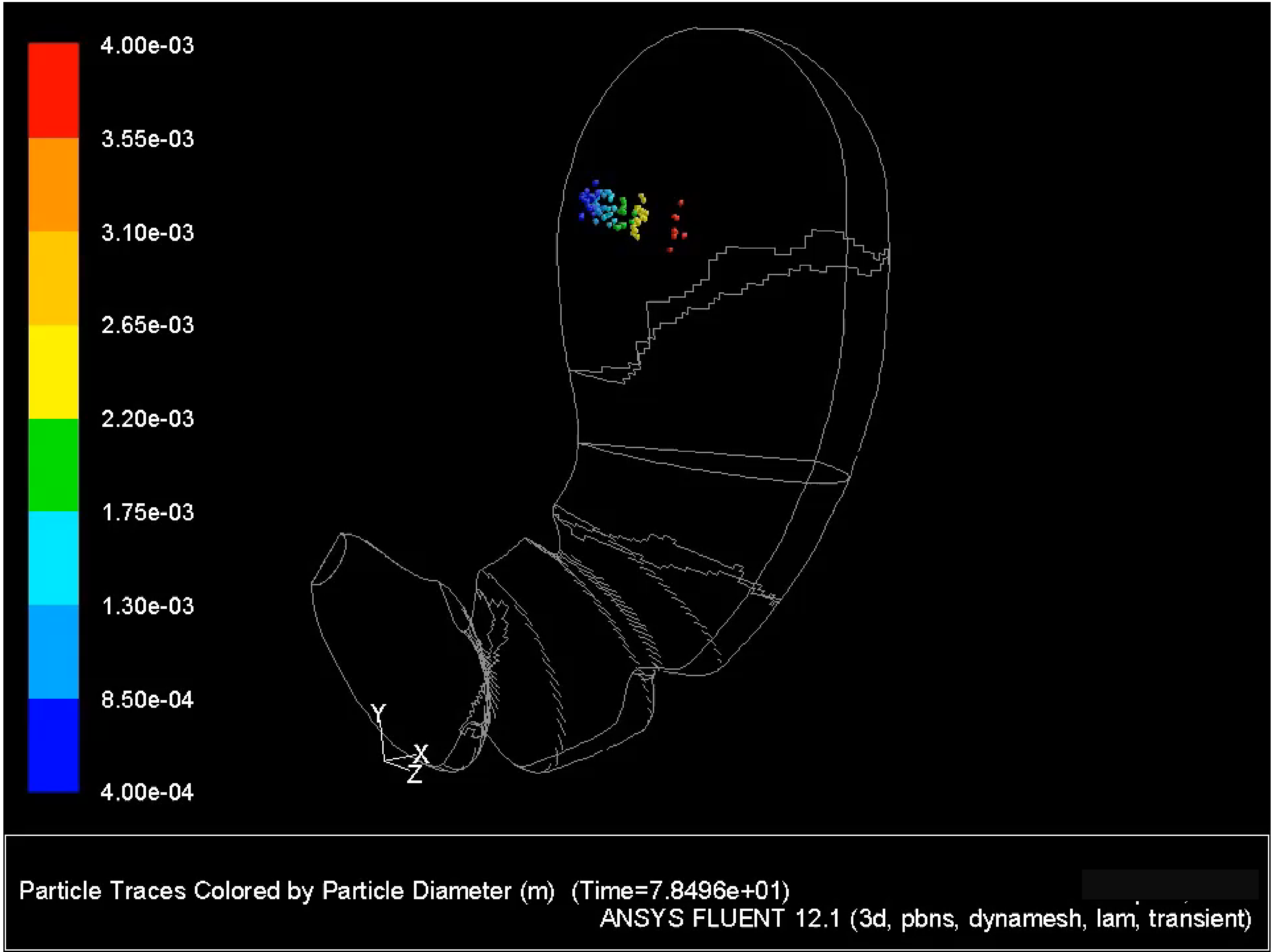


Newtonian
(1000 cP)

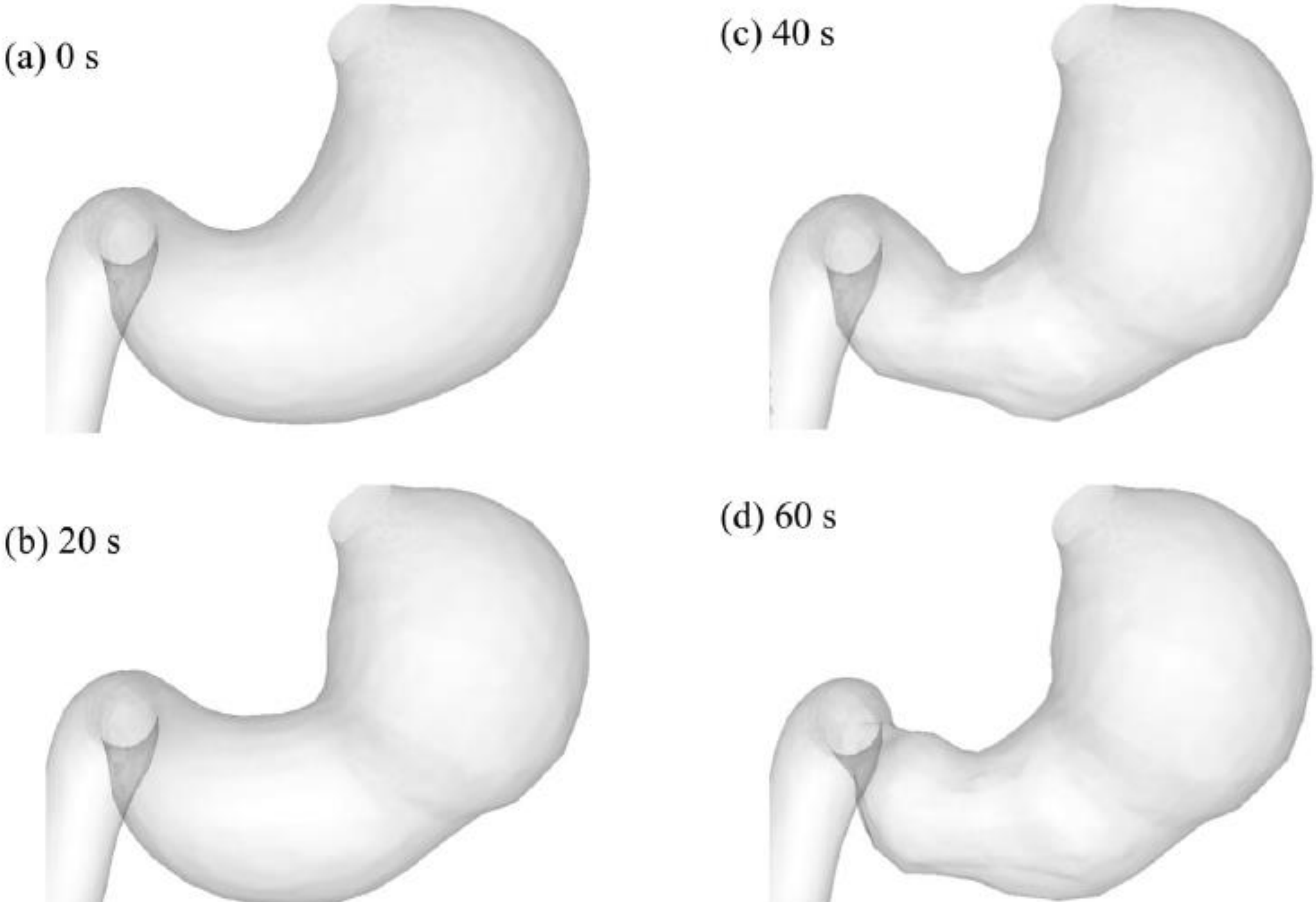


Non-Newtonian-shear thinning
(40-570 cP)

- Eddy structures are confined to smaller regions closer to the gastric walls.

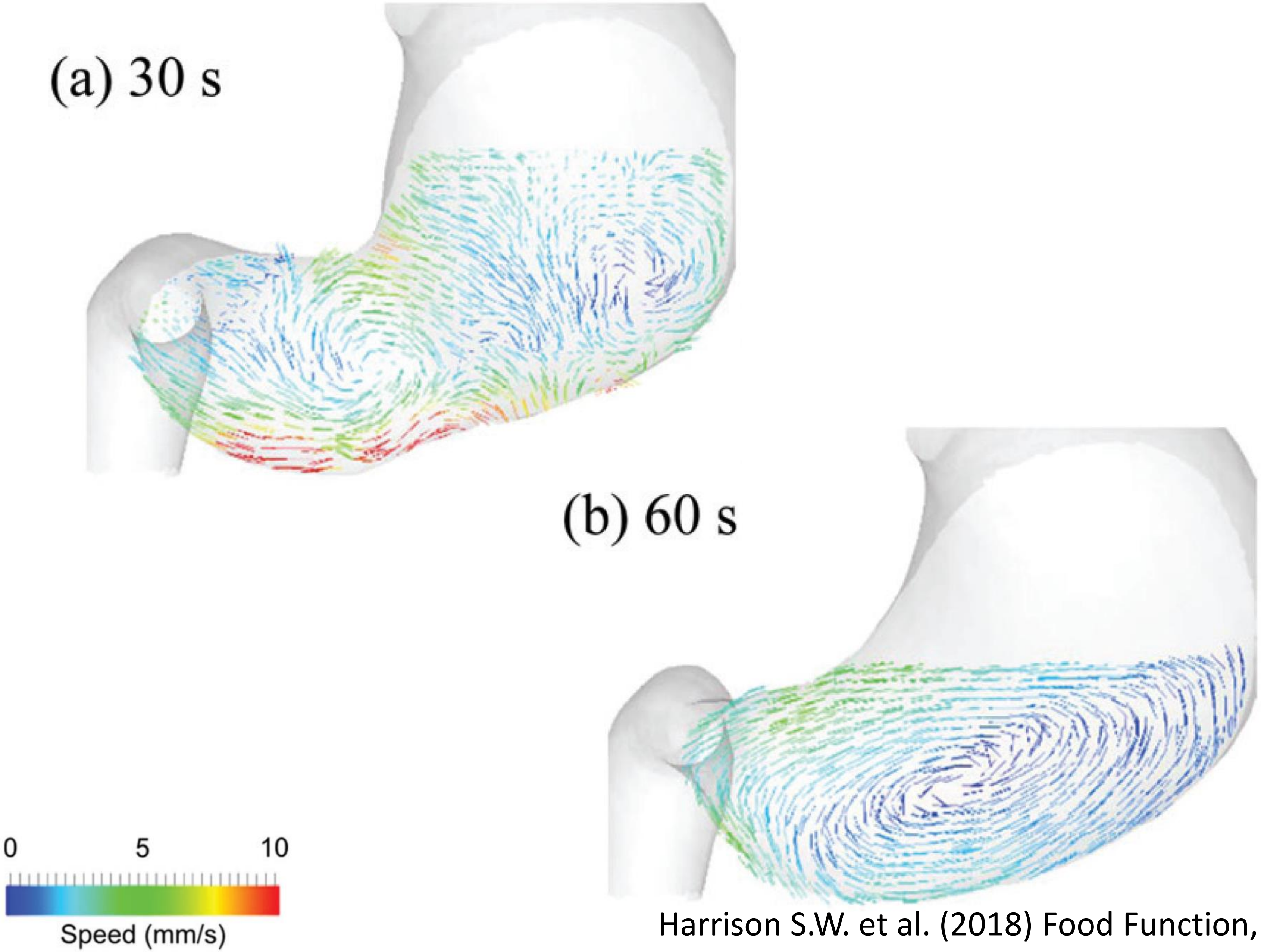

4.00e-03
3.55e-03
3.10e-03
2.65e-03
2.20e-03
1.75e-03
1.30e-03
8.50e-04
4.00e-04
Y
X
Z
Particle Traces Colored by Particle Diameter (m) (Time=7.8496e+01) [redacted]
ANSYS FLUENT 12.1 (3d, pbns, dynamesh, lam, transient)

Computational Modeling – SPH (Smoothed Particles Hydrodynamics)



Harrison S.W. et al. (2018) Food Function, 9.3202

Computational Modeling – SPH (Smoothed Particles Hydrodynamics)



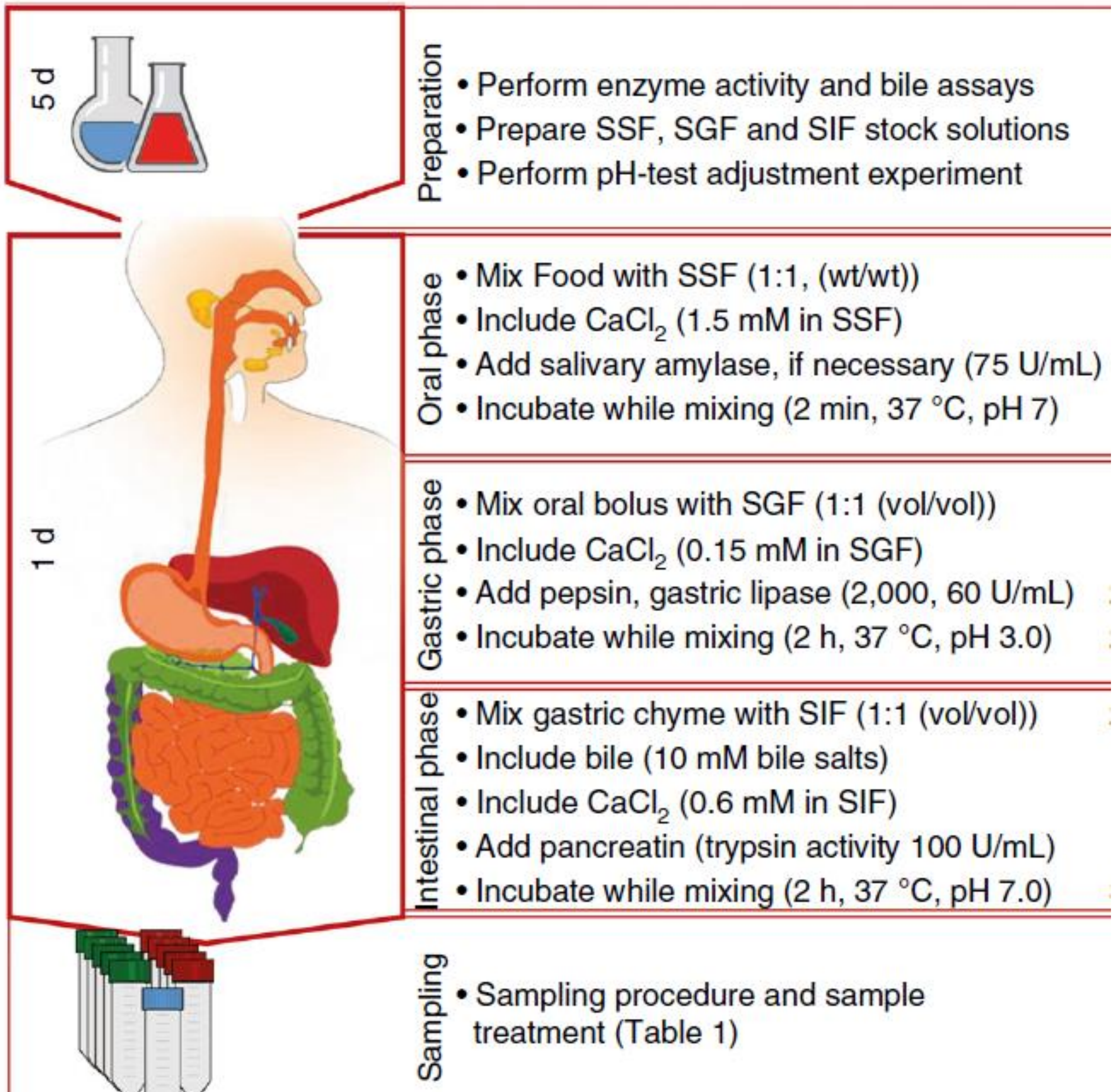
Harrison S.W. et al. (2018) Food Function, 9.3202

In vitro systems

- To study food disintegration and digestion

Shaking bath

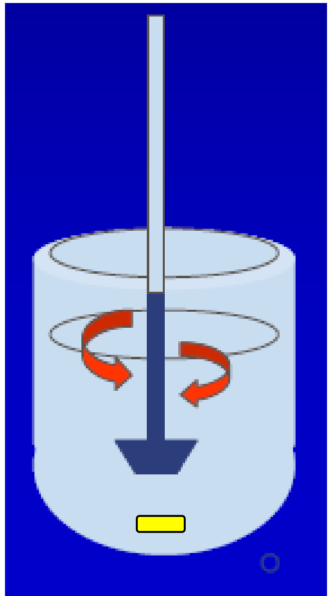
- Used in many studies and pharmaceutical research
- Advantages
  - Ease
  - Minimal physical damage
  - High level of control
- Disadvantages
  - No physical impact (peristalsis)
  - No emptying
  - Just not how a gastric system functions



