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Mechanisms explaining the role of viscosity and post-deglutitive pharyngeal residue on *in vivo* aroma release: a combined experimental and modeling study

M. Doyennette^{*1}, C. de Loubens¹, I. Déléris¹, I. Souchon¹, I. C. Trelea¹

¹UMR 782 Génie et Microbiologie des Procédés Alimentaires, INRA/AgroParisTech, CBAI
78850 Thiverval Grignon, France

* Corresponding author: Marion Doyennette, marion.doyennette@grignon.inra.fr; fax: +33 (0)1 30 81 55 97

12 **Abstract**

13 The objective of this study was to analyze the viscosity effect of liquid Newtonian products on aroma
14 release, taking human physiological characteristics into account. *In vivo* release of diacetyl from
15 glucose syrup solutions varying widely in viscosity (from 0.7 to 405 mPa s) was assessed by five
16 panelists using Proton Transfer Reaction Mass Spectrometry (PTR-MS). The physicochemical
17 properties of the solutions and the physiological parameters of subjects were experimentally measured.
18 In parallel, a mechanistic model describing aroma release while eating a liquid food was developed.
19 Model predictions based on the characteristics of the glucose syrup solution were invalidated when
20 compared to *in vivo* measurements. Therefore, the assumption that the post-deglutitive pharyngeal
21 residue was considerably diluted with saliva was introduced into the model. Under this hypothesis, the
22 model gives a satisfactory prediction of the *in vivo* data. Thus, relevant properties to be considered for
23 *in vivo* release were those of product-saliva mixes.

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25

26 **Keywords:** Flavor release; saliva dilution; swallowing; dynamic modeling; rheology.

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29 **1. Introduction**

30 Aroma compound release and perception determine the aromatic quality of food products and
31 contribute to consumer choices and preferences. During consumption, flavor delivery is particularly
32 determined by product properties (structure and composition) and individual physiology.
33 Understanding the key mechanisms of release is of great practical interest for rational food design and
34 formulation (Linthorpe & Taylor, 2000).

35 In the present work, the focus has been placed on the effect of matrix viscosity. This subject has
36 already been discussed in the literature but there appears to be no consensus. On the one hand, some
37 authors observed no effect of product viscosity on aroma release kinetics (Cook, Hollowood, Linthorpe
38 & Taylor, 2003; Hollowood, Linthorpe & Taylor, 2002; Weel, Boelrijk, Burger, Verschueren, Gruppen,
39 Voragen et al., 2004). These authors studied solutions viscosified with hydrocolloids. Their analysis
40 may have been biased by the fact that the concentration of the viscosifying agent modified both
41 rheological and physico-chemical properties. On the other hand, some authors found an impact of
42 viscosity on aroma release (Saint-Eve, Martin, Guillemin, Semon, Guichard & Souchon, 2006). They
43 obtained different rheological properties by a mechanical treatment that does not modify the product
44 composition and that therefore leaves physico-chemical properties such as air/product partition
45 coefficients unchanged (Kora, Souchon, Latrille, Martin & Marin, 2004). In that way, authors were
46 able to uncouple rheological and physico-chemical properties in their study. Saint-Eve et al. (2006)
47 showed a strong influence of yogurt complex viscosity on aroma release and hypothesized that these
48 differences were due to different mechanical behaviors of the products in the mouth or in the pharynx.
49 However, yogurts present complex rheological properties such as viscoelasticity and yield stress.
50 These complex behaviors, leading to different experimental conditions when compared with the other
51 studies, could explain the conflicting results.

52 In this context, the objective of this study was to analyze the Newtonian viscosity effects on the aroma
53 release kinetics of the products. To this end, we measured *in vivo* aroma release kinetics by Proton
54 Transfer Reaction Mass Spectrometry (PTR-MS) after the ingestion of glucose syrup solutions. These
55 solutions were Newtonian liquids for which a wide range of viscosities could be obtained.

56 Increasing the carbohydrate concentration of the solutions increased the Newtonian viscosity but
57 modified the air/product partition and mass transfer coefficients as well. In order to quantify these
58 effects independently, we developed a mechanistic model that described aroma release during
59 consumption of a liquid and semi-liquid food. Most of the model parameters related to the products or
60 to the subjects were measured experimentally. Comparing the model predictions under different
61 assumptions with the experimental data allowed us to understand the influence of viscosity on aroma
62 release.

63 The mechanistic model describing aroma release in the present study was developed on the basis of
64 the work described by Trelea, Atlan, Deleris, Saint-Eve, Marin & Souchon (2008). The sensitivity
65 analysis of the previous model highlighted the parameters that have a major influence on aroma
66 release kinetics. For example, the residual product layer thickness reduction in the pharynx accelerates
67 the volatile compound depletion by the breath flow rate, whereas its increase induces a longer
68 persistence effect. The breath flow rate also influences the aromatic persistence. In addition, increasing
69 the equilibrium partition coefficient or the mass transfer coefficient increases the aroma concentration
70 in the nasal cavity.

71 Most of these key parameters can be determined experimentally or evaluated from the literature.
72 However, the residual thickness of a product is an unknown parameter that should depend both on the
73 product viscosity and on the individual physiology. Due to the presence of saliva on the pharyngeal
74 mucosa, two hypotheses can be formulated about the nature of this post-deglutitive pharyngeal
75 residue. The first one considers that the initial saliva thickness in the pharynx is very thin compared to
76 the deposited thickness of the product, or is swept out during swallowing: a pure product layer coats
77 the mucosa. In the second hypothesis, we consider that the amount of saliva on the mucosa is large:
78 the deposited residue layer is a mix of saliva and the product.

79 These two assumptions were tested successively. In order to do this, the present work was carried out
80 in successive steps. First, a model of aroma release during ingestion was developed. In parallel,
81 relevant physico-chemical and physiological parameters were measured using *in vitro* or *in vivo*
82 experiments, or were calculated from the literature or experimental data. Finally, model predictions
83 under the two hypotheses were compared to measured *in vivo* release data.

