How structure and assembly across different length scales influence protein digestion

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Why are we interested in understanding food digestion?

Gut = interface between food and human body
Digestion releases food components that can have a beneficial or a deleterious effect on human health

... but the mechanisms of food disintegration during digestion remain unclear since the gastrointestinal tract has been considered as a black box so far

By increasing our knowledge on food digestion, we will increase our knowledge on the effect of food on human health
**Our goals**

- To understand the mechanisms of breakdown of food matrices and their constituents in the gut and identify the beneficial/deleterious food components released during digestion.
- To determine the impact of the structure of food matrices on these mechanisms.
- To model these phenomena in order to develop a reverse engineering approach.

**Bioactivities**
- Bioactive peptides
- Amino acids
- Fatty acids
- Minerals...

**Gut**
- Immune System
- Microbiota

**Mathematical modelling**

**Reverse engineering**

**Processing**

- Raw material
- Structured food

**Bioactivities**
- Healthy Adult
- Neonate
- Elderly
The digestive process

- **Storage, grinding, and mixing in the stomach**
- **Chewing and deglutition**
- **Gastric phase** = a very complex but crucial step for the whole digestion process

**Stomach**
- **Pepsin**
- **Gastric lipase**
- **HCl**
- **Fasted pH 1.3-2.5**

**Small intestine**
- **Duodenum**
  - pH 6.5-6.8
- **Jejunum**
- **Ileum**

**Large intestine**

**Nutrient absorption**

From Roger Lentle, Massey Univ. NZ

Kong and Singh, 2008
Thermal aggregation of natively unfolded proteins slows down their kinetics of hydrolysis during digestion.

Kinetics of proteolysis of different domains among one specific protein.

Design of model infant formulas with different heat-treatments and in vitro digestion using an infant model.

- Dupont et al. 2010. Mol Nutr Food Res, 54, 767-80
- Dupont et al. 2010. Mol Nutr Food Res, 54, 1677-89
- Dupont et al. 2010 Food Digestion, 1, 28-39

Identification of the resistant areas.
Thermal aggregation of globular proteins \textit{accelerates} their kinetics of hydrolysis during digestion

Ovalbumin (OVA) was taken as a model

Heat-treatments at different pH and ionic strength (IS)

\begin{itemize}
  \item pH 9/ IS 0,03M
  \item pH 7/ IS 0,03M
  \item pH 7/ IS 0,3M
  \item pH 5/ IS 0,8M
  \item Control: Non-aggregated
\end{itemize}

\textbf{In vitro digestion}

\begin{itemize}
  \item Linear
  \item Linear-branched
  \item Spherical
  \item Spherical-agglomerated
  \item Non-aggregated OVA
\end{itemize}


Nyemb et al., 2014. Food Res. Int., 63, 192-202
The microstructure of egg-white gels made from different types of aggregates affects the kinetics of proteolysis.

<table>
<thead>
<tr>
<th>Aggregates</th>
<th>Rate of in vitro hydrolysis</th>
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<tbody>
<tr>
<td>linear</td>
<td>+++</td>
</tr>
<tr>
<td>branched</td>
<td>++</td>
</tr>
<tr>
<td>spherical</td>
<td>+</td>
</tr>
</tbody>
</table>

Gels

Folded structure
Unfolded structure
Aggregated structure
Gel network

SEM
CRYO-TEM

Folded structure
Unfolded structure
Aggregated structure
Gel network

Rate of in vitro hydrolysis

+++
++
+

Nyemb et al., 2016. Food Hydrocolloid, 54, 315-27
Nyemb et al., 2016. Food Res. Int., in Press
Spatio-temporal evolution of pH during an *in vivo* digestion

**pH 7.0**

- **Gel pH 5**
- **Gel pH 7**
- **Gel pH 9**

**Digestion time**

- 20 min
- 60 min
- 120 min
- 240 min
- 360 min

$n=33$
Physical state of food controls gastric emptying and amino acid bioavailability in mini-pigs

Barbe et al. 2013. Food Chem. 136, 1203-12
Barbe et al. 2014, Food Chem, 143, 1-8
Mathematical model of transit and absorption

Le Feunteun et al. 2014. Food Bioprocess Tech. 7, 1099-1113
Conclusion

- The effect of heat treatment on protein kinetics of digestion directly depends on the structure of the protein:
  - natively unfolded
  - globular

- The trends determined for protein aggregates sensitivity to digestion cannot be extended to gels made with these aggregates

- The physical state (liquid/gel) of dairy products drives the kinetics of protein digestion and amino acid bioavailability

- The structure of food can be a way to control nutrient release and make it adapted to specific populations (infant, elderly, overweight...)

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