Brodkorb et al. (2019) INFOGEST static in vitro simulation of gastrointestinal food digestion, Nature Protocols

In Vitro Dissolution Testing of Oral Dosage Forms: USP apparatus

- Apparatus 1 - Basket (37º)
- Apparatus 2 - Paddle (37º)
- Apparatus 3 - Reciprocating Cylinder (37º)
- Apparatus 4 - Flow-Through Cell (37º)
- 500 ml –1000 ml (900 ml)
- Agitation speed: 50-100 rpm for basket method, and 25-75 rpm for paddle method.
- Aqueous dissolution medium composed of 0.1 N HCl (or pH 1.2)



Needs in Pharmaceutical research

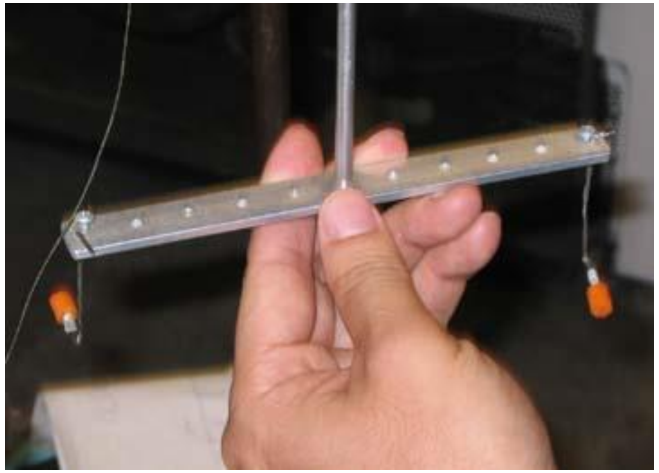
- *“... mechanical functions of stomach and duodenum are well defined in terms of viscoelastic properties, movement patterns of their walls….flow phenomenon to digestion remains to be established…contribution of pressure forces, shear stresses, flow reversals and vortical flow remains to be quantified.”*

Schulze (2006)

Food Disintegration System

- Custom-built turntable
- Jacketed glass chamber
- On-line Force measuring apparatus

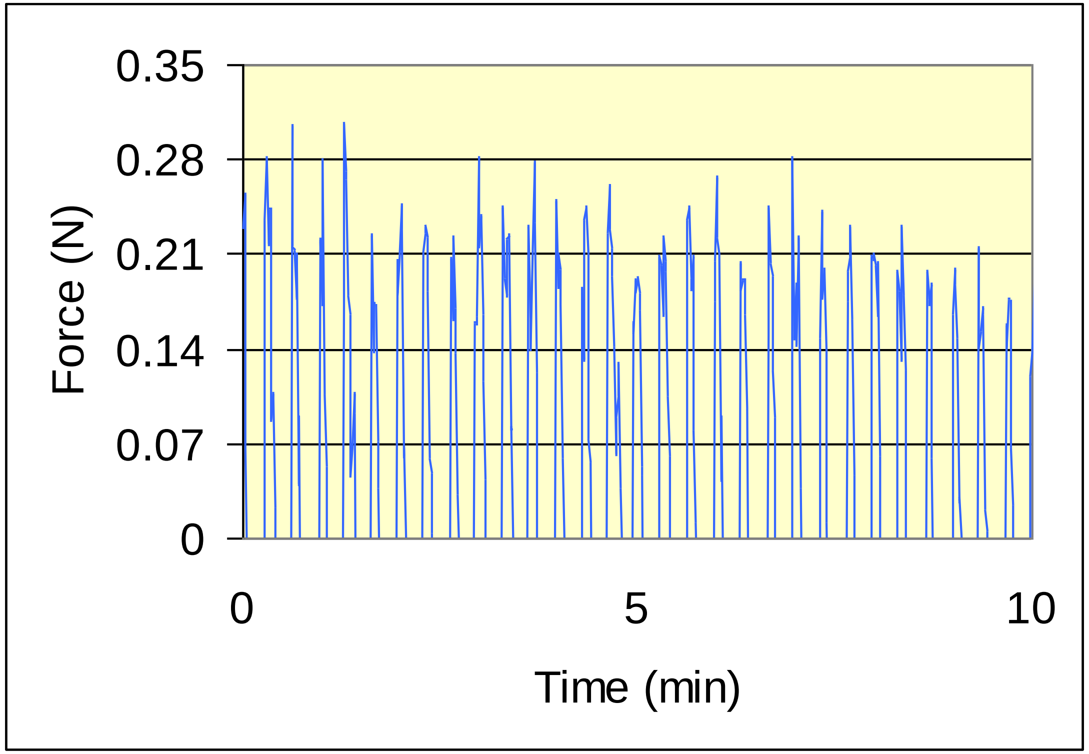
GP-22 ABS plastic beads
(~3 mm dia)



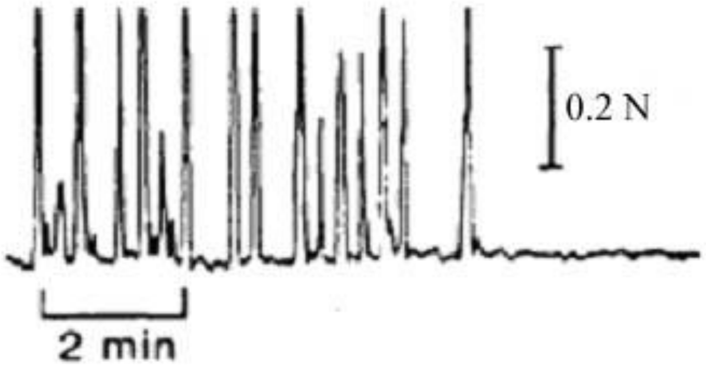
Sample holder

Kong and Singh (2008) *J Food Sci*

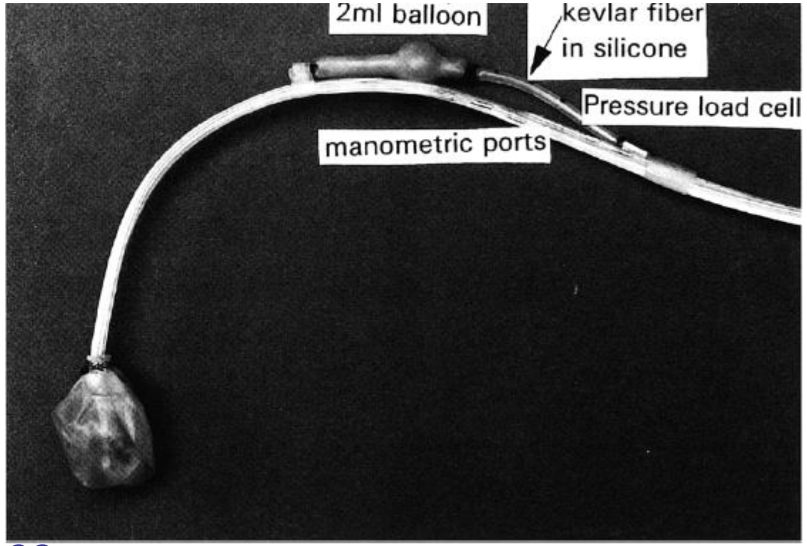
Profile of periodic force



In vitro

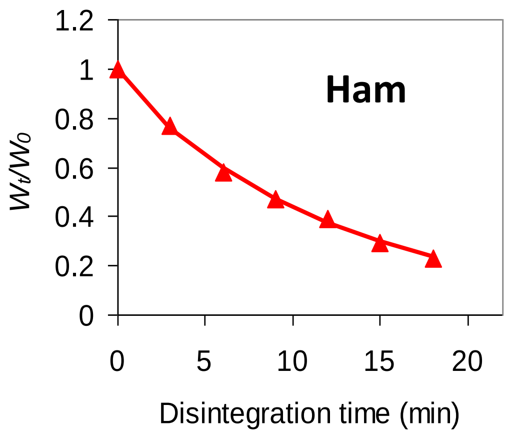


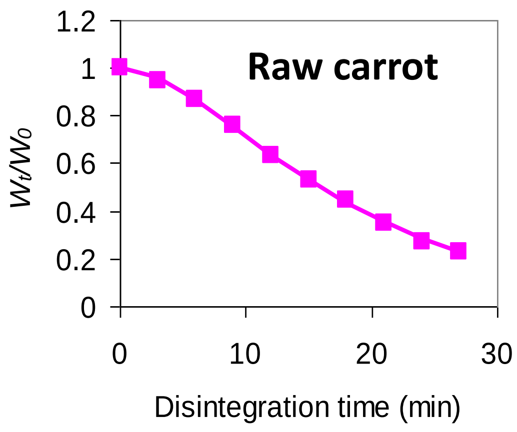
In vivo

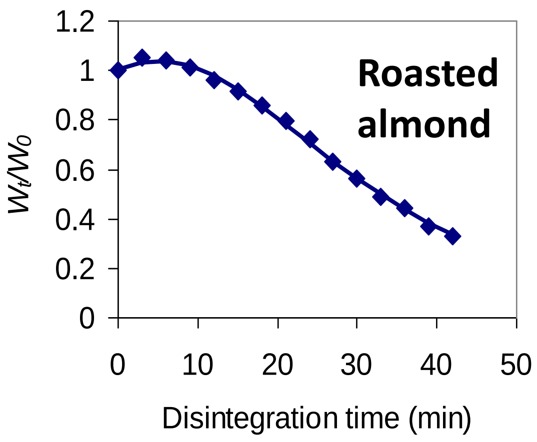


Vassallo MJ, et al. 1992.

Typical disintegration profiles

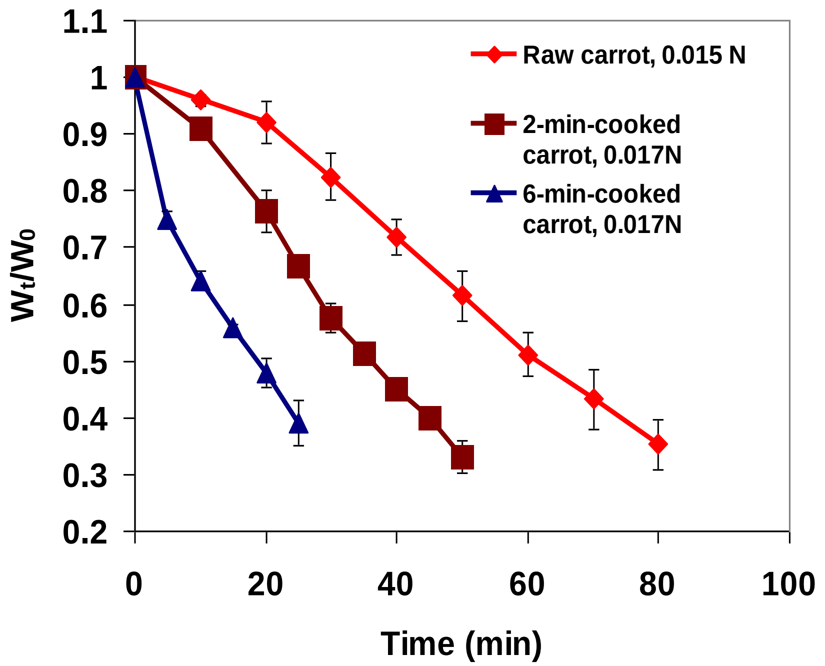






- Exponential: canned kidney beans, ham, Gummy bear candy, apple bar
- Reverse Sigmoidal: fruits such as raw carrots
- Delayed reverse sigmoidal: dry foods such as peanuts, almonds, fried dough products

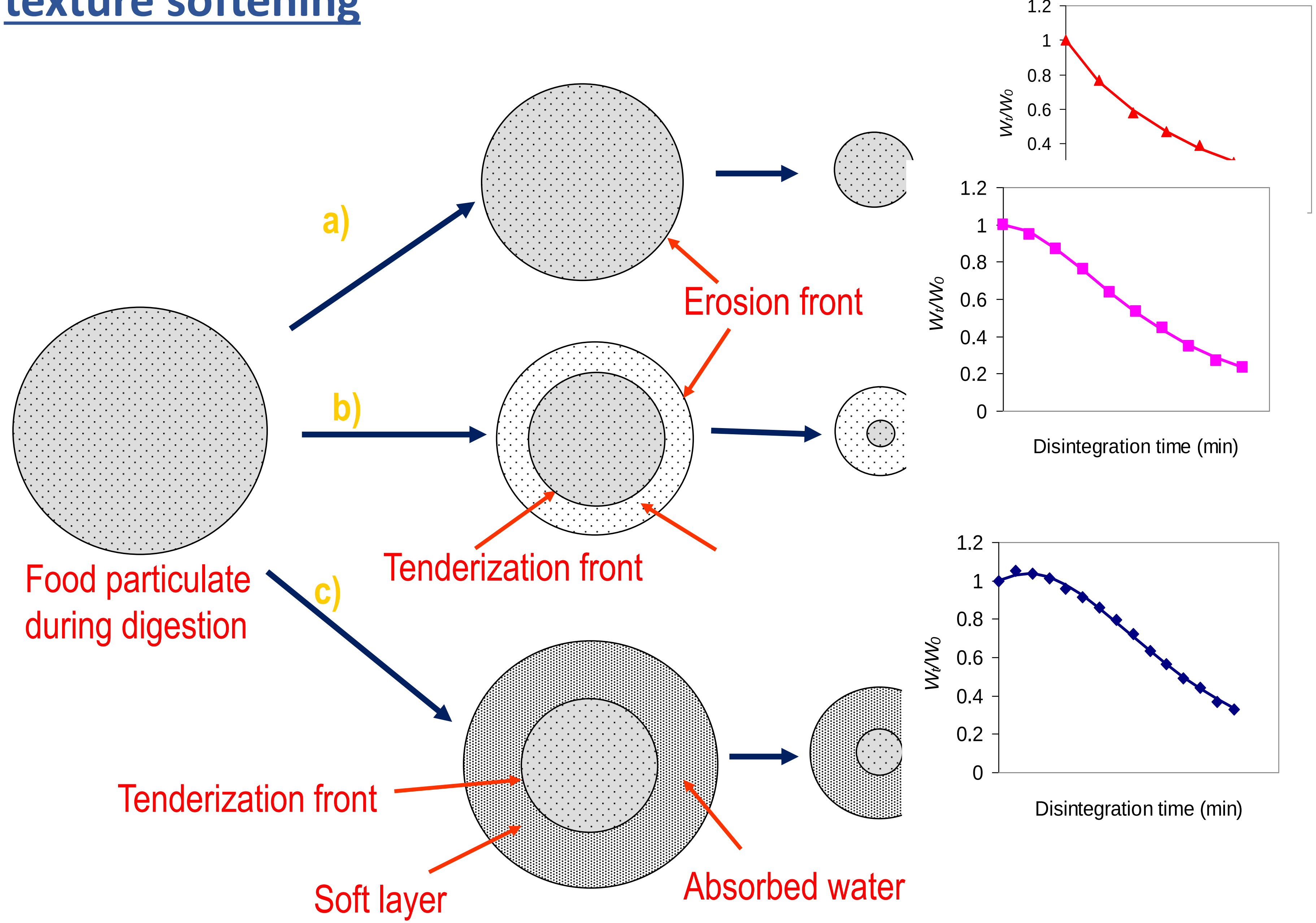
Carrot disintegration



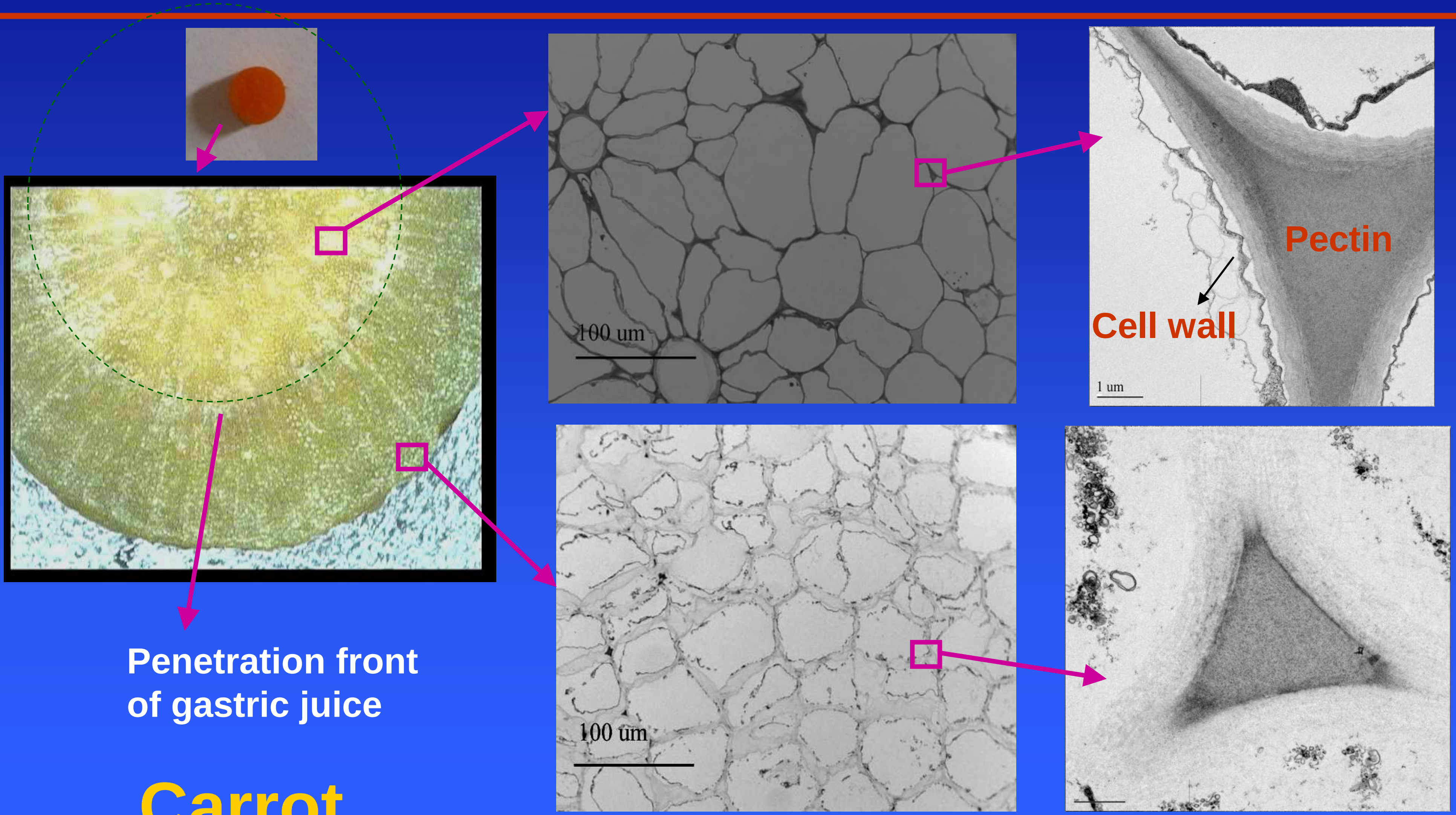
Disintegration profiles of carrot (n=6)