85 **Nomenclature**

| Symbol | Unit | Parameter |
|-------------|------------------------|-----------------------------------------------------------------------------|
| A_{FAP} | cm^2 | Air/product contact area in the pharynx |
| A_{OAP} | cm^2 | Air/product contact area in the oral cavity |
| C_{FA} | g/cm^3 | Aroma concentration present in the air in the pharynx |
| C_{FP} | g/cm^3 | Aroma concentration present in the product in the pharynx |
| C_{FP}^* | g/cm^3 | Aroma concentration present at the air/product interface in the pharynx |
| C_{NA} | g/cm^3 | Aroma concentration present in the air in the nasal cavity |
| C_{OA} | g/cm^3 | Aroma concentration present in the air in the oral cavity |
| C_{OP} | g/cm^3 | Aroma concentration present in the product in the oral cavity |
| C_{OP}^* | g/cm^3 | Aroma concentration present at the air/product interface in the oral cavity |
| e | μm | Residual product layer thickness |
| F_R | Number of cycles/s | Respiratory frequency |
| K_{AP} | | Air/product partition coefficient |
| k_p | m/s | Mass transfer coefficient in the product layer |
| t_{deg} | | Swallowing moment |
| Q_{NA} | cm^3/s | Respiratory flow rate |
| Q_S | cm^3/s | Salivary flow rate |
| V_{FA} | cm^3 | Volume of air in the pharynx |
| V_{FP} | cm^3 | Volume of the product in the pharynx |
| V_{lung} | cm^3 | Lung volume |
| V_{NA} | cm^3 | Volume of air in the nasal cavity |
| V_{OA} | cm^3 | Volume of air in the oral cavity |
| V_{OP} | cm^3 | Volume of product in the oral cavity |
| V_{OPres} | cm^3 | Volume of residual product in the oral cavity |
| V_T | cm^3 | Tidal volume |

| | | |
|--------------|-----|-----------------------------------------------------------------------|
| ϕ_{FPA} | g/s | Volatile mass flux between the product and the air in the pharynx |
| ϕ_{OPA} | g/s | Volatile mass flux between the product and the air in the oral cavity |
| τ | s | Characteristic time of the aroma release decay |

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89

90 **2. Material and Methods**

91 2.1. Mathematical model for *in vivo* release

92 2.1.1. Principle of the model

93 A model describing aroma compound release during liquid and semi-liquid food consumption was
 94 previously developed by Trelea et al. (2008). It is based on a physiological representation of the
 95 deglutition process as described by Buettner, Beer, Hannig & Settles (2001). A schematic
 96 representation of the various compartments involved in the modeling design, as well as their
 97 connections, is given in Fig. 1A. We considered that the oral cavity (index O), the pharynx (index F)
 98 and the nasal cavity (index N) were interconnected compartments containing product and/or air phase.
 99 In the present study, two main simplifications were performed with the aim of eliminating parameters
 100 that have little impact on model predictions and which are difficult to determine experimentally.

101 The first simplification concerns the number of swallowing steps. In the original model, the product
 102 consumption process was decomposed into a series of four steps. Three of them concerned the
 103 deglutition event. However, they were very short and quite difficult to validate experimentally.
 104 Therefore, the new version of the model considers only three steps: product residence in the mouth,
 105 swallowing and release after swallowing. The swallowing step includes simultaneous contraction of
 106 the oral cavity and of the pharynx, leading to air and product expulsion, followed by relaxation and
 107 filling with fresh air. Figure 1B shows the successive steps modeled in the present work.

108 The second simplification of the model consisted in neglecting the aroma compound transfer
109 resistance in the air at the gas/product interface compared to the resistance in the product.

110 After these model simplifications, the number of physicochemical and physiological parameters that
111 needs to be known is reduced from 24 to 16. A comparison of the new model with the previous one
112 shows that these simplifications do not change the predictions in any significant way.

113 Therefore, the model simulates the relative concentration of a specific aroma compound in the nose
114 space of the subject. Aroma compound concentrations in all compartments (oral cavity, pharynx and
115 nasal cavity) were calculated using mass transfer equations and mass balances. Isothermal conditions
116 were assumed. Moreover, aroma compounds have a strong preference for the aqueous phase compared
117 to the air, and the contact area between air and lungs is very large ($\sim 100 \text{ m}^2$) (Menache, Hanna, Gross,
118 Lou, Zinreich, Leopold et al., 1997). Thus, it seems reasonable to assume that aroma compounds are
119 quickly absorbed into the lungs. It was therefore assumed that the air coming from the trachea (i.e., the
120 lungs) would be aroma-free. If we take a closer look at the anatomy of the nose, we can subdivide the
121 nasal cavity into the nasal vestibule, the anterior turbinate and the posterior turbinate with different
122 volumes and airflow rates (Wen, Inthavong, Tu & Wang, 2008). Similarly, it could be possible to take
123 aroma compound-mucosa interactions into account. These additional phenomena were tentatively
124 incorporated into a provisional model but were not retained in the final model, as will be explained
125 below in the Results and Discussion section.

126 Moreover, concerning the presence of saliva on the pharyngeal mucosa, two different hypotheses
127 about the nature of the bolus that coats the pharyngeal mucosa after swallowing were considered. The
128 first one (H1) assumes that a pure product layer is deposited on the pharyngeal mucosa. The second
129 one (H2) assumes that the product coating the pharyngeal mucosa is significantly diluted with saliva.
130 In that case, contrarily to the first hypothesis, the physico-chemical parameters of the bolus have to be
131 recalculated on the basis of the dilution rate.

132

133

134 2.1.2. Mathematical model description

135 We refer to the time of product introduction in mouth and the time of deglutition as t_0 and t_{deg} ,
 136 respectively.

137

138 Step 1: product residence in the mouth

139 ✓ **Product in the oral cavity**

140 The mouth is closed during this step and does not exchange aroma compounds with other
 141 compartments. The volume of the product in the oral cavity V_{op} increases due to dilution by saliva.

$$142 \quad \frac{dV_{OP}(t)}{dt} = Q_S \quad (1)$$

143 The volatile mass flux ϕ_{OPA} is given by the difference between the product concentration (C_{OP}) and the
 144 interfacial concentration (C_{OP}^*):

$$145 \quad \phi_{OPA}(t) = A_{OAP} \times k_p \times (C_{OP}(t) - C_{OP}^*(t)) \quad (2)$$

146 where k_p is the mass transfer coefficient of the aroma compound in the product.