- The different profiles are a result of competition among surface erosion, texture softening and absorption of gastric juice

Simultaneous surface erosion, absorption of gastric juice and texture softening



Penetration front of gastric juice in carrot



Carrot

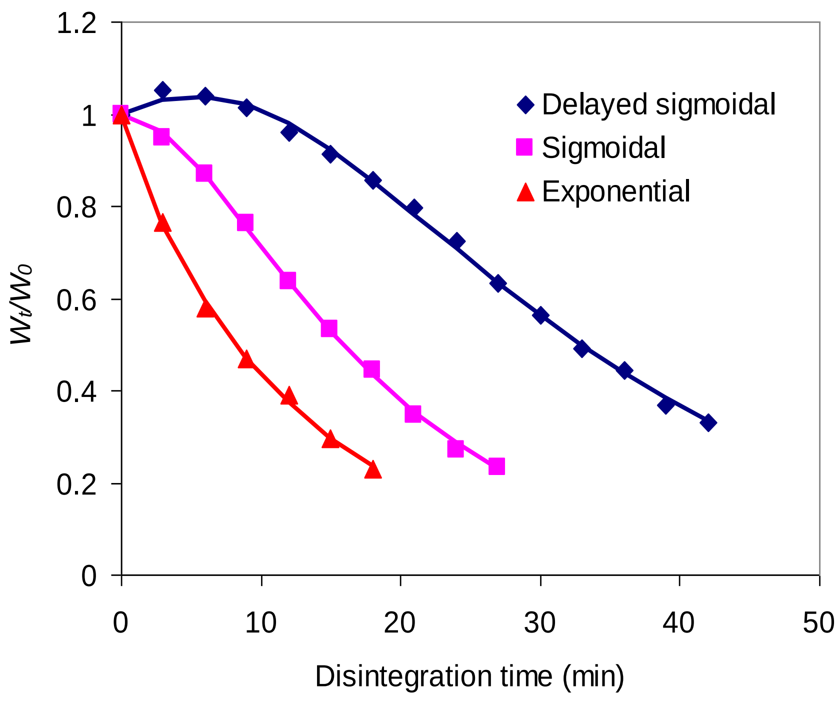
Categorize foods based on their structural breakdown in gastric environment?

- Linear-exponential equation:

$$y(t) = (1 + k \cdot \beta \cdot t) \cdot e^{-\beta \cdot t}$$

  - k: increase in weight with time t (min)
  - β : the concavity of the time-weight retention relationship (β >0)

Candy, apple bar, Canned kidney beans	<5 min
Ham, breakfast pretzels, fried dough (no yeast)	5-10 min
Apple, raw carrots	10-20 min
Raw almond and peanut	>10 hours



- Half time($t_{1/2}$)
  - Can be derived by regression
  - Express as disintegration rates

Food Breakdown Classification System

Class	Initial Hardness (N)	Rate of Softening/Dissolution (1/s)	Examples
A	High	Fast	Confectionary (Hard Candy)
B	High	Slow	Nuts (almonds, peanuts)
C	Medium	Fast	Apple, Cheese
D	Medium	Slow	Pasta
E	Low	Fast	Cooked Rice, Ham, Soft fruit (peach)
F	Low	Slow	Cooked Meat

Post oral mastication of foods

Food Breakdown Classification System

Class	Initial Hardness (N)	Rate of Softening/Dissolution (1/s)	Examples
A	High		
B	High		
C	Medium		
D	Medium		
E	Low		
F	Low		

<u>Key Parameters</u>:
Moisture Content
Processing/Cooking Conditions

Food Breakdown Classification (FBC) System

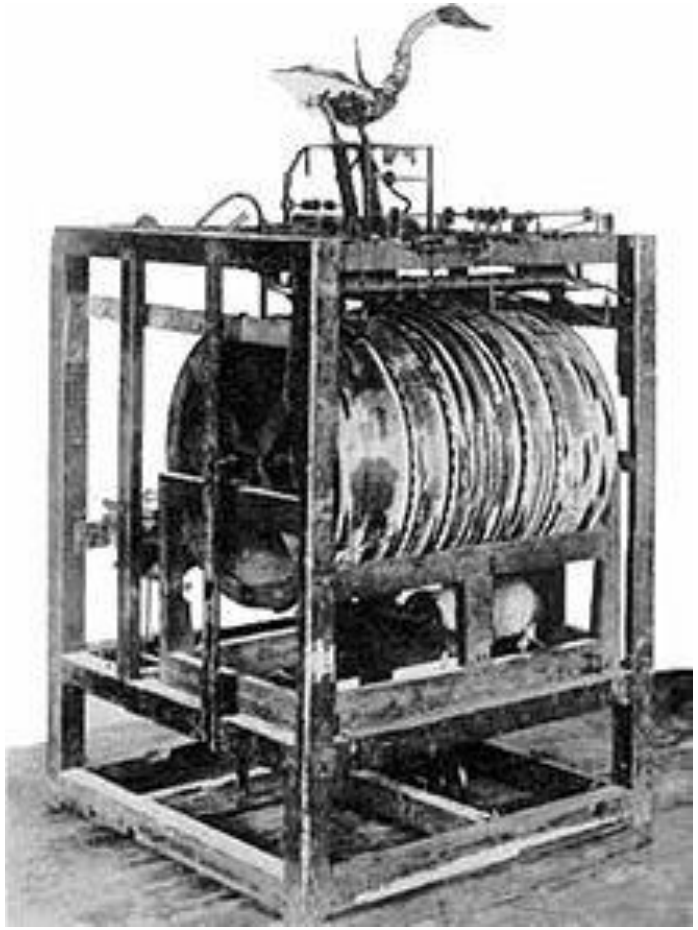
FB Class	Initial Hardness (N)	Rate of Softening/Dissolution (1/s)	Examples
A		**Fast**	Confectionary (Hard Candy)
B		**Slow**	Nuts (almonds, peanuts)
C		**Fast**	Apple, Cheese
D		**Slow**	Pasta
E		**Fast**	Cooked Rice, Ham, Soft fruit (peach)
F		**Slow**	Cooked Meat

Key Parameter:

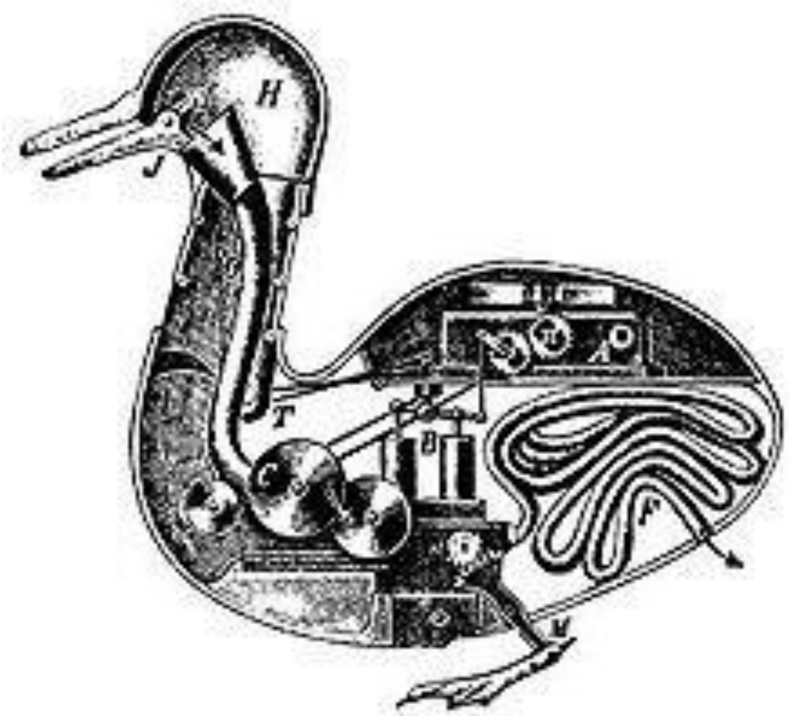
Food Structure

Dynamic *in vitro* systems

Canard Digerateur
Jacques de Vaucanson, 1739

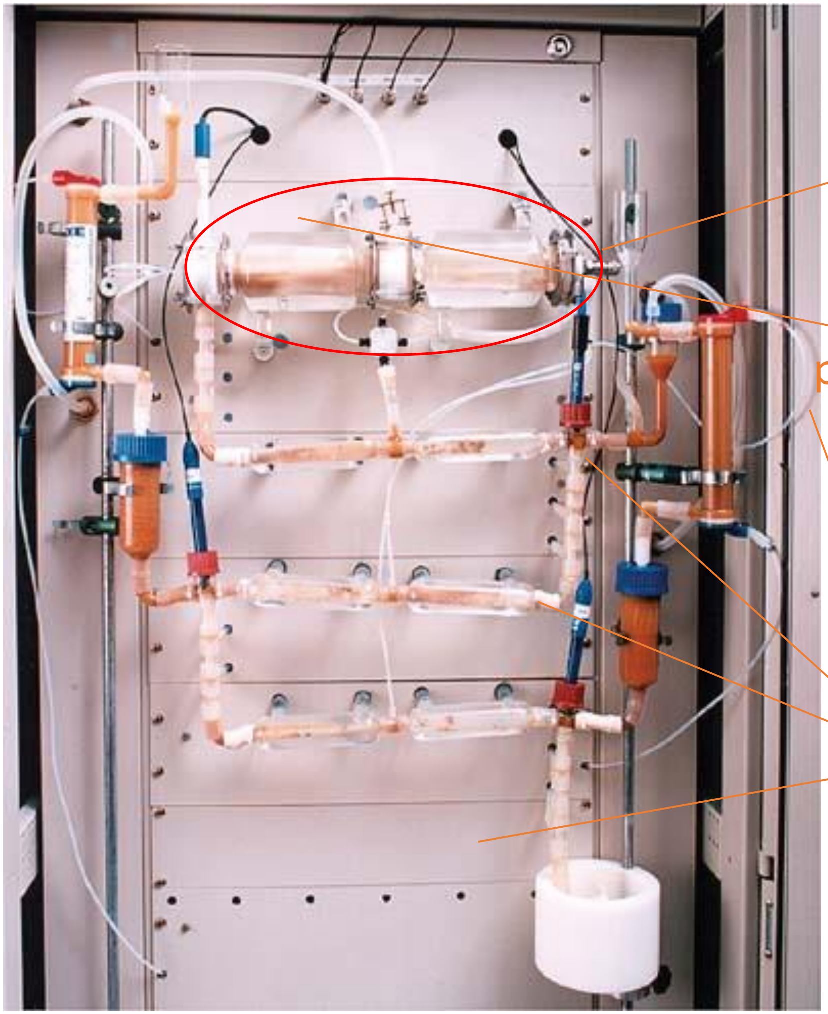


The Digesting Duck



Voltaire wrote that "without...the duck of Vaucanson, you will have nothing to remind you of the glory of France."
(*"Sans...le canard de Vaucanson vous n'auriez rien qui fit ressouvenir de la gloire de la France."*)

https://commons.wikimedia.org/wiki/File:Vaucanson_duck1.jpg

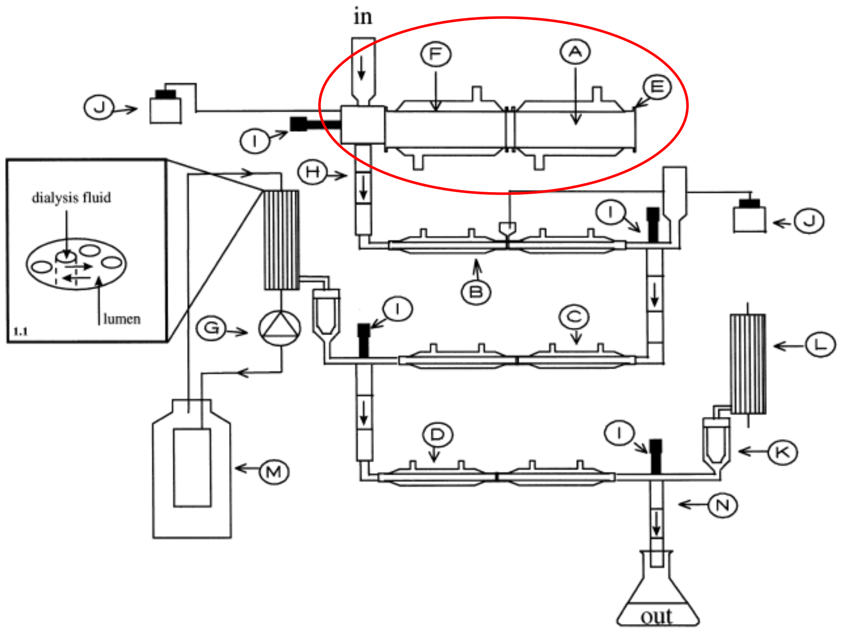


Stomach

pH electrode

Hollow fiber membranes simulating the absorption

Intestine

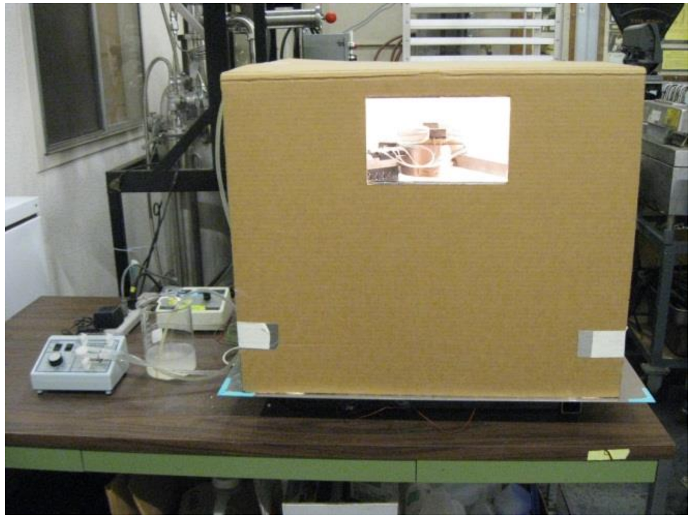


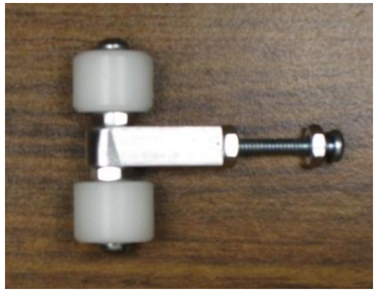
TNO Nutrition and Food Research

Human Gastric Simulator (HGS)