147 The variation of the aroma concentration present in the product C_{OP} is due to release to the air in the
 148 mouth (transfer through the product-air interface A_{OAP}) and to dilution by saliva flow Q_S :

$$149 \quad V_{OP}(t) \times \frac{dC_{OP}(t)}{dt} = -\phi_{OPA}(t) - Q_S \times C_{OP}(t) \quad (3)$$

150

151 ✓ **Air in the oral cavity**

152 The variation of aroma concentration in the air C_{OA} is due to the volatile flux from the product in the
 153 mouth ϕ_{OPA} :

$$154 \quad V_{OA} \times \frac{dC_{OA}(t)}{dt} = \phi_{OPA}(t) \quad (4)$$

155

156 ✓ **Interfacial conditions**

157 The interfacial aroma compound concentration on the product side was calculated using the partition
 158 conditions at the interface (Cussler, 1997). Since transfer resistance on the air side was assumed to be
 159 negligible, the interfacial air concentration is the same as the bulk air concentration:

$$K_{AP} = \frac{C_{OA}(t)}{C_{OP}^*(t)} \quad (5)$$

161 where K_{AP} is the air/product partition coefficient.

162

163 Initial conditions for Step 1: product residence in the mouth

164 At the beginning of Step 1, the product introduced into the mouth (C_{OPini}) is the only compartment
165 containing aroma compounds. Hence, the initial conditions are:

$$C_{OP}(t_0) = C_{OPini} \quad (6)$$

$$C_{OA}(t_0) = C_{FP}(t_0) = C_{FA}(t_0) = C_{NA}(t_0) = 0 \quad (7)$$

168

169 Step 2: Swallowing

170 The deglutition step is very short compared to the mouth residence step. The main modeling
171 implication is that the transfer to the gaseous phase is negligible during deglutition.

172 To describe this sequence of very quick contraction and relaxation events, the following notation is
173 used (Fig. 1B):

- 174 • t_{deg-} corresponds to the product and air status immediately before the oral and pharyngeal
175 contraction begins. It is the end of Step 1;
- 176 • t_{deg} corresponds to the status between the end of the contraction and the subsequent relaxation
177 of the pharynx and mouth;
- 178 • t_{deg+} corresponds to the moment just after pharynx and mouth relaxation. This is the end of
179 Step 2 and the beginning of Step 3.

180

181 **✓ Product in the oral cavity**

182 After the oral cavity contraction, the residual amount of product is assumed to be equal to the usual
183 residual amount of saliva:

$$V_{OP}(t_{deg}) = V_{OPres} \quad (8)$$

184

185 Since Step 2 is very short, the aroma compound concentration in the oral cavity is unchanged during
 186 deglutition (negligible dilution by saliva and transfer to air):

$$187 \quad C_{OP}(t_{\text{deg}+}) = C_{OP}(t_{\text{deg}}) = C_{OP}(t_{\text{deg}-}) \quad (9)$$

188

189 **✓ Product in the pharynx**

190 During deglutition, it is assumed under hypothesis (H1) that the saliva film in the pharynx is swept out
 191 by the large amount of product coming from the mouth:

$$192 \quad C_{FP}(t_{\text{deg}+}) = C_{OP}(t_{\text{deg}-}) \quad (10)$$

193 Under hypothesis (H2), only a small part of the product coming from the mouth is mixed with
 194 the saliva film in the pharynx. This corresponds to the dilution factor discussed below.

195 **✓ Air in nasal cavity, pharynx and mouth**

196 Assuming that during the contraction, the expelled air is well mixed in the mouth, pharynx and nose,
 197 the intermediate aroma compound concentration in the nasal cavity, after contraction, is given by the
 198 total mass divided by the total volume:

$$199 \quad C_{NA}(t_{\text{deg}}) = \frac{V_{OA} \times C_{OA}(t_{\text{deg}-}) + V_{FA} \times C_{FA}(t_{\text{deg}-}) + V_{NA} \times C_{NA}(t_{\text{deg}-})}{V_{OA} + V_{FA} + V_{NA}} \quad (11)$$

200 After the contraction, the amount of aroma compound present in the upper airway is $V_{NA} \times C_{NA}(t_{\text{deg}})$.

201 After relaxation, this amount is diluted by ambient air. Assuming good mixing, the final
 202 concentrations will be:

$$203 \quad C_{NA}(t_{\text{deg}+}) = C_{FA}(t_{\text{deg}+}) = C_{OA}(t_{\text{deg}+}) = \frac{V_{NA} \times C_{NA}(t_{\text{deg}})}{V_{OA} + V_{FA} + V_{NA}} \quad (12)$$

204

205

206 Step 3: Release after swallowing

207 The initial conditions of Step 3 are the final values of Step 2 (at $t_{\text{deg}+}$).

208

209 **✓ Product in the pharynx**

210 The residual product in the pharynx releases aroma compounds into the adjacent air. The volatile flux
 211 ϕ_{FPA} is given by:

$$212 \quad \phi_{FPA}(t) = A_{FAP} \times k_p \times (C_{FP}(t) - C_{FP}^*(t)) \quad (13)$$

213 The mass balance of the aroma compound in the product layer gives:

$$214 \quad V_{FP} \times \frac{dC_{FP}(t)}{dt} = -\phi_{FPA}(t) \quad (14)$$

215 The product volume in the pharynx V_{FP} can be expressed as the product of the residual layer thickness
 216 e and the pharynx area A_{FAP} , i.e. $V_{FP} = A_{FAP} \times e$. The previous equation can be further simplified to:

$$217 \quad \frac{dC_{FP}(t)}{dt} = -\frac{k_p}{e} \times (C_{FP}(t) - C_{FP}^*(t)) \quad (15)$$

218

219 ✓ Air in the pharynx

220 The air in the pharynx exchanges aroma compounds with the residual product coating the pharynx
 221 walls and with the airflow Q_{NA} from the nasal cavity (inhalation) or the lungs (expiration).

$$222 \quad V_{FA} \times \frac{dC_{FA}(t)}{dt} = \phi_{FPA}(t) + \begin{cases} Q_{NA}(t) \times (C_{NA}(t) - C_{FA}(t)) & \text{if } Q_{NA}(t) \geq 0 \text{ (inhalation)} \\ -Q_{NA}(t) \times (0 - C_{FA}(t)) & \text{if } Q_{NA}(t) < 0 \text{ (expiration)} \end{cases} \quad (16)$$