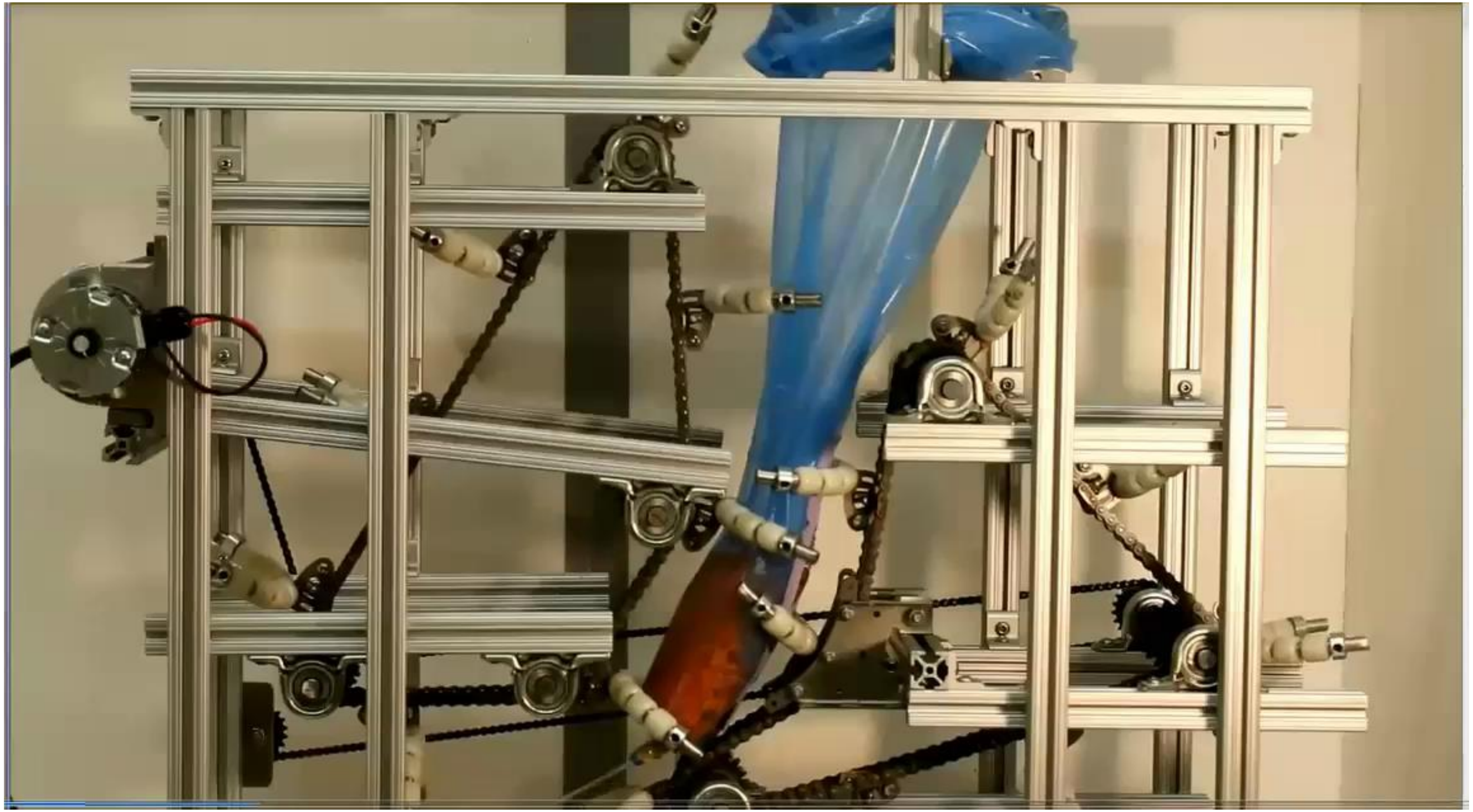
- Create peristaltic movement of walls
- Simulate gastric secretion (enzyme and acid) and stomach emptying
- Study size distribution of food particulates in digesta, nutrient release, and rheological properties
- Study physiological effects (pH, emptying, contraction) on digestion

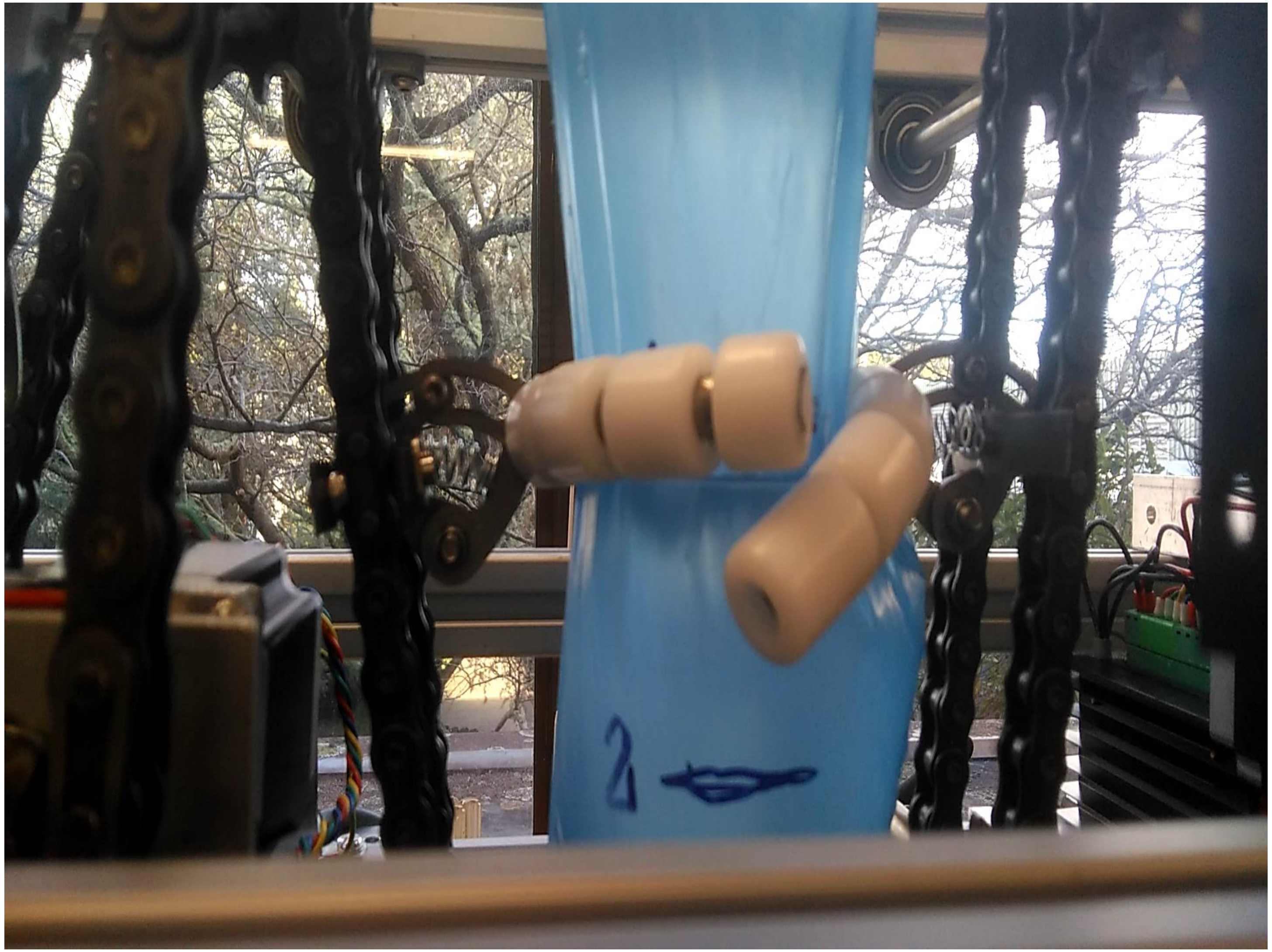
(Kong and Singh, 2010)





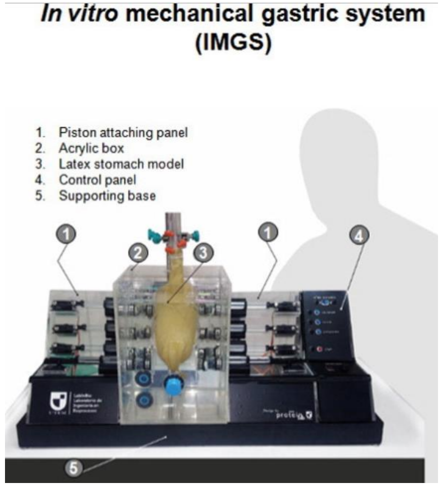
Human Gastric Simulator (HGS-1)





3D printing to fabricate human stomach

Novel Dynamic Systems



Barros, L., Retamal, C., Torres, H., Zúñiga, R. N., & Troncoso, E. (2016). Development of an in vitro mechanical gastric system (IMGS) with realistic peristalsis to assess lipid digestibility. *Food research international, 90*, 216-225.

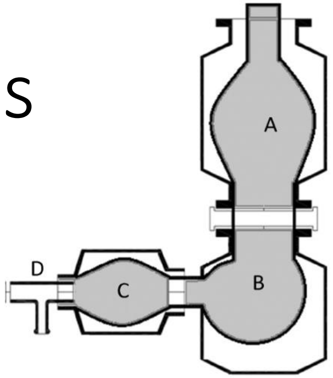
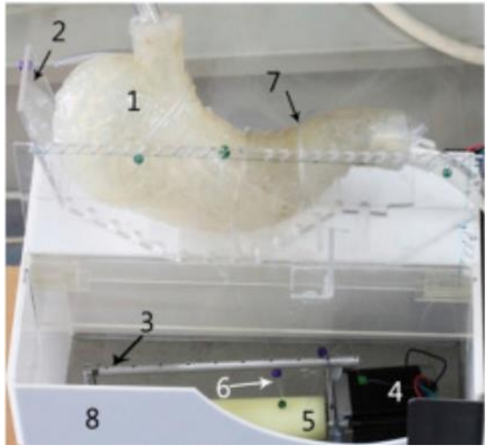
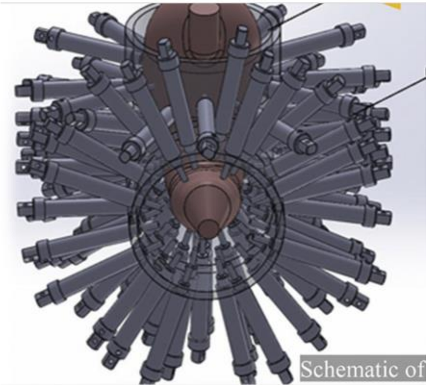


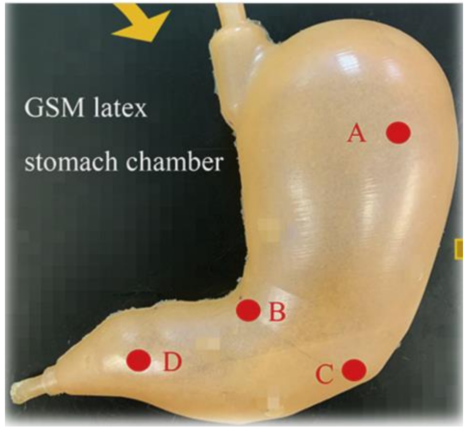
Fig. 4. TIMagc representing A: gastric body; B: proximal antrum; C: distal (terminal) antrum; D: pyloric sphincter.

Bellmann, S., Lelieveld, J., Gorissen, T., Minekus, M., & Havenaar, R. (2016). Development of an advanced in vitro model of the stomach and its evaluation versus human gastric physiology. *Food research international, 88*, 191-198.



Chen, L., Xu, Y., Fan, T., Liao, Z., Wu, P., Wu, X., & Chen, X. D. (2016). Gastric emptying and morphology of a ‘near real’in vitro human stomach model (RD-IV-HSM). *Journal of Food Engineering, 183*, 1-8.

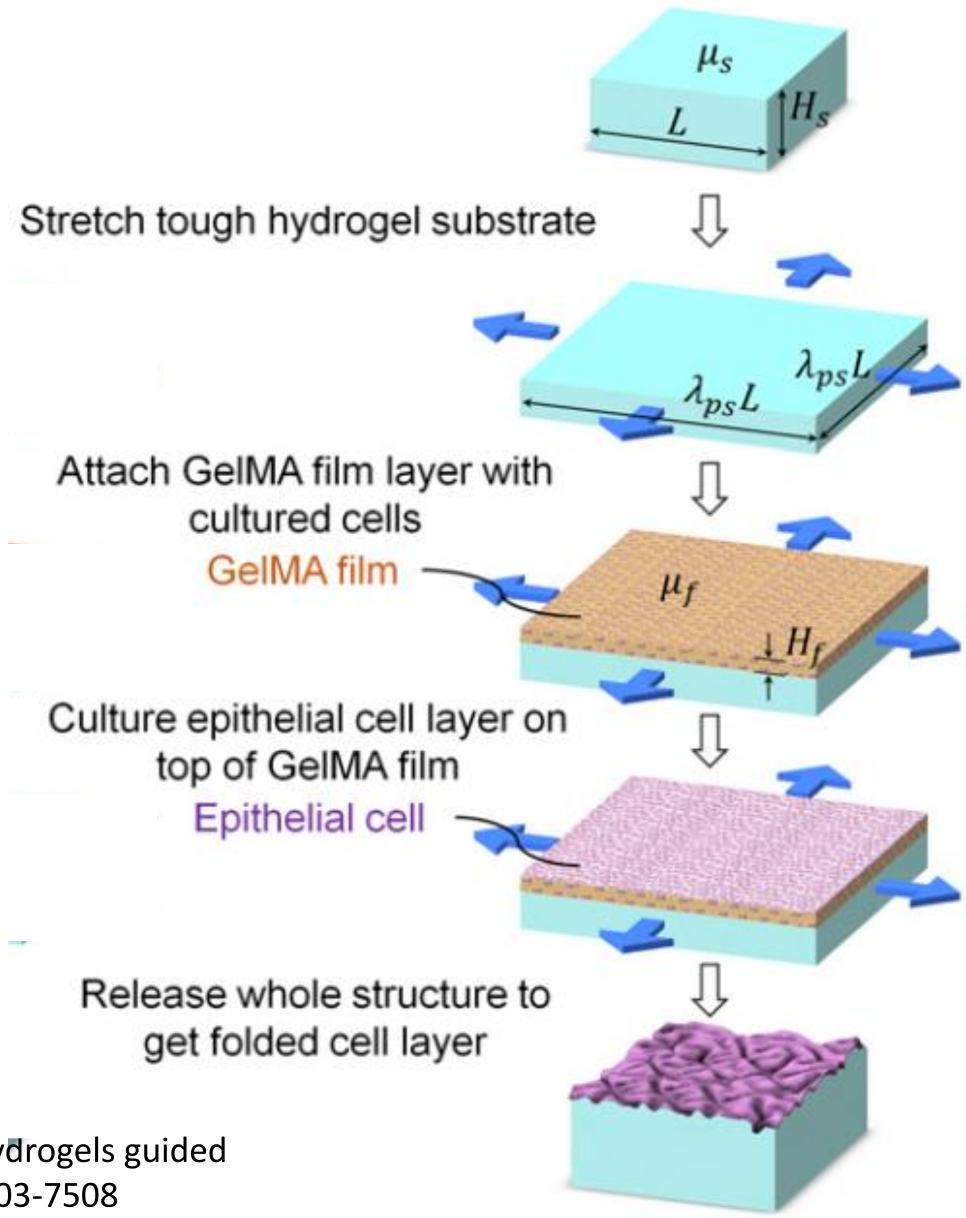




Li, Y., Fortner, L., & Kong, F. (2019). Development of a Gastric Simulation Model (GSM) incorporating gastric geometry and peristalsis for food digestion study. *Food research international, 125*, 108598

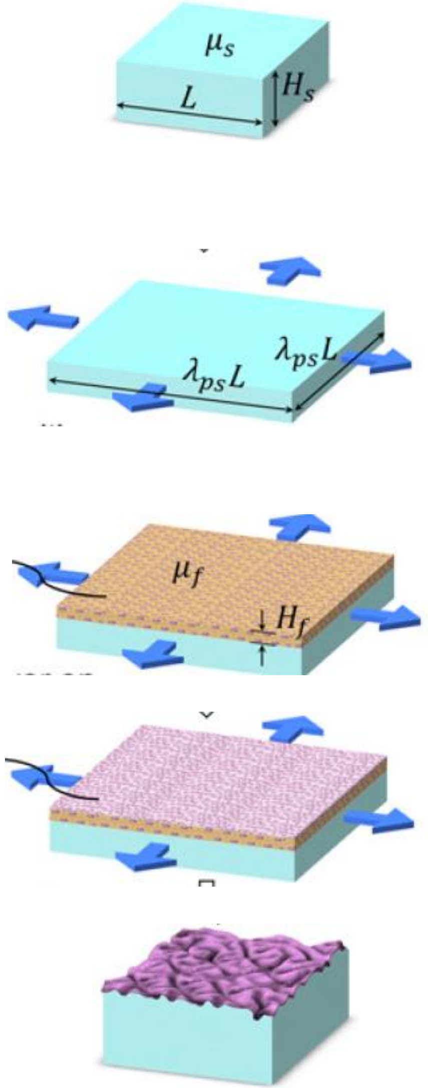
Gastric mucosa

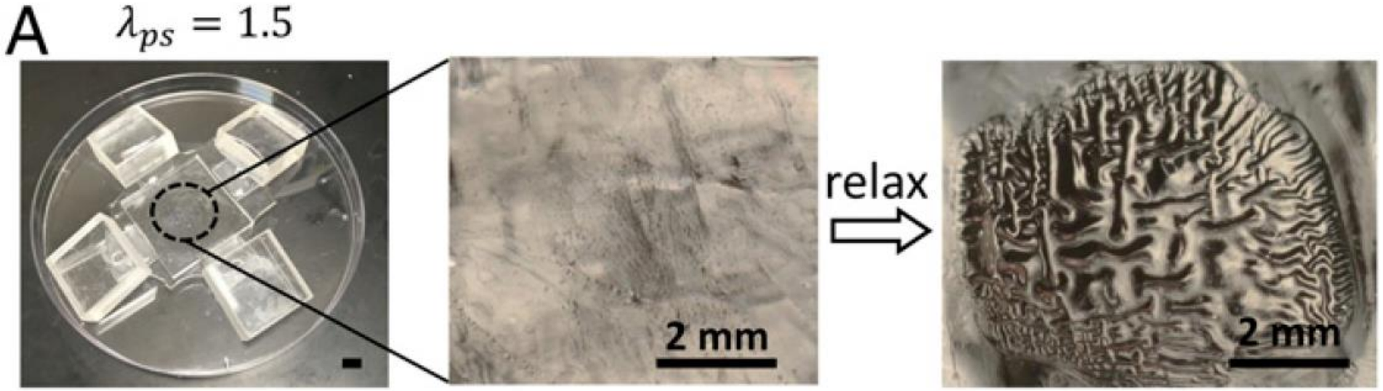
Folding artificial mucosa with cell-laden hydrogels



Chan et al. Folding artificial mucosa with cell-laden hydrogels guided by mechanics models PNAS July 17, 2018, 115(29) 7503-7508

Folding Mucosa





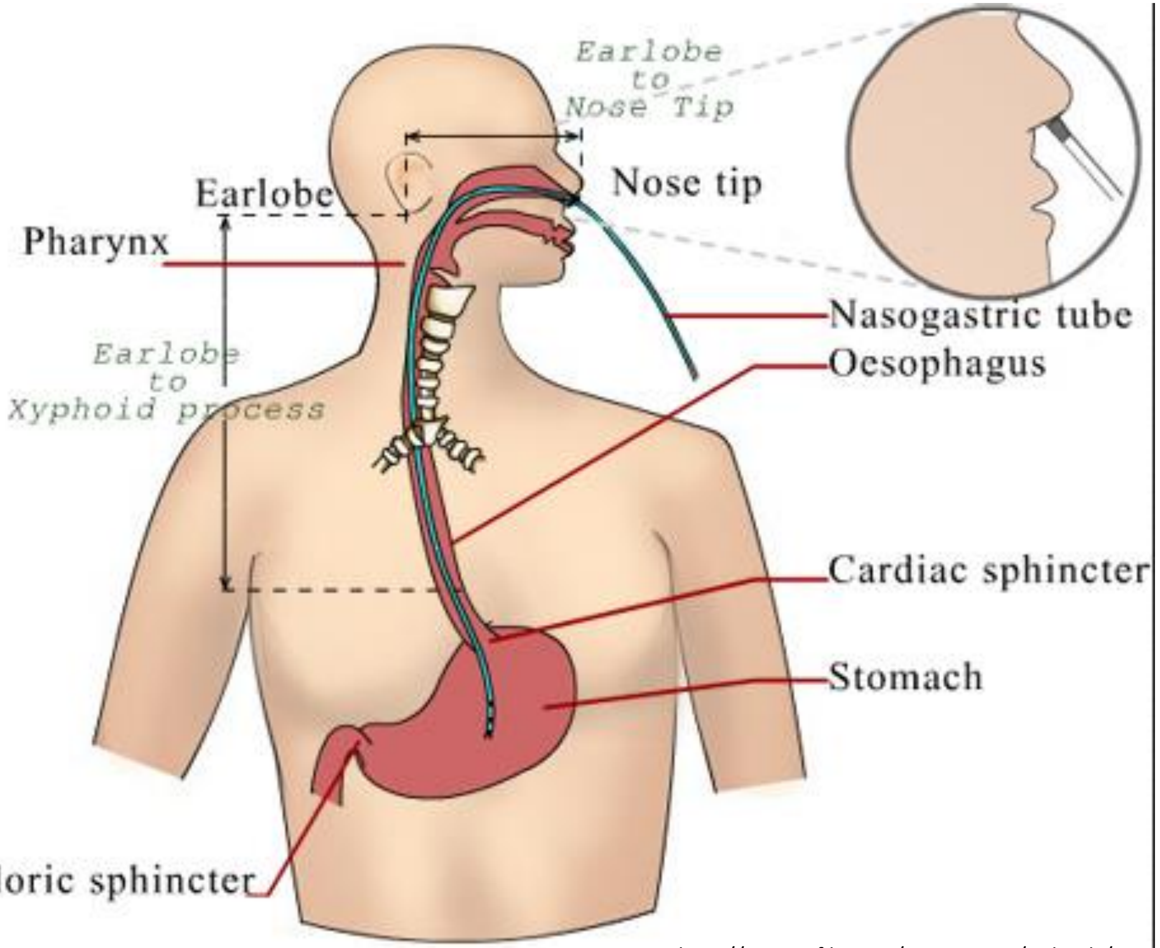
Chan et al. Folding artificial mucosa with cell-laden hydrogels guided by mechanics models PNAS July 17, 2018, 115(29) 7503-7508

In vivo studies

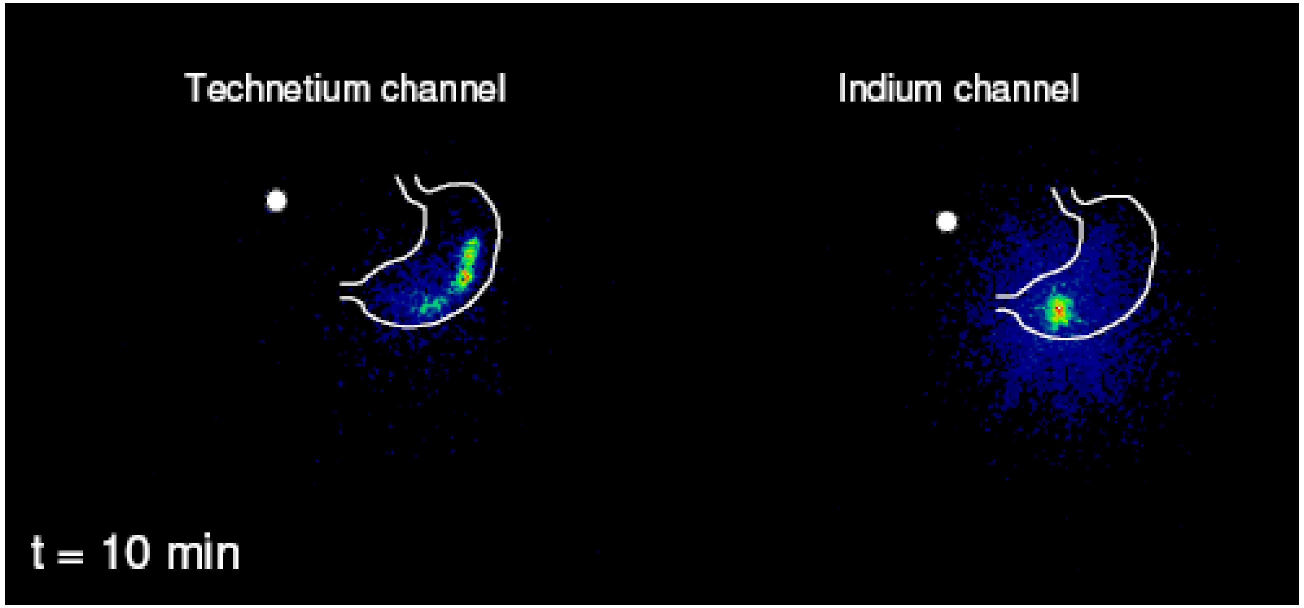
- To study food disintegration and digestion

In vivo methods to assess gastric disintegration and emptying rate

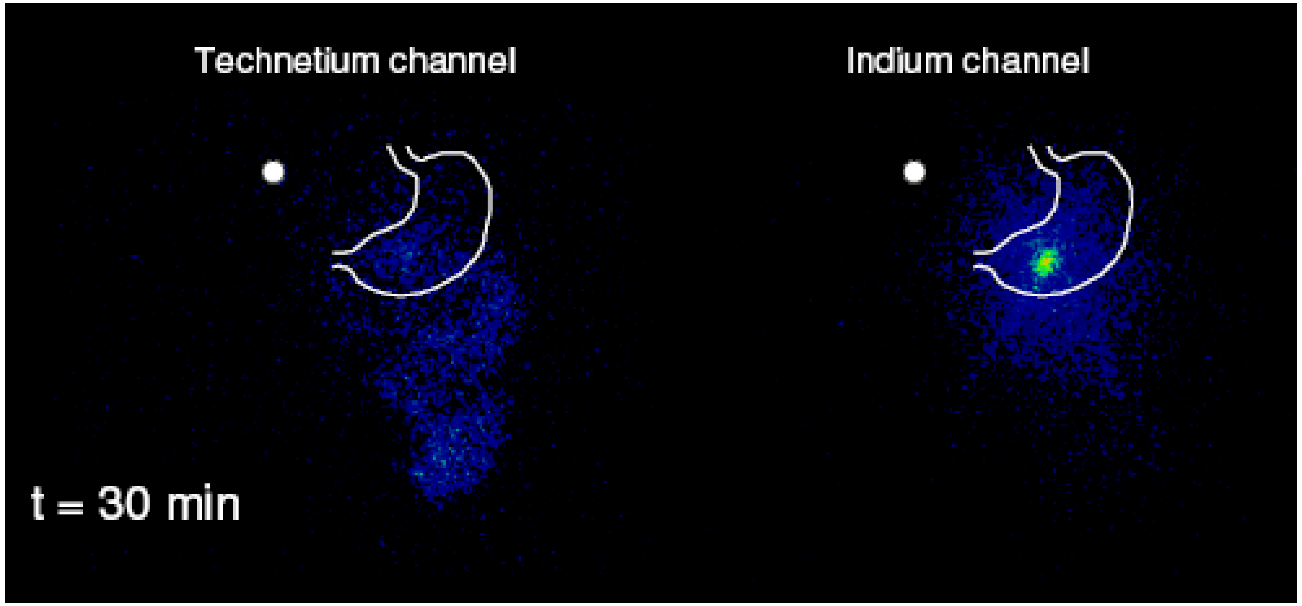
- Feeding study
  - acquiring the digesta samples using **naso-gastric tube**

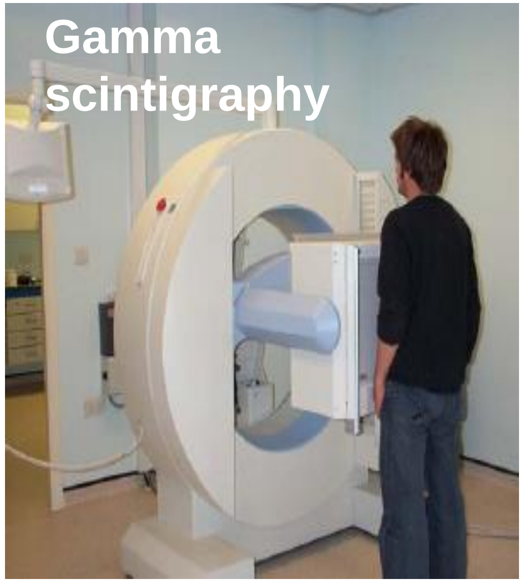


http://nursingfile.com/wp-content/uploads/2011/06/nasogastric-tube.jpg



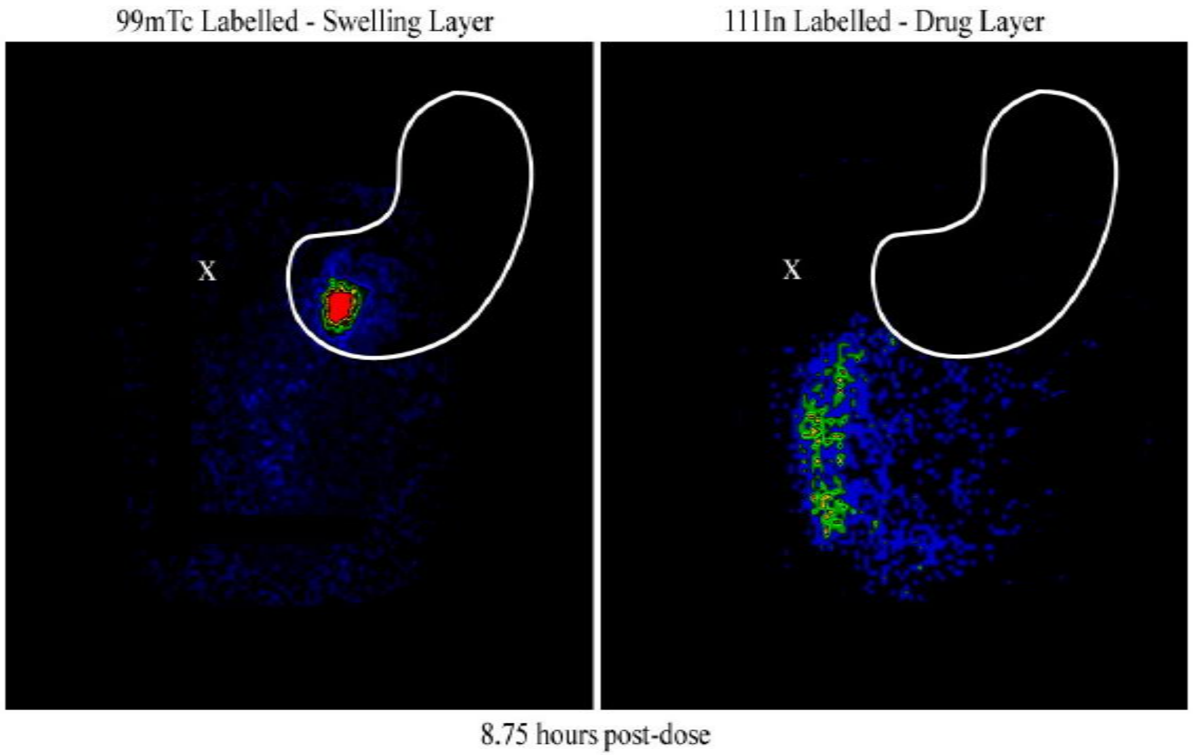
Scintigraphic images shows capsule disintegration and gastric emptying of its contents)

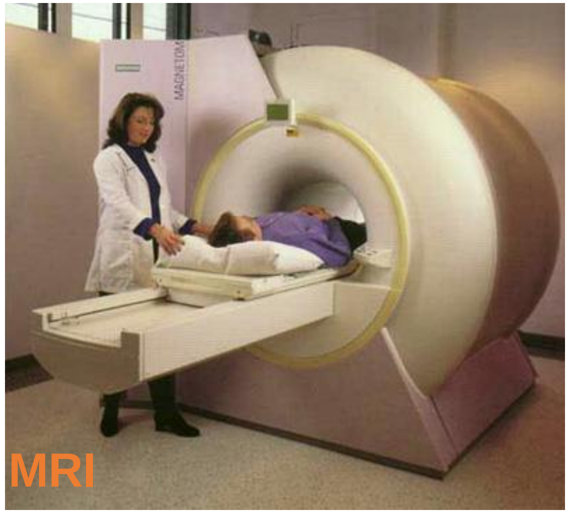




www.bio-images.co.uk/AAPS2002.pdf

MRI images showing disintegration and gastric emptying of drug tablet





www.pharmprofiles.co.uk/UserFiles/File/pdf/DepomedPresentation.pdf

In vivo trials

- Animal trials
  - Rats
  - Pigs
    - Canulated
    - Euthanized

http://t1.gstatic.com/

Approach

- Selected **growing pig** as model system
  - Similar upper GI tract to humans
  - Sufficient amount of food consumed
  - Comparable digestibility to humans

Overall *in Vivo* Objectives

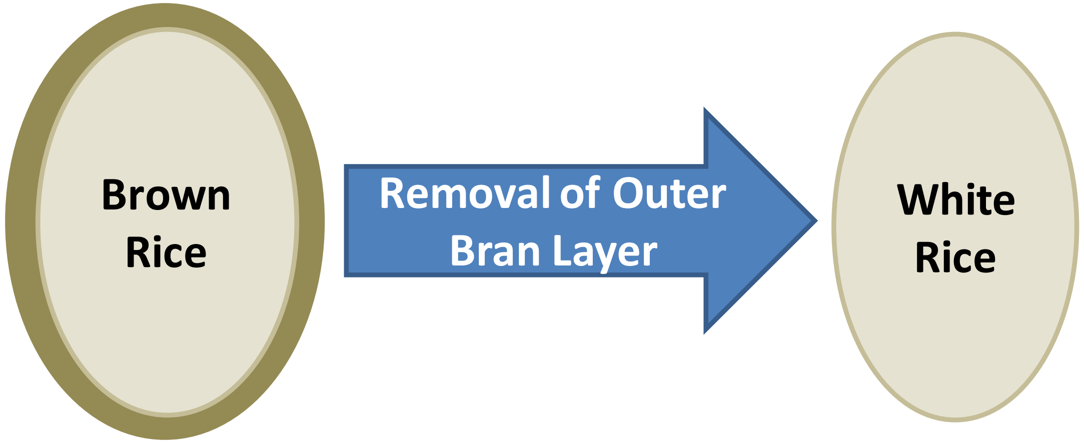
1. Determine the **rate of breakdown** of foods with varying initial properties during gastric digestion