223

224 ✓ Air in the nasal cavity

225 The concentration of aroma compounds in the nasal cavity results from a dilution with the ambient air
 226 during inhalation and with air coming from the pharynx during expiration:

$$227 \quad V_{NA} \times \frac{dC_{NA}(t)}{dt} = \begin{cases} Q_{NA}(t) \times (0 - C_{NA}(t)) & \text{if } Q_{NA}(t) \geq 0 \text{ (inhalation)} \\ -Q_{NA}(t) \times (C_{FA}(t) - C_{NA}(t)) & \text{if } Q_{NA}(t) < 0 \text{ (expiration)} \end{cases} \quad (17)$$

228

229 ✓ Interfacial conditions

230 Similarly to what happens in the oral cavity (Equation (5)), the interfacial air concentration in the
 231 pharynx is the same as the bulk air concentration:

$$K_{AP} = \frac{C_{FA}(t)}{C_{FP}^*(t)} \quad (18)$$

233

234 ✓ Calculation of the respiratory flow rate

235 We based our calculation of the airflow rate Q_{NA} on the assumption that the volume of air inhaled and
 236 exhaled by the panelist had a sinusoidal shape. The tidal volume V_T and the respiratory frequency F_R
 237 were required for this calculation (Section 2.6 for details about this data acquisition).

238 The time shift $(t - t_{deg})$ was introduced to ensure that the deglutition event is always followed by
 239 expiration, as physiologically observed. This is referred to as a swallow breath.

240 Assuming that lung volume variation is as follows:

$$241 \quad V_{lung}(t) = const + \frac{V_T}{2} \times \cos(\pi \times 2 \times F_R \times (t - t_{deg})) \quad (19)$$

242 where the constant accounts for the average air volume in the lungs, the expression of Q_{NA} will be:

$$243 \quad Q_{NA}(t) = \frac{dV_{lung}(t)}{dt} = -\pi \times F_R \times V_T \times \sin(\pi \times 2 \times F_R \times (t - t_{deg})) \quad (20)$$

244

245

246 2.1.3. Model parameters

247 Model parameters can be related to the product, the consumer or the interaction between them.

248 1. Parameters related to the product

249 These parameters include the initial aroma compound concentration, the air/product partition
 250 coefficient and the mass transfer coefficient. The first parameter above is directly calculated from the
 251 product flavoring protocol (Section 2.2), and the second one is estimated *via* the non linear phase ratio
 252 variation method described in Atlan, Trelea, Saint-Eve, Souchon & Latrille (2006). The mass transfer
 253 coefficient was measured with the headspace method (Lauverjat, de Loubens, Deleris, Trelea &
 254 Souchon, 2009). Experimental protocols are described in detail in Section 2.4.

255 2. Parameters related to consumer anatomy and physiology

256 These parameters include the areas and volumes of the various compartments of the oro-nasal-
257 pharyngeal sphere, as well as the saliva and airflow rates. Data collection protocols are described in
258 detail in the Section 2.6.

259 3. Parameters related to product-consumer interaction

260 These parameters are the residual amounts of the product and the air/product contact areas (both in the
261 mouth and in the pharynx). Residual product left in the mouth after swallowing was arbitrarily set to
262 1% of the initial volume of product in the oral cavity. The air/product contact areas of the mouth and
263 pharynx were calculated as detailed in Appendix A. The thickness of the post-deglutitive pharyngeal
264 residue coating the pharynx was the degree of freedom of the model. Since it only affected the part of
265 the curve related to the persistence of aroma, it was determined so that the model fitted the decay time
266 of the experimental curve for each panelist, product and replicate.

267 The effects of these parameters on model prediction were investigated and are presented in the
268 “Results and Discussion” section.

269

270

271 2.2 Preparation of flavored products

272 Seven solutions were prepared with a glucose syrup (C*Sweet M01623, Cerestar, Europe) and mineral
273 water (Evian). The dry matters of final solutions varied from 0 g/100 g to 70 g/100 g. All preparations
274 presented a Newtonian behavior, i.e., viscosity was constant regardless of the shearing rate applied.
275 Viscosities were measured with Physica MCR301 rheometer (Anton Paar Germany GmbH, Ostfildern,
276 Germany) and were between 0.7 and 405 mPa s at 35°C. The characteristics of the solutions are
277 summarized in Table 1. The solutions investigated in this paper were labeled according to their
278 approximate percentage of dry matter (for example, G60 had a dry matter of 61.11g/100g). These
279 solutions were flavored with diacetyl and ethyl hexanoate, which had been previously dissolved in
280 99.46% of propylene glycol (Aldrich, France). Final concentrations of diacetyl and ethyl hexanoate in
281 the solutions studied were approximately 20 mg/L and 88 mg/L, respectively, for the *in vivo*
282 experiments, 140 mg/L and 8.3 mg/L, respectively, for the *in vitro* determination of air/product

283 partition coefficients, and 1.5 mg/L and 0.85 mg/L, respectively, for the *in vitro* determination of mass
284 transfer coefficients.

285 For the rest of this work, we focused on the diacetyl results. Data concerning ethyl hexanoate will be
286 used for the validation step.

287

288 2.3. Measurement of *in vitro* and *in vivo* aroma release by Proton Transfer

289 Reaction–Mass Spectrometry

290 The dynamic release of aroma compounds for *in vitro* and *in vivo* experiments was measured online
291 using a Proton Transfer Reaction Mass Spectrometer (PTR-MS, Ionicon, Innsbruck, Austria).

292 The PTR-MS inlet was connected to samples or to the subject's nose via a 1/16" PEEK tube
293 maintained at 60°C. The PTR-MS instrument drift tube was thermally controlled ($T_{\text{drift}} = 60^\circ\text{C}$) and
294 operated at $P_{\text{drift}} = 200$ Pa with a voltage set of $U_{\text{drift}} = 600$ V. Measurements were performed with
295 the multiple ion detection mode on specific masses with a dwell time of 50 ms per mass. Diacetyl was
296 monitored with m/z 87 (molecular ion). For *in vivo* experiments, m/z 59 (acetone) was also monitored
297 as a breath marker, as described in Normand, Avison & Parker (2004) and Trelea et al. (2008).