2. Examine the role of **food processing** in the **breakdown mechanisms** of food in the stomach

3. Quantify **mixing of gastric secretions with foods (liquid-solid)** and **overall meal mixing (solid-solid)** during gastric digestion

Rice Gastric Digestion

- Key factors impacting **rice digestion**
  - Physicochemical properties
  - Cooking method
  - **Rice structure**



References: Miller et al., 1992; Goddard et al., 1983; Panlasigui et al., 1991; Lee et al., 2005; Benmoussa et al., 2007; Hallfrisch & Behall, 2000

Almond Gastric Digestion

- Key factors impacting **almond digestion**
  - **Physical structure** (i.e. ground, whole)
  - **Roasting**/processing **conditions** (i.e. blanched, roasted)
  - **Particle size** of almond pieces

In Vivo Trial Setup

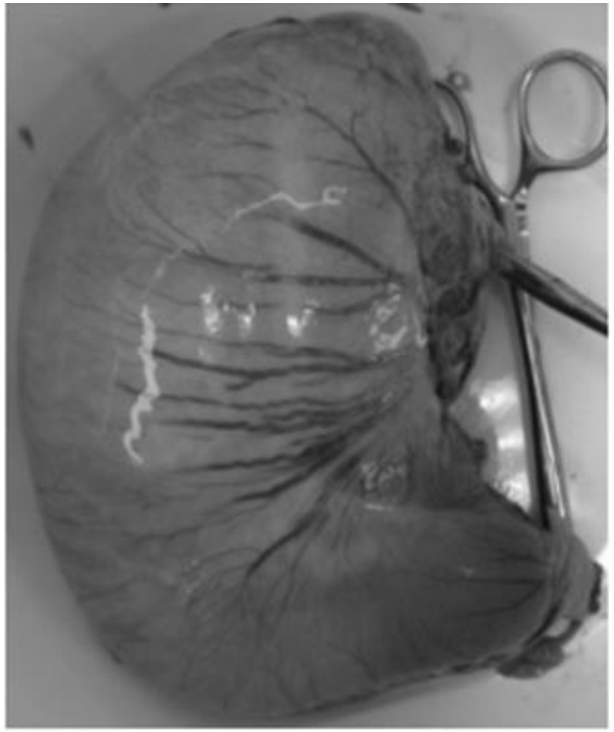
- **Pigs purchased from farmers**
  - 144 male pigs (23 ± 1.5 kg)
  - Housed in metabolic cages
  - 7 day acclimation period
- **Final meal**
  - Prior to final meal 18 hr fast
  - 2 hr without water
  - Meal of *only* rice or almonds

In vivo experimental protocols are approved by Massey University Ethics Committee

Methods

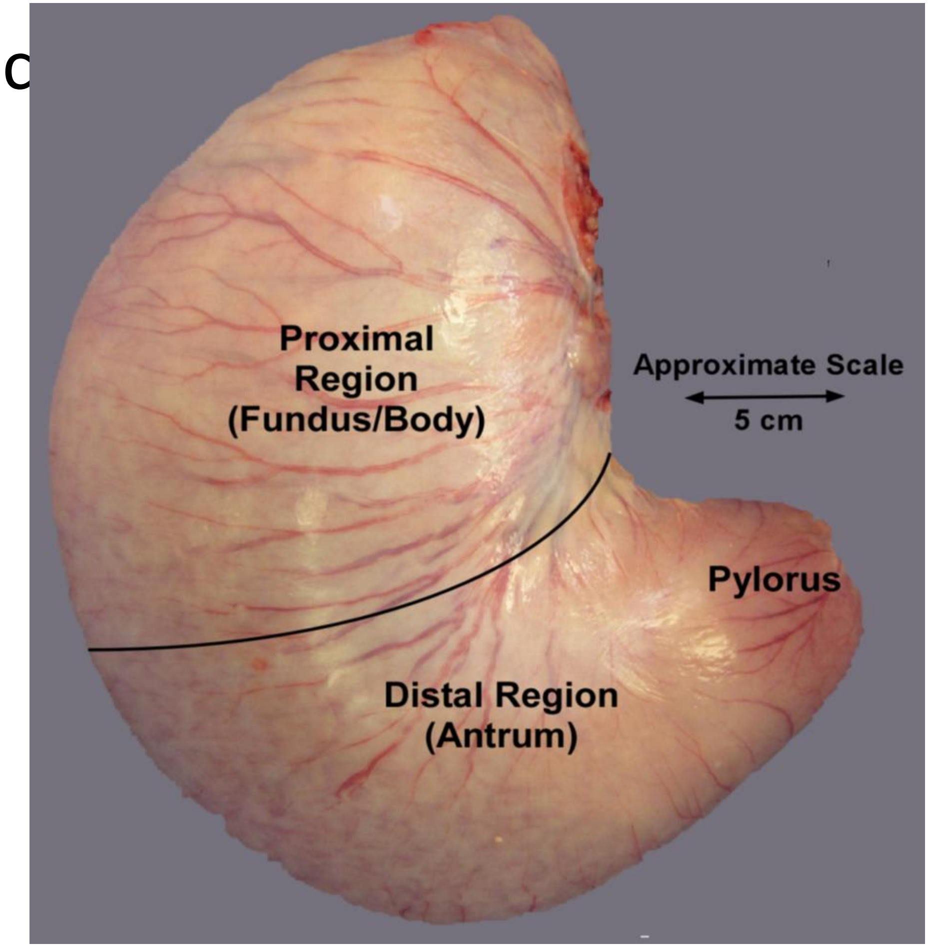
- Pigs euthanized at 0, 60, 120, 180, or 300 min after feeding brown or white rice meal, or raw and roasted almonds

Pig Surgery

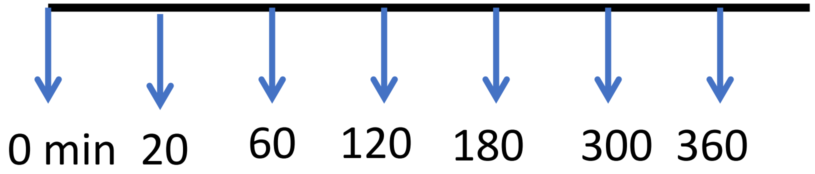


Samples (Digesta) -

- Stomac



Sampling Time (min)



Fresh samples

- pH
- Moisture content
- Textural properties
- Rheological flow behavior
- Particle size distribution

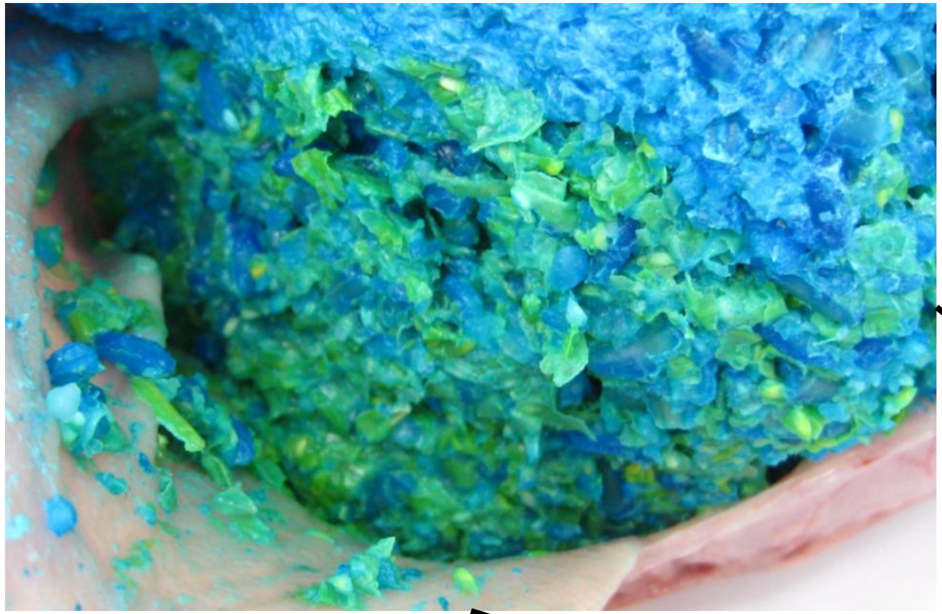
Freeze Dried

- Protein
- Starch(Rice)/Lipid(Almonds)

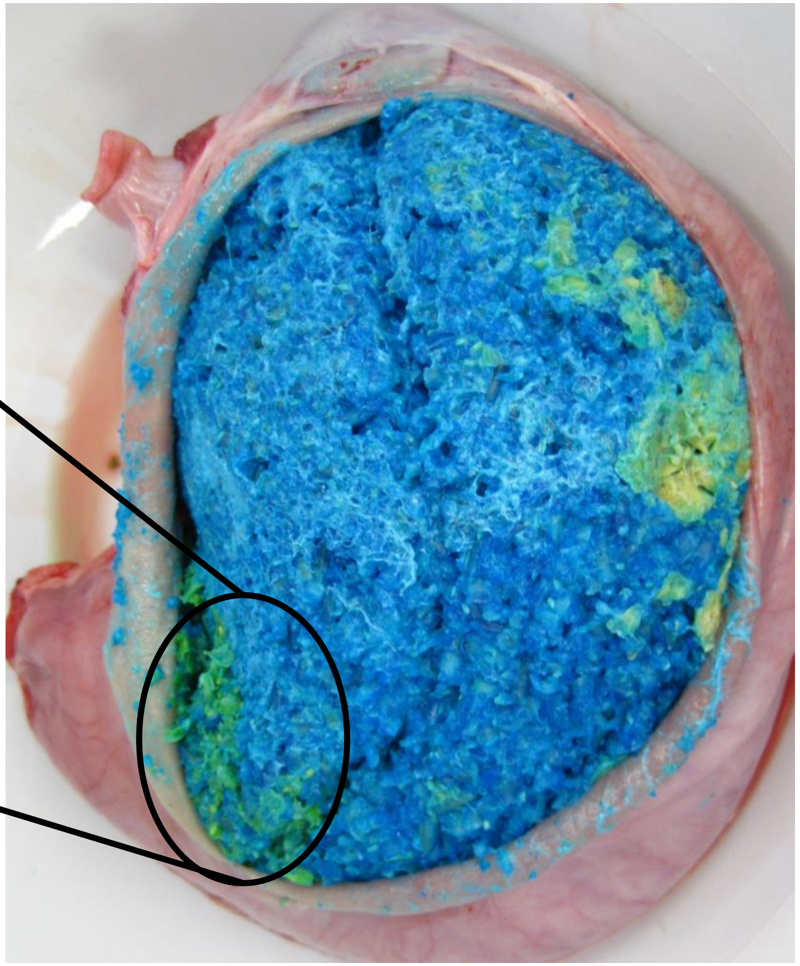
Results:
20 min white rice

More “liquid-like” portion in antrum

Results: 20 min brown rice



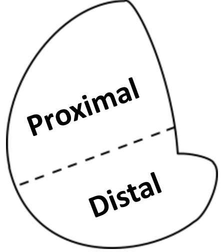
Evidence of “antral grinding” → outer bran layer broken off of inner endosperm layer