298 In addition, masses m/z 21 (signal for $\text{H}_3^{18}\text{O}^+$) and m/z 37 (signal for water clusters $\text{H}_2\text{O}-\text{H}_3\text{O}^+$) were
299 monitored with a dwell time of 100 ms to check the instrument performances and cluster ion
300 formation. m/z 21 intensity was $(1.34 \pm 0.51) \times 10^4$ cps for *in vitro* experiments and $(9.46 \pm 0.035) \times$
301 10^3 cps for *in vivo* experiments. In both cases, the ratio of intensities of m/z 37 and 21 variation was
302 lower than 5%. These differences were considered sufficiently small to ensure accurate PTR-MS
303 measurements. For both *in vitro* and *in vivo* measurements, a minimum of three replicates were
304 performed for each condition studied.

305 Air was sampled from the subject's nose at a flow rate of 35 cm³/min. Nose space air was sampled *via*
306 two inlets of a stainless nosepiece placed in both of the assessor's nostrils.

307

308

309

310 2.4. Determination of physicochemical parameters of diacetyl

311 2.4.1. Determination of air/product partition coefficients

312 The air/product partition coefficient of diacetyl K_{AP} was measured for each solution with the Phase
313 Ratio Method using headspace gas chromatography (Ettre, Welter & Kolb, 1993). A known amount of
314 solution was placed in vials (22.4 cm³, Chromacol, France) and incubated at 35°C for 5 hours. After
315 this equilibration time, 2 cm³ of the headspace above the product was sampled and injected with an
316 automatic HS CombiPal sampler (CTC Analytics, Switzerland) into a gas chromatograph HP (GC-FID
317 HP6890, Germany) equipped with an HP-INNOWax polyethylene glycol semi-capillary column J&W
318 Scientific (30 m x 0.53 mm, with a 1 µm-thick film) and a flame ionization detector. The temperatures
319 of the gas chromatograph injector and detector (GC-FID HP6890, Germany) were both set at 250°C.
320 The oven program was 12 min long, starting at 40°C, for 5°C/min up to 60°C, then for 10°C/min up to
321 120°C, and 2 min at 120°C. The carrier gas was helium (flow rate: 8.4 cm³/min, corresponding to a 57
322 cm/s average velocity at 50°C). Peak areas were measured using Hewlett-Packard Chemstation
323 integration software.

324 A non-linear regression was performed on the data set as described in Atlan et al. (2006). A minimum
325 of three replicates were performed for each solution tested.

326

327

328 2.4.2. Determination of mass transfer coefficients

329 The method used for mass transfer coefficient measurements was based on two studies: the Static
330 Equilibrium and Headspace Dilution Analysis (Marin, Baek & Taylor, 1999) and the Volatile Air
331 Stripping Kinetic (VASK) method (Lauverjat, de Loubens, Deleris, Trelea & Souchon, 2009).

332 Five g of solution were poured into 134.8-cm³ vials (three replicates/solution). The samples were left
333 for a minimum of 12 h at 35°C to establish thermodynamic equilibrium. The headspace was then
334 stripped by a gaseous flow at a controlled rate of 1.45 cm³/s (Brooks Digital Mass Flow Meter, Brooks
335 Instrument 5860s). The evolution over time of headspace concentration of these vials was measured
336 by PTR-MS for 25 minutes. The experiment time had to be longer than four times the characteristic

337 time of the headspace stripping $\frac{V}{Q}$, where V is the volume of the headspace, and Q the stripping
338 airflow rate. In fact, when the experiment time is shorter than $\frac{V}{Q}$, the headspace concentration is
339 mainly governed by dilution with the airflow rate and not by the transfer from the product to the air.
340 Fitting the diacetyl release model (Appendix B for detailed equations) to experimental data made it
341 possible to determine the mass transfer coefficient of this aroma compound in the solutions.

342

343 2.5. In-nose measurements of aroma release and data processing

344 Five panelists (three females and two males, all Caucasian) aged between 25 and 38 years old were
345 recruited for this study. Only the four solutions presenting the widest range of viscosities (G0, G40,
346 G60 and G70) were investigated *in vivo*. The 10-cm³ samples were first left at 35°C for 2 hours to
347 allow thermal equilibrium. Panelists were then instructed to pour the sample into their mouth, keep it
348 while they were connecting to the PTR-MS (1-2 seconds) and to then swallow. Subjects had to
349 continue to breathe normally through the nose (and with their mouth closed) for approximately one
350 minute, during which time the nose-space PTR-MS signal was recorded. Each experiment was
351 repeated three times.

352 An additional protocol consumption was applied for G0: panelists had to suck up a mouthful of the
353 headspace vial with a straw, swallow it and continue to breathe normally through the nose.

354

355 On the basis of data treatment observed in the literature, the aroma release curve is rarely analyzed in
356 its entirety. In the modeling studies of Buffo, Rapp, Krick & Reineccius (2005) and Linforth et al.
357 (2000) on aroma compound persistence in human breath, analyses were performed on the ratio
358 between the corresponding intensities of the second and the first expirations after swallowing for each
359 subject and each aroma compound investigated. Hodgson, Langridge, Linforth & Taylor (2005)
360 proceeded differently and calculated the decay exponent of the maximum intensity of the second and
361 subsequent breath peaks plotted against time (setting apart the first aroma release peak).

362 Figure 2 represents the data processing results of our experimental aroma release kinetics for one
363 panelist and one solution. Each kinetic presented a sinusoidal pattern due to the cyclic shape of the
364 breath. For clarity, we smoothed the breath-by-breath aroma release profiles by plotting a curve
365 linking the maxima of the sinusoids (referred to as the “peak curve” in Fig. 2), including the swallow-
366 breath peak. Then, for each product, each panelist and for the three replicates, a mean curve and an
367 envelope curve were built based on the peak lines. This last one represents the standard deviation of
368 the replicates and, as a result, the intra-individual variability.

369 In order to validate model prediction against experimental measurements, simulated data were also
370 represented as a peak line. For ease of comparison among different release curves, the deglutition
371 event was always synchronized at time zero.

372 In the “Results and Discussion” section, two main characteristics of the curves were analyzed during
373 *in vivo*/simulation comparison: the intensity of the first peak after swallowing, and the decay time of
374 the curve (which is representative of the aroma persistency and related to the thickness of the post-
375 deglutitive residue in the pharynx).

376

377

378 2.6. Determination of physiological parameters

379 Volumes of oral, nasal and pharyngeal cavities were measured with the Eccovision Acoustic
380 Rhinopharyngometer from Eccovision (Sleep Group Solutions, North Miami Beach, FL 33162). The
381 air/product contact areas in the mouth and in the pharynx were calculated for each panelist as
382 described in Appendix A. However, for the air/product contact area in the mouth, we only took 60% of
383 the calculated value, since we estimated that the brief in-mouth product residence did not allow the
384 subjects to spread the product over the full surface of the mouth before swallowing.

385 The volume of solution introduced into the mouth was fixed by the experimental protocol at 10 cm³,
386 which corresponds to a realistic “mouthful”. In-mouth saliva volume was set at 1.1 cm³ based on data
387 from Dawes (2008), and stimulated saliva flow rate was measured for each panelist (under a parafilm
388 stimulation).

389 The tidal volume of each panelist was measured with a spirometer (SpeeDyn from Dyn'R group) and
390 the respiratory frequency was calculated from the acetone signal measured by PTRMS during the
391 resting time preceding each experiment.

392

393 Prior to their participation in the experiments, a written consent was obtained from all participants
394 after a full explanation of the purpose and nature of the study.

395

396

397 **3. Results and Discussion**

398 3.1. Experimental data

399 3.1.1. Air/product partition coefficients of diacetyl

400 Results from PRV experiments are shown in Table 2. The diacetyl air/product partition coefficient for
401 the pure water at 35°C was 1.28×10^{-3} . This value is quite close to the ones obtained by Bakker,
402 Boudaud & Harrison (1998) at 37°C, ranging between 1.16×10^{-3} and 1.78×10^{-3} . Additional values of
403 the diacetyl partition coefficient for pure water can be found in the literature, but mostly for
404 experiments performed at 25°C or below. By using the Arrhenius law on data obtained by Atlan et al.
405 (2006), it is possible to calculate an activation energy of 40.7 kJ/mol and to extrapolate a partition
406 coefficient value of 1.18×10^{-3} at 35°C, which is very close to the value found in the present work.

407 We can observe that the air/product partition coefficient increases with the dry matter for values
408 greater than 5% of dry matter solution. Values range from 0.57×10^{-3} for G5 up to 2.5×10^{-3} for G70.

409 Most of the data available in the literature are for sucrose. For example, Friel, Linforth & Taylor
410 (2000) showed a similar trend in the air/product partition coefficient for diacetyl for a variation of
411 sucrose concentrations. These phenomena could be explained by a loss of free water due to hydration
412 of sugar molecules. Increasing the sucrose concentration makes the solvent character of a solution
413 more hydrophobic. Therefore, for a hydrophilic aroma compound such as diacetyl, its affinity for the

414 product would be reduced (Nahon, Koren, Roozen & Posthumus, 1998; Nawar, 1971; Thanh,
415 Thibeau, Thibaut & Voilley, 1992).

416

417 3.1.2. Mass transfer coefficients of diacetyl

418 The mass transfer coefficients calculated with the headspace dilution method are presented in Table 2.
419 They ranged between 1.1×10^{-6} m/s (pure water) and 3.31×10^{-8} m/s (G70) at 35°C. We observe a
420 decrease in the mass transfer coefficient of diacetyl with the dry matter content of the solution. Nahon,
421 Harrison & Roozen (2000) reported similar results within a range of 0 to 60% w/w of sucrose
422 concentration.

423 Marin et al. (1999) measured a mass transfer coefficient for diacetyl at 35°C of 2×10^{-6} m/s for an
424 aqueous solution. Bakker et al. (1998) found a value of 2.7×10^{-6} m/s at 37°C for pure water and
425 showed that an increase in viscosity induced a decrease in the mass transfer coefficient, similarly to
426 our work.

427

428

429 3.1.3. Physiological parameters

430 In order to make the model as accurate as possible, all of the physiological parameters (except the
431 thickness of the product layer coating the pharynx) were measured for each panelist. The variation
432 ranges of the physiological parameters are presented in Table 3.

433 We observe that all physiological parameters present a wide range of variation. For example, the
434 volumes of oral cavity, nasal cavity and pharynx obtained by rhinopharyngometry are about 37 ± 8 ,
435 11 ± 4 and 29 ± 9 cm³, respectively. The contact areas in the oral cavity and the pharynx are 102 ± 14 cm²
436 and 60 ± 13 cm², respectively.

437

438

439 3.1.4. Typical experimental results

440 We observed that the aroma release curve (“single repetition” curve in Fig. 2) has a sinusoidal shape,
441 and is synchronized with breath (data not shown): when a subject exhales, he/she brings aroma to
442 his/her nasal cavity (corresponding to the rising part of the sinusoid pattern), whereas during
443 inhalation, fresh air is delivered to the nose (decreasing part of the sinusoid pattern). We can also
444 observe that the first breath peak of the aroma release is the highest and corresponds to the delivery
445 that occurs immediately after the first swallow. The aroma concentration then gradually decreases, and
446 secondary peaks are due to the continuous aroma release induced by the flavored post-deglutitive film
447 coating the pharynx, which is permanently in contact with the breath airflow.

448 Figure 3 represents the mean peak curves of aroma release for the four solutions consumed by one
449 panelist. The global shapes of the kinetics are the same, regardless of the panelist or the product.
450 However, similarly to Buffo et al. (2005) and Linforth et al. (2000), we observed differences in
451 PTRMS responses for each subject due to their physiological characteristics. Nevertheless, G0
452 presents the highest intensity for the swallow-breath peak of aroma compound release for all panelists.
453 This observation was confirmed by a statistical analysis. Since our data were not normally distributed,
454 we performed a Friedman test (non parametric) with an excel macro developed by P. Georgin et M.
455 Gouet (available online at www.AnaStats.fr) on the *in vivo* release data, normalized by the initial
456 aroma concentration in the product, to see if we could observe a solution effect. The three analyzed
457 descriptors of the kinetics were: (1) the normalized area under the curve, (2) the normalized maximum
458 intensity I_{NAmax}/C_{OPini} (first peak intensity), and (3) the decay time of the curve τ . Results show that
459 there is a product effect on the first peak intensity (level of significance 0.05). Confirming the
460 empirical observation in Fig. 3, the classification performed with a multiple comparison test
461 (Bonferroni method with a macro developed by G. Le Page, available online at www.AnaStats.fr)
462 (Table 4) shows that the first diacetyl peak for flavored pure water (G0) is significantly higher than for
463 the other solutions (G40, G60 and G70) (level of significance 0.05).

464 The normalized area under the curve and the characteristic decay time of the curve were not
465 statistically different between the glucose syrup solutions.