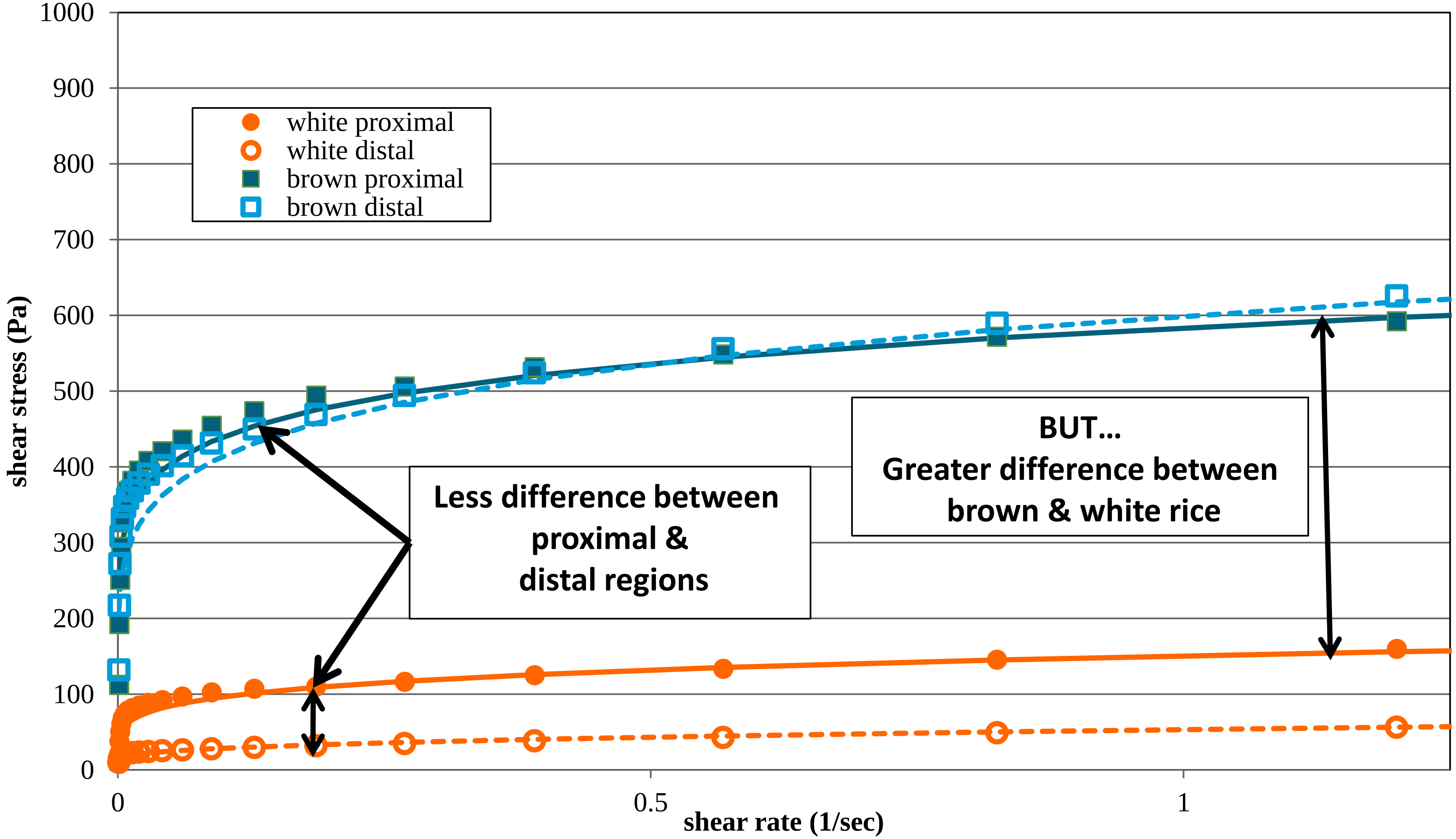
300 min digestion

Brown rice -- antrum

White rice -- antrum

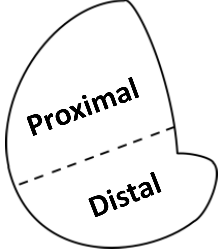


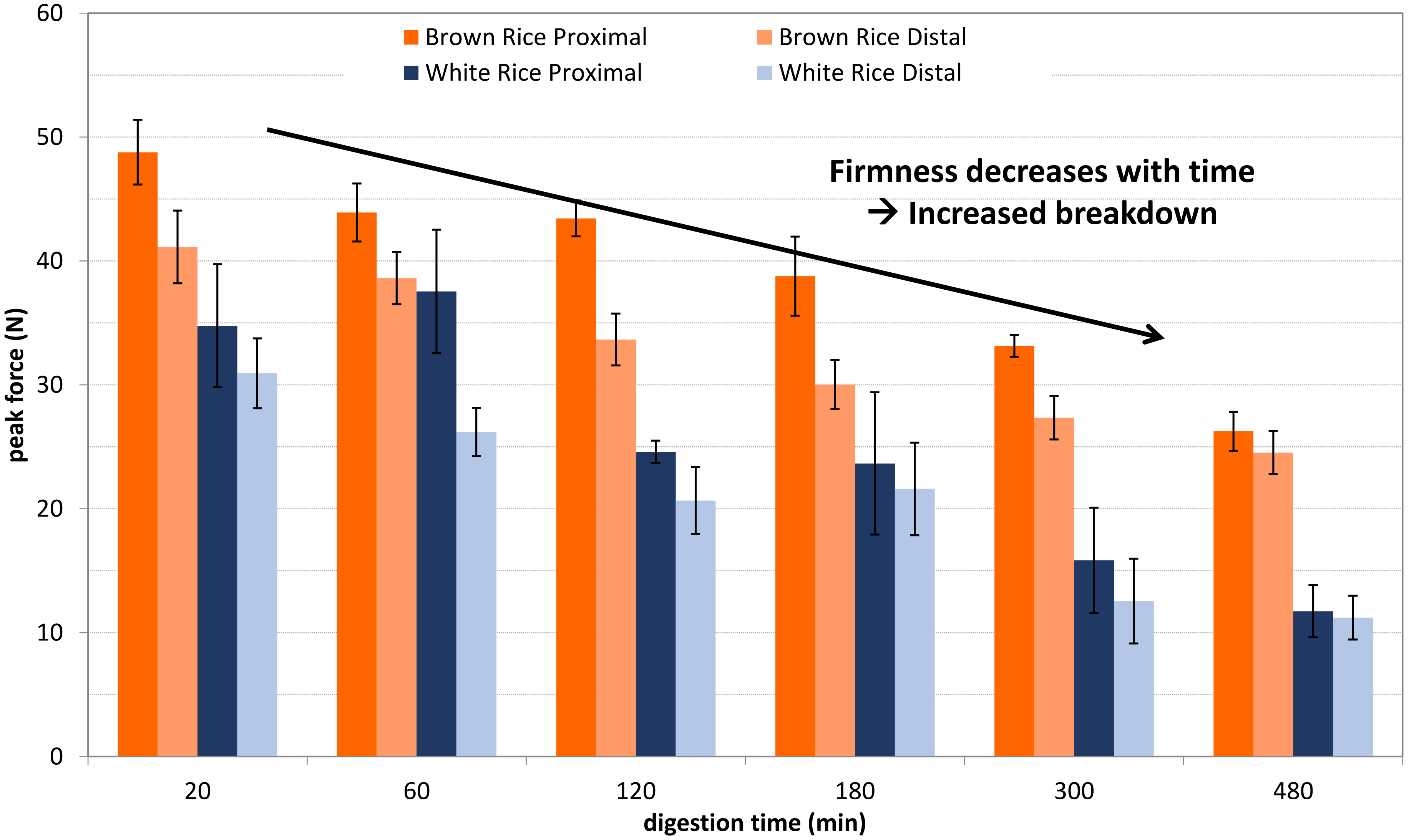
120 min digestion



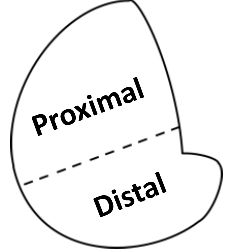
Data points are experimentally measured values. Lines represent Hershel-Bulkely model predictions.

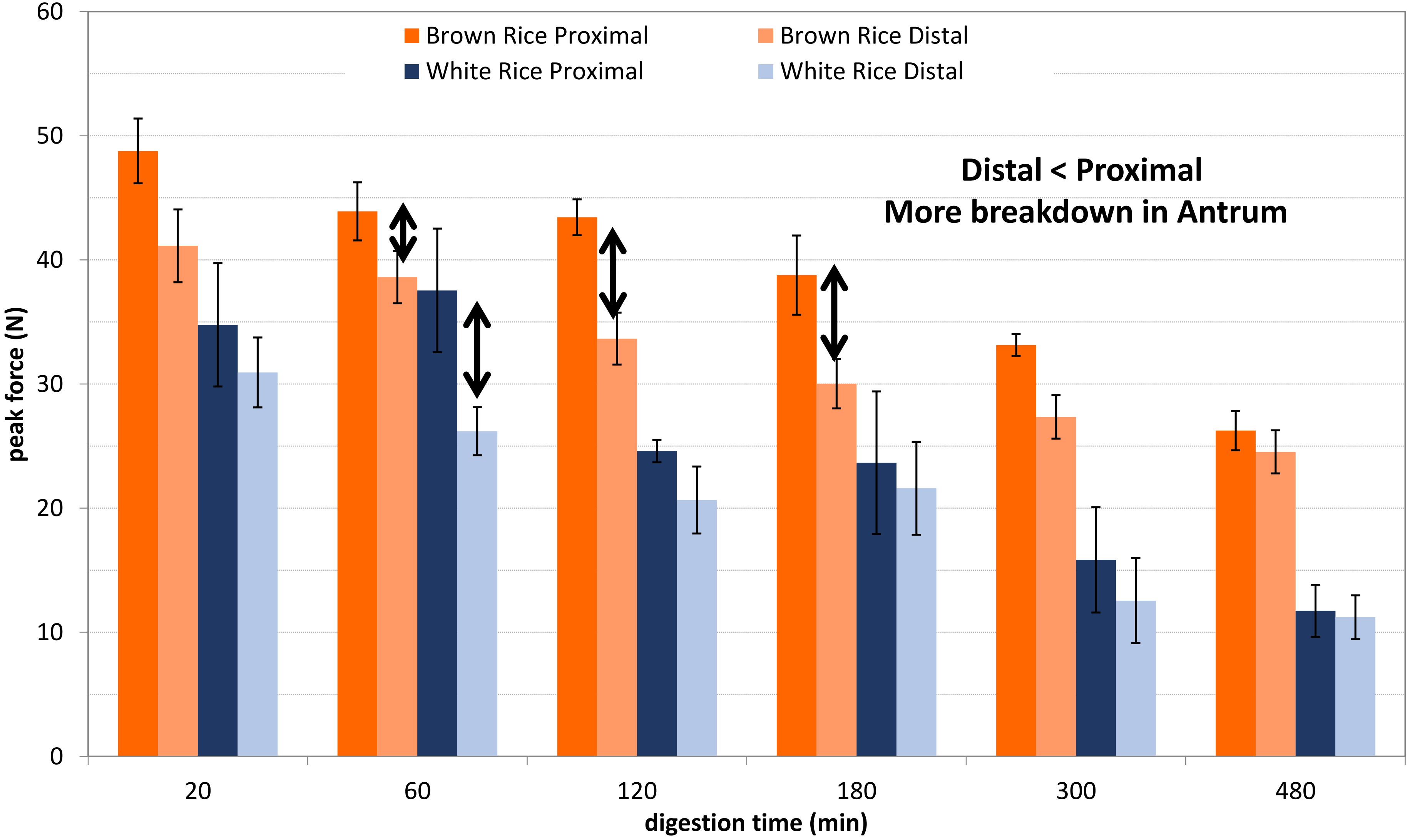
Rice Grain Compression





Rice Grain Compression





Mixing of Digesta in Stomach?

- 50% of daily dry matter requirement of almonds
- 25% water
- 0.3% indigestible marker evenly mixed with sample
  - Titanium dioxide (TiO_2)
  - Chromium oxide (Cr_2O_3)



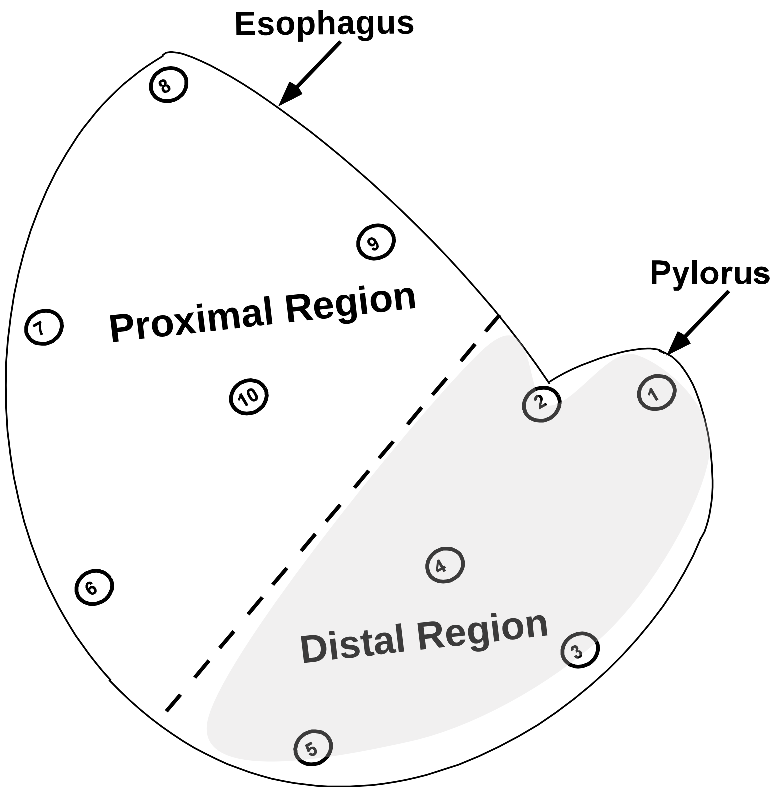


Particle Mixing using Markers

- Each meal → divided into 2 portions

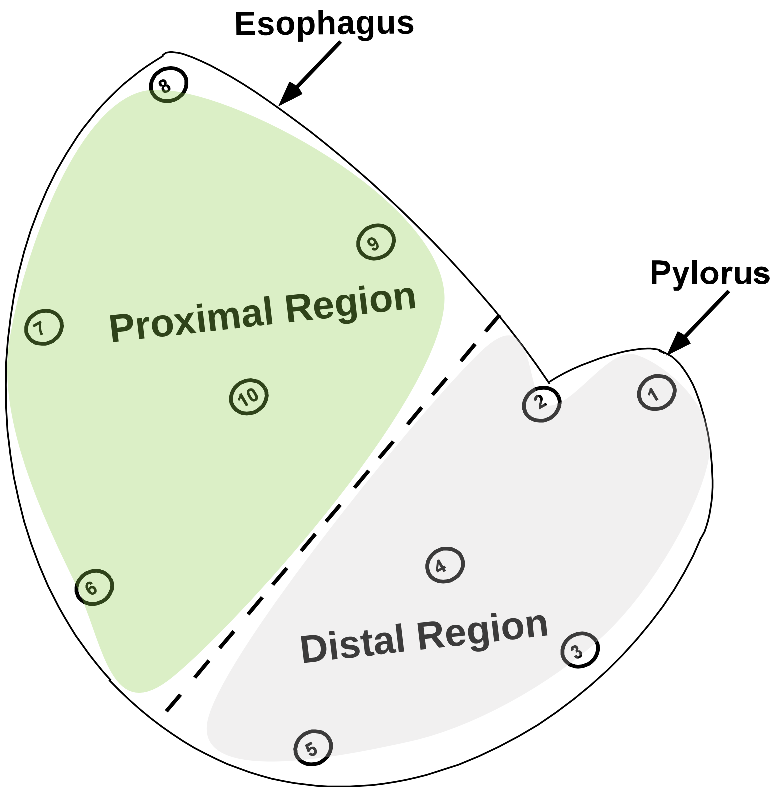
Particle Mixing using Markers

- Each meal → divided into 2 portions
  - Portion 1: **Titanium Dioxide (TiO_2)**

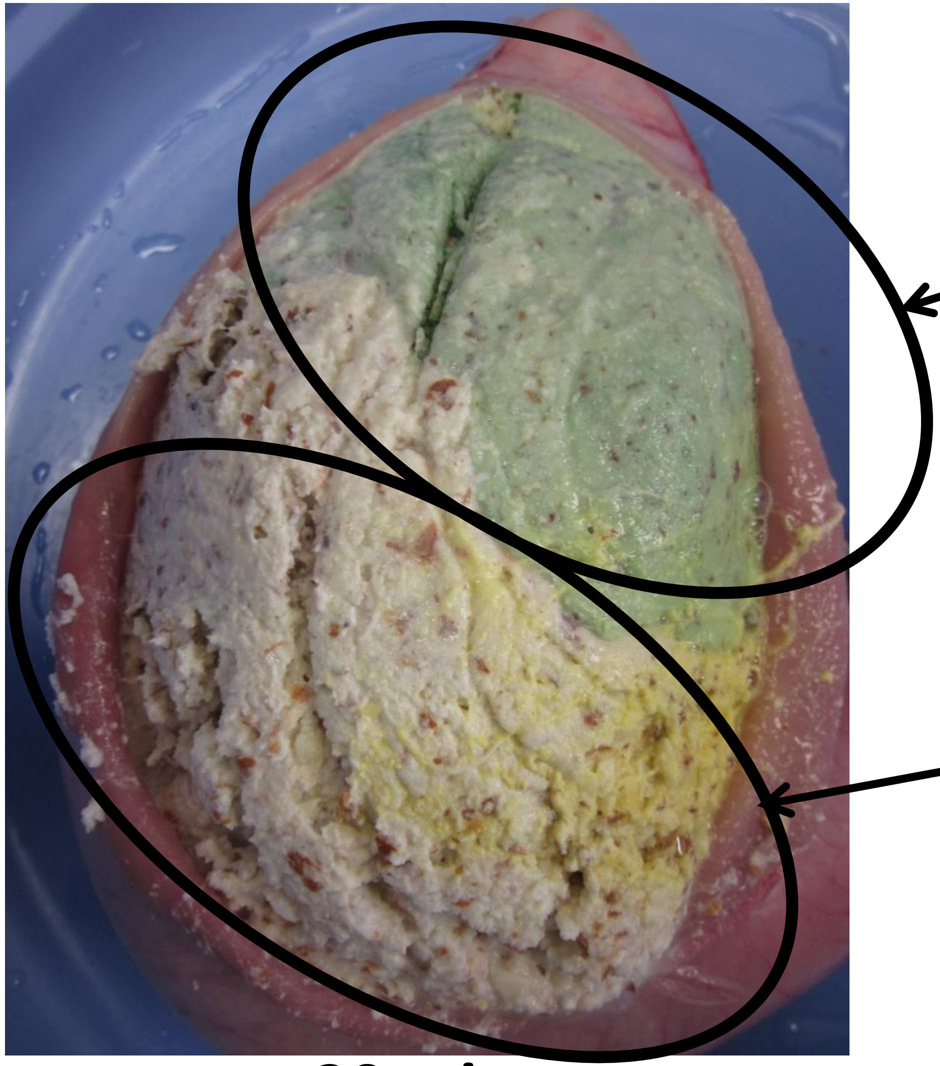


Particle Mixing using Markers

- Each meal → divided into 2 portions
  - Portion 1: **Titanium Dioxide (TiO_2)**
  - Portion 2: **Chromium Oxide (Cr_2O_3)**