466

467

468 3.2. Parameter effects on model predictions

469 As mentioned in Section 2.1, the simplifications of the model were validated by comparing the
470 kinetics obtained with the current model and the previous one with the same parameters. A sensitivity
471 analysis of the new model was conducted.

472 We found that an increase in the mass transfer coefficient of the product induced an increase in the
473 aroma concentration in the nasal cavity and a decrease in the characteristic decay time τ .

474 The post-deglutitive residual thickness layer in the pharynx influences the characteristic decay time of
475 the curve τ . In fact, this time period follows the relationship:

$$476 \quad \tau \propto \frac{e}{k_p} \quad (21)$$

477 where e is the residual thickness layer in the pharynx and k_p the mass transfer coefficient (Equation
478 (15)). Moreover, this parameter has no influence on the height of the first aroma release peak. Last but
479 not least, the lower the respiratory frequency is, the higher the aroma persistence will be.

480

481

482 3.3. Comparison of model predictions with experimental data

483 This section is dedicated to the comparison of model prediction with experimental data. Firstly, we
484 verified that the aroma compound investigated in this study, i.e., diacetyl, does not specifically interact
485 with the mucosa of the different compartments of the oro-pharyngeal sphere and the airways.
486 Hodgson, Parker, Linforth & Taylor (2004) stated that while volatile molecules are transferred through
487 the upper airways, they absorb to the nasal mucosa. To check the absence of mucosa interaction,
488 panelists were asked to absorb aroma compounds either in gaseous phase or in liquid phase, as
489 described in the “Material and Methods” section. A typical result of each type of consumption
490 protocol is illustrated in Fig. 4. On the one hand, we observe a curve for the liquid ingestion protocol
491 (solid line) that shows secondary aroma release peaks due to persistence phenomena. On the other
492 hand, the aroma release after inhaling the aroma compound in gaseous phase (dotted line) has only one
493 major peak. This shows that no significant mucosa retention occurred. This is in agreement with the

494 work of Normand et al. (2004), stating that short persistence of the aroma release (less than 1 min,
495 which is the case in our study) is considered to be mainly due to saliva coating, whereas longer
496 persistence is due to volatile adsorption in the mucosa. Therefore, introducing an additional mucosa
497 compartment into the model was unnecessary for this aroma compound.

498 Secondly, another assumption of the model that was investigated was that complex airflow in the
499 airways could have a significant effect on aroma kinetics. Tentatively, the model was implemented by
500 considering an additional “lung” compartment and/or by subdividing the nasal cavity into several
501 compartments, i.e., the nasal vestibule, the anterior turbinate and the posterior turbinate, with
502 corresponding volumes and airflow fractions (Hahn, Scherer & Mozell, 1993). It appeared that the
503 effect of these additional compartments on model predictions was minor (results not shown).
504 Therefore, we did not keep those compartments in the final version of the model.

505

506 Finally, two different hypotheses concerning the nature of the post-deglutitive residue coating the
507 pharyngeal mucosa after swallowing were developed.

508 The first hypothesis assumed that a pure product layer is deposited on the pharyngeal mucosa. In this
509 case, the air/product partition coefficients as well as the mass transfer coefficients are those obtained
510 earlier in Section 3.1.

511 The second hypothesis assumed that the product coating the pharyngeal mucosa is highly diluted with
512 saliva. In that case, the physico-chemical parameters of the bolus need to be recalculated according to
513 the dilution rate.

514 These two hypotheses will be tested and discussed in the following sections.

515

516 3.3.1. Assumption of the pure product layer (H1)

517 By fitting the model to experimental data, we found a residual thickness layer in the pharynx of
518 $14.6 \pm 3.4 \mu\text{m}$ for G0, and of $2.9 \pm 1.1 \mu\text{m}$, $2.5 \pm 1 \mu\text{m}$, and $0.8 \pm 0.2 \mu\text{m}$ for G40, G60 and G70,
519 respectively. In their work, Wright, Hills, Hollowood, Linforth & Taylor (2003) found a thickness of
520 film saliva (which is equivalent to our post-deglutitive residue) of $55 \mu\text{m}$ for flavored aqueous

521 solutions with only 2% of sucrose (which is close to our reference G0). Their thickness value is almost
522 four times higher than ours. This difference could result from individual variability or the
523 determination method used.

524 We then observed that similarly to *in vivo* measurements (Fig. 3), simulations predicted that the
525 highest peak intensity was reached for G0 (results not shown). The second set of bars in Fig. 5 shows
526 that the model prediction for the first aroma release peak for the aqueous solution is five times higher
527 than for the glucose syrup solutions. These differences are due to the differences that we found in the
528 mass transfer coefficients for the solutions studied. However, the *in vivo* data (first set of bars) do not
529 reveal such a large gap between the aqueous and the glucose syrup solutions (which reaches between
530 58% and 83% of G0's I_{max} , depending on the solution and the panelist). These discrepancies between
531 experimental observations and model predictions led us to consider that the product properties
532 considered in the model (mass transfer and air/product partition coefficients) might be misevaluated
533 due to saliva dilution.

534

535 3.3.2. Assumption of the product dilution by saliva (H2)

536 Under the saliva dilution hypothesis, the aroma release profile of any glucose syrup solution predicted
537 by the model is expected to be closer to the reference solution (G0), as observed *in vivo*, because the
538 physico-chemical properties of the newly formed mixtures would be closer to the properties of water.

539 It is difficult to check this assumption *in situ* and, more specifically, to determine the quantity of saliva
540 present in the pharyngeal junction, as well as the amount of product left in the pharynx after
541 swallowing. Therefore, in order to validate this assumption, additional simulations were performed
542 and compared to *in vivo* data. Since the sensitivity analysis of the model showed that the residual
543 thickness layer does not have an impact on the first peak intensity of aroma release, we fixed this
544 parameter to the averaged value found for G0, i.e., 14.6 μm . After several tests, a common dilution
545 factor was determined for all solutions such that the model predictions fit the *in vivo* release data.
546 Physico-chemical parameters for dilutions not present in Table 2 were interpolated with the formulas
547 indicated below Table 2.