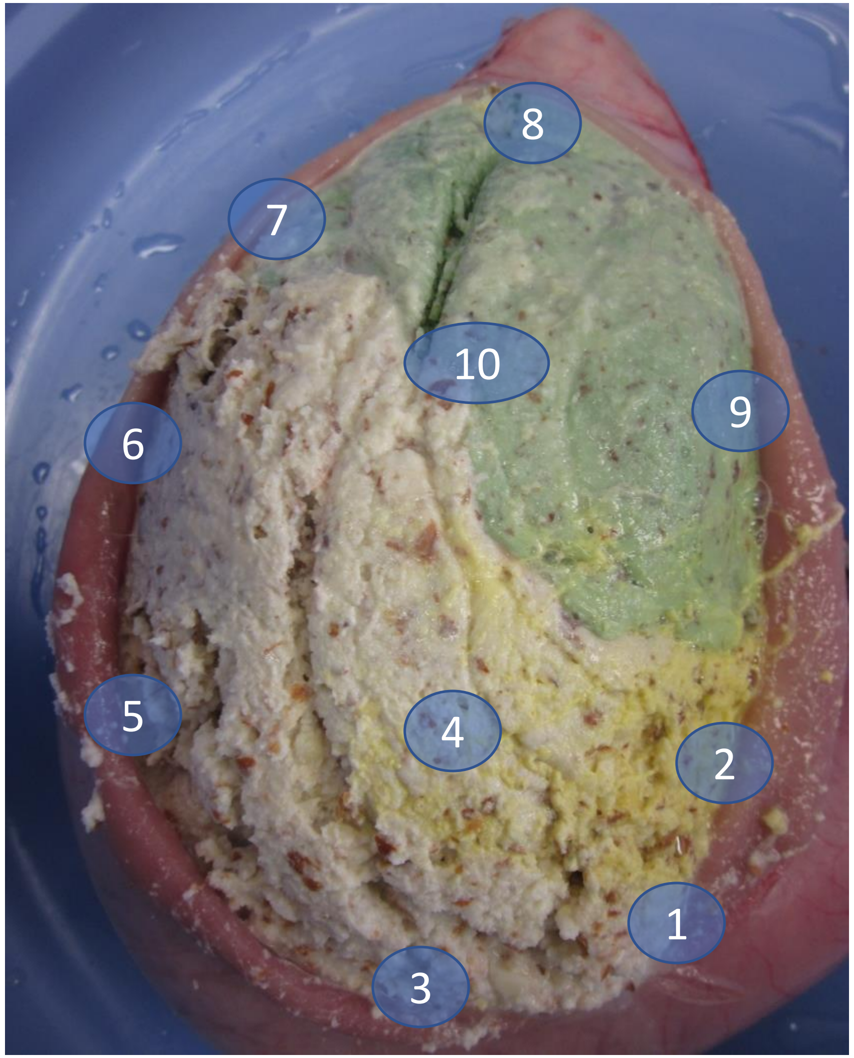


Raw Almond Digestion

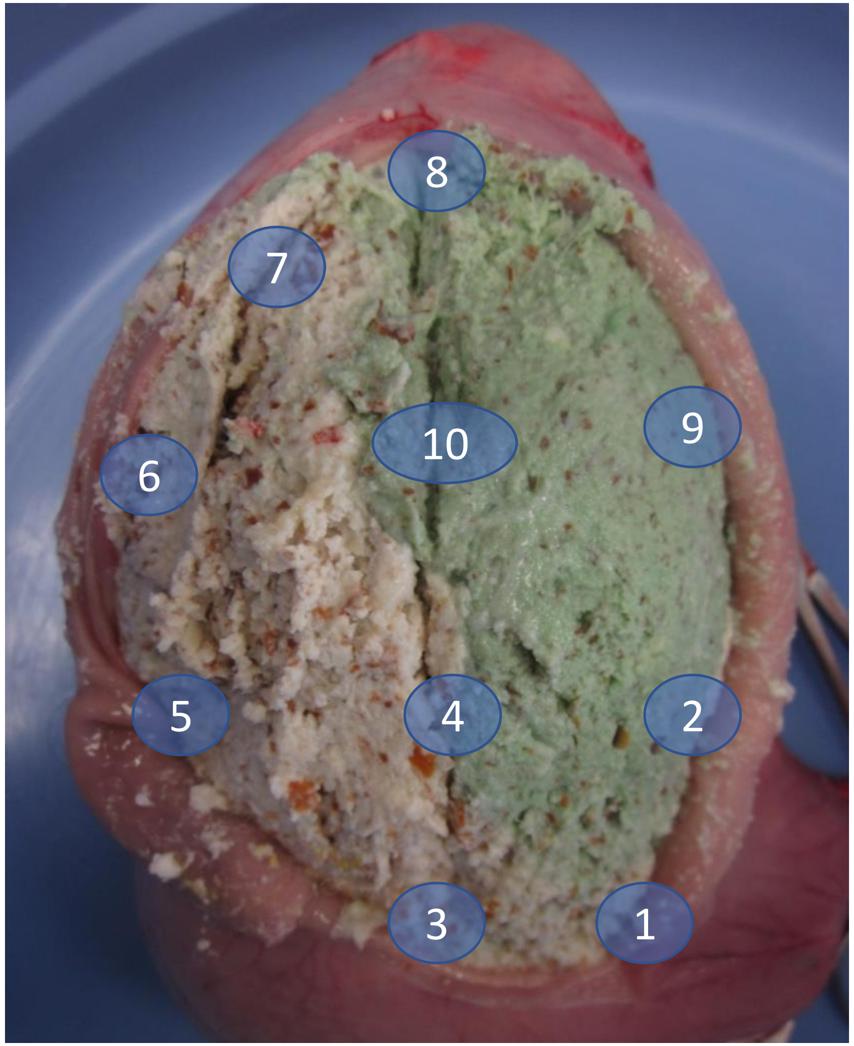


20 min

Raw Almond Digestion

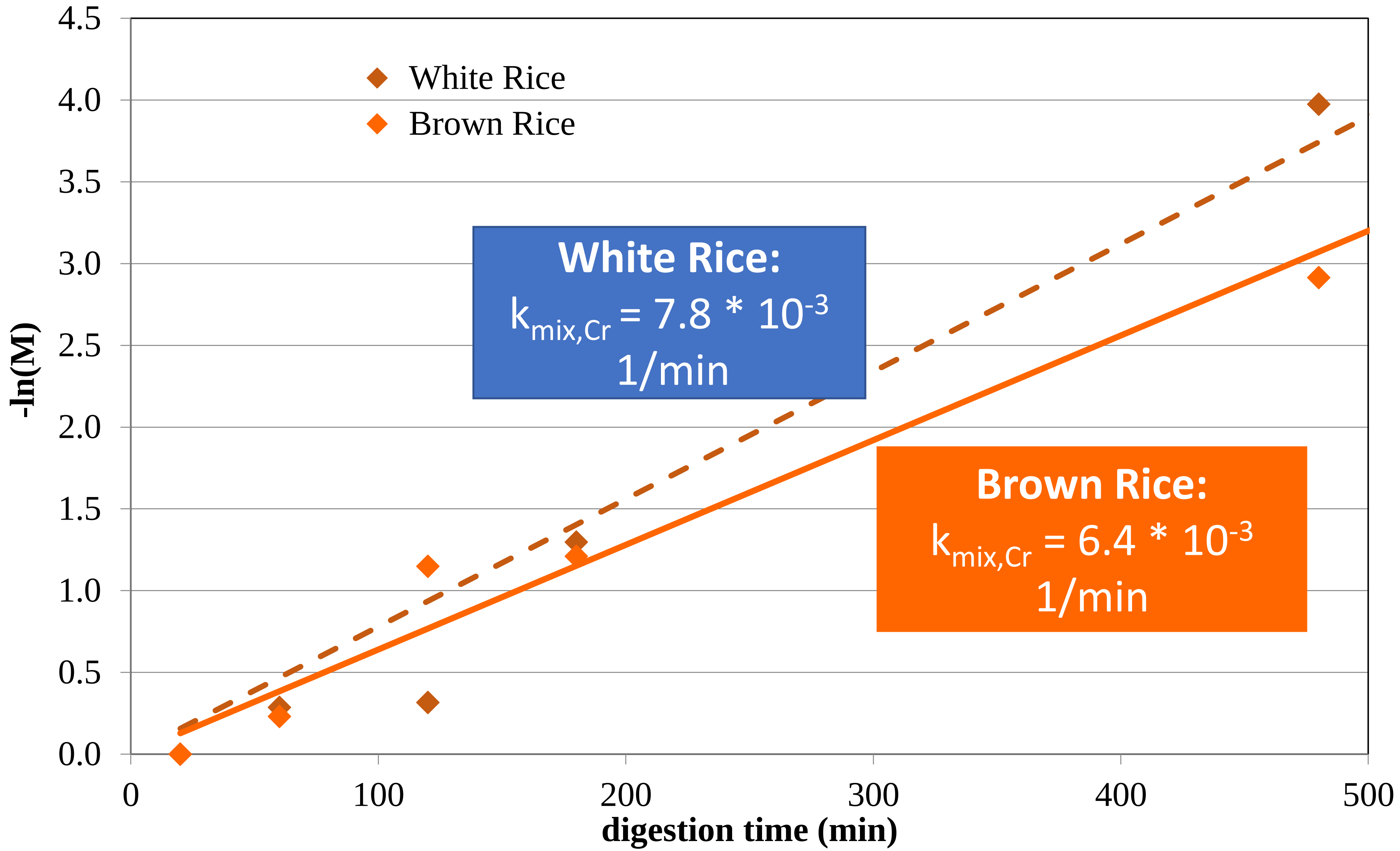


20 min



1 hour

Mixing Index Calculation: Cr

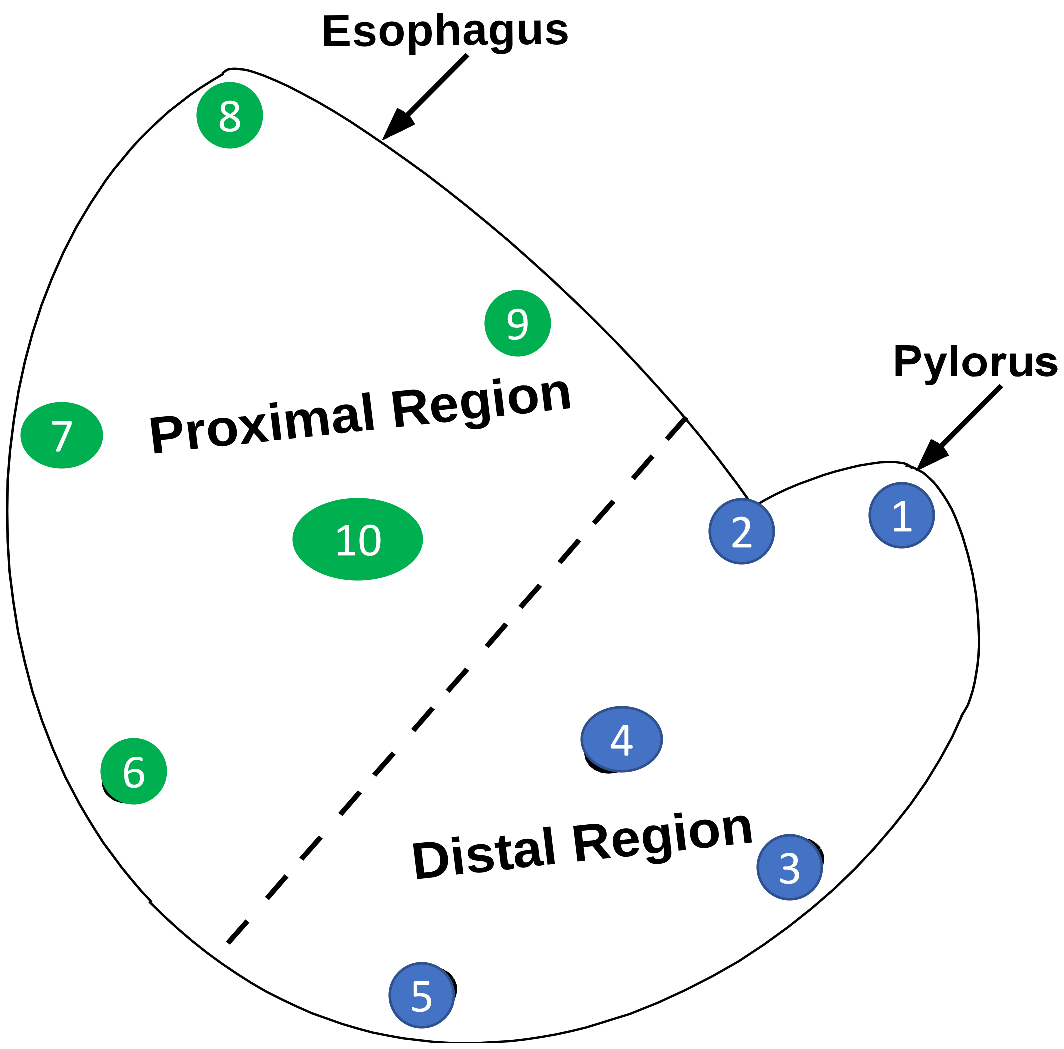


Gastric Regional pH Distribution

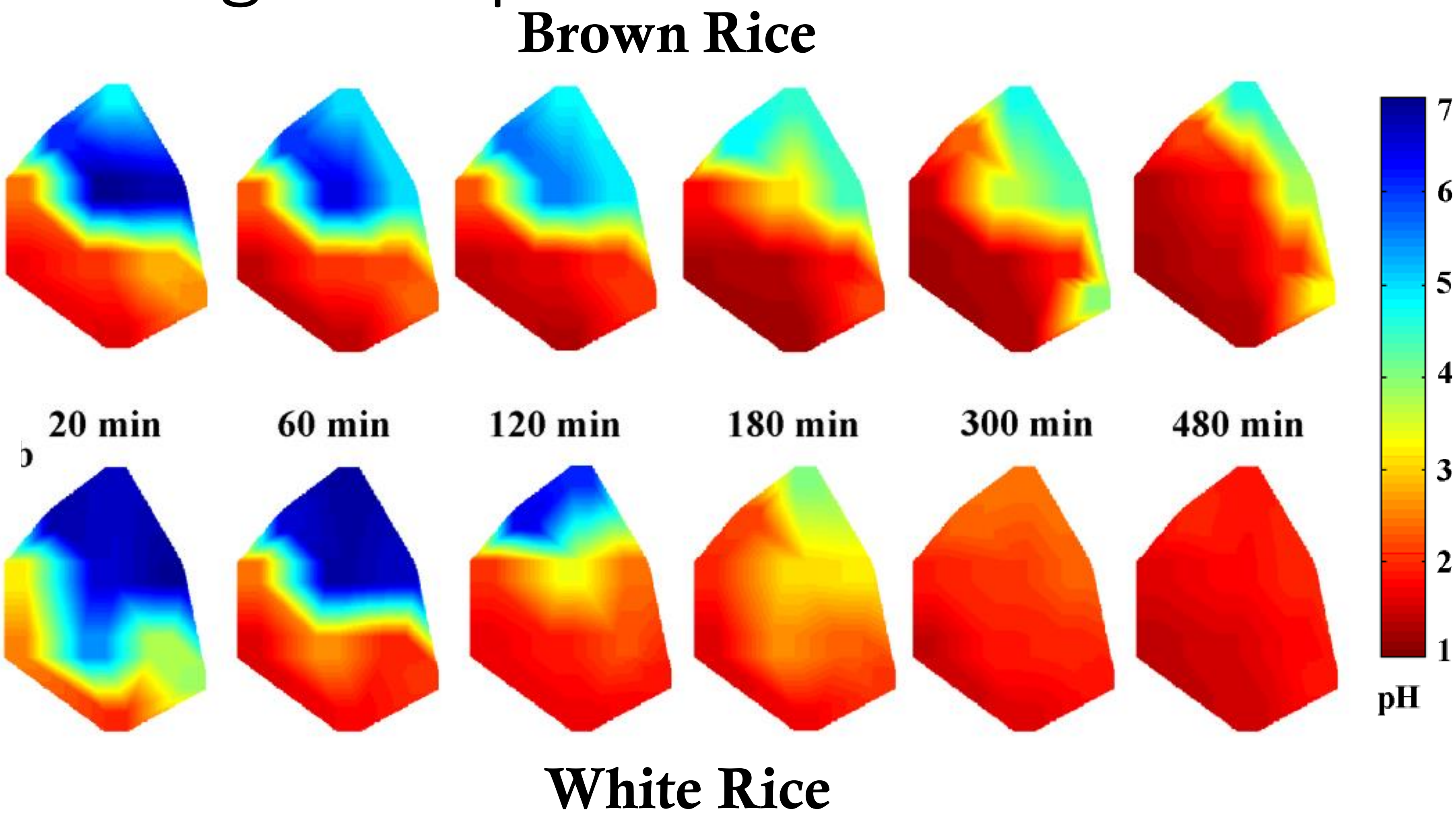
Intragastric pH

Mixing of Secretions with Meal Bolus

Sampling Throughout Stomach



Rice Intragastric pH

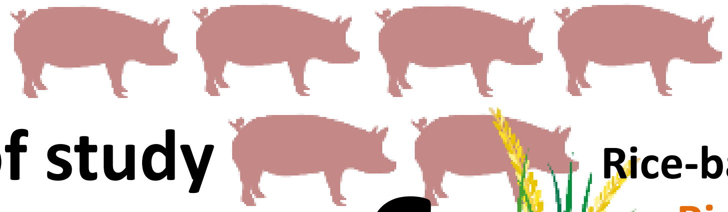


In Vivo Study Update

27th February – 29th May 2019 (99 days)

145 pigs

2 stages of study



6 diets

Rice-based diets
- Rice grains
- Rice noodle
- Rice couscous

Wheat-based diets
- Semolina
- Fettuccine
- Couscous

Blood glucose response measurement

- 18 pigs, catheterized on the ear vein
- Blood sampling at 18 time points (-15 minutes to 360 minutes after meal)
- Feeding the pigs with 4 different diets, including white bread as reference food

Digesta collection

- 127 pigs + 18 pigs from stage 1
- 1 pig = 1 type of diet and 1 digestion time point (20/60/120/240 min)

Data Collected

Blood glucose response measurement

- Pre-prandial & postprandial plasma glucose profile
- Pre-euthanasia plasma glucose response from 5 vein locations

Digesta collection

- **Measurements**: pH mapping & masses of digesta and stomach
- **Physical properties analysis**
  - Rheology
  - Texture analysis
  - Particle size distribution (image analysis/mastersizer)
  - Moisture content
- **Chemical & microstructural analysis:**
  - Reducing sugar, amylase activity, degree of protein hydrolysis assays
  - Titanium dioxide measurement (for gastric emptying calculation)
  - Confocal microscopy, SEM

Food Breakdown = Physical + Chemical

Cooked Food

During Gastric Digestion

Rice Noodles

White Rice

Summary

- Food structure breakdown in gastric digestion remains a poorly understood process
- A quantitative understanding is required to develop next generation of foods for health
- Strong collaborations among food scientists and engineers and researchers from medical, nutrition, and pharmacology fields are necessary to advance science in this area.

Acknowledgements

- **UC Davis**
    - Gail Bornhorst
    - David Phinney
    - Ryan Mayfield
    - Jerry Xue
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    - Betty Burri
- **Riddet Institute**
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    - Francisco Perez
    - Trent Olson
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