548 The dilution factor was selected to keep the ratio “Intensity of the first peak for the investigated
549 solution”/“Intensity of the first peak for G0” as close as possible to *in vivo* experimental observations.
550 Results presented in Fig. 5 (first versus last series of bars in the chart) showed that it was possible to
551 find a common dilution factor that reproduces the intensity ratios observed *in vivo*.
552 Results indicated that all glucose syrup solutions were highly diluted in the pharynx (by a factor of
553 10).
554 We validated the saliva dilution assumption with an additional aroma compound, ethyl hexanoate.
555 This molecule was chosen for its hydrophobicity, in contrast to diacetyl. Similarly to diacetyl, the
556 absence of retention by mucosa was checked. Since the two molecules were investigated together, we
557 performed simulations with the same residual thickness layer and with the same dilution factor that
558 was previously determined with diacetyl. Due to the introduction of the dilution factor, the physico-
559 chemical parameters of ethyl hexanoate in the glucose syrup solutions, G0, G5, G10 and G20, were
560 measured. On the basis of the results presented in Table 5, we can observe that the air/product
561 partition coefficient values for the three glucose syrup solutions are all higher than G0, but very close
562 to each other. For the mass transfer coefficient, we observe an opposite trend: the three glucose syrup
563 solutions values are lower than G0, but also close to each other. Similarly to the diacetyl,
564 interpolations of the experimental points were necessary to perform the simulations. For both the
565 air/product partition and mass transfer coefficients, we decided to use a linear regression between G0
566 and G5, and to calculate an averaged value between G5 and G20.
567 Comparison of the ratios “Intensity of the first peak for the investigated solution”/“Intensity of the first
568 peak for G0” between *in vivo* experiments and model predictions for ethyl hexanoate are presented in
569 Fig. 6. They show that the model provides a satisfactory prediction for all solutions under the saliva
570 dilution assumption, given the wide range of experimental variability (standard deviation bars on Fig.
571 6).
572
573 These results lead to the conclusion that the viscosity of the initial product has a limited effect on
574 aroma release for products with Newtonian properties within the wide range of viscosities studied, and
575 confirm the results of Hollowood et al. (2002). The combined modeling and experimental approach

576 conducted in this work suggests a possible explanation for this limited effect: viscous solutions are
577 highly diluted by saliva during the swallowing step and the relevant properties are those of relatively
578 similar product-saliva mixtures.

579

580

581 3.4. Conclusions

582 This work aimed at studying the influence of food viscosity on flavor release during ingestion of a
583 liquid food. The originality of this study was the combination of experimental and modeling
584 approaches that allowed us to gain insights into the aroma compound release mechanisms, based on
585 the example of the diacetyl release from glucose syrup solutions. When considering the consumption
586 of a liquid product, it can be assumed that the saliva dilution is relatively low due to the short
587 residence time in the mouth. Therefore, the hypothesis that a pure product layer was deposited on the
588 pharynx walls after ingestion of a liquid food was stated at first. This assumption was invalidated by
589 the comparison of model predictions to *in vivo* measurements. This result led us to consider the
590 dilution of the product during swallowing. This new hypothesis, stating that the film coating the
591 pharyngeal walls was a mixture of saliva and product, provided predictions compatible with
592 experimental observations for the aroma compound investigated (diacetyl). Simulations showed that
593 the dilution factors by saliva determined were quite similar, regardless of the initial dry matter of the
594 solution: approximately 10% of the initial solution was kept in the final diluted mixture. With these
595 dilution factors, we tentatively extended the model to a highly hydrophobic molecule (ethyl
596 hexanoate) with satisfactory results.

597 The formulated hypothesis has to be further confirmed based on the study of the release of other
598 aroma compounds with different physico-chemical characteristics. In parallel, work is in progress on
599 the pharynx mucosa coating to increase the understanding of these phenomena based on a mechanical
600 approach. Combining mechanical and mass transfer studies should help us to gain new insights into
601 the complex phenomena of *in vivo* aroma compound release.

602

603

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607

608

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- 719
- 720
- 721
- 722

723 **Figure legends**

724

725 Figure 1. A. Schematic representation of the nasal cavity, pharynx and oral cavity as interconnected
726 reactors. B. Chronological steps of the consumption of a semi-liquid food.

727

728 Figure 2. Example of data processing for *in vivo* aroma release experiments (solution G0, with
729 16.5mg/L of diacetyl). Dotted line: diacetyl intensity signal recorded by PTR-MS. For clarity, only
730 one single replicate is shown. Solid line: peak curve of the shown replicate. Bold line: mean of the
731 three peak curves for the three replicates of the experiment. Gray area: envelope of the peak curves for
732 the three replicates.

733

734 Figure 3. Example of *in vivo* diacetyl release for the four Newtonian solutions (panelist 1).
735 Representation of the mean peak curves.

736

737 Figure 4. Example of *in vivo* diacetyl release during two consumption protocols. Solid line: ingestion
738 of aromatized solution; dotted line: aspiration of aromatized air.

739

740 Figure 5. “Imax of a solution/Imax of G0” ratios for diacetyl: comparison of experimental data with
741 the model simulations under the “pure product layer (H1)” and the “saliva dilution (H2)” assumptions.

742

743 Figure 6. “Imax of a solution/Imax of G0” ratios for ethyl hexanoate: comparison of experimental data
744 with the model simulations under the “saliva dilution (H2)” assumption.

745

746

747 **Tables**

748

749 Table 1. Characteristics of the analyzed glucose syrup solutions.

750

| Solutions | Dry Matter (g/100g) | Viscosity at 35°C (mPa s) |
|------------------|----------------------------|----------------------------------|
| G0 | 0.00 | 0.7 |
| G5 | 5.13±0.19 | 0.8 |
| G10 | 8.99±0.30 | 1.1 |
| G20 | 20.19±0.73 | 1.5 |
| G40 | 45.94±1.70 | 7.6 |
| G60 | 61.11±1.19 | 25.0 |
| G70 | 75.68±2.65 | 405.0 |

751

752

753

754 Table 2. Diacetyl air/product partition coefficient (K_{ap}) and mass transfer coefficient (k_p) as a function
 755 of the dry matter content for Newtonian glucose syrup solutions at 35°C.

756

| Solutions | K_{ap} (g/g) [†] | k_p (m/s) [‡] |
|------------|-----------------------------|--------------------------|
| | $\times 10^{-4}$ | $\times 10^{-7}$ |
| G0 | 12.84±3.11 | 11.03±3.9 |
| G5 | 5.72±2.21 | 4.26±2.18 |
| G10 | 6.78±3.27 | 4.50±2.85 |
| G20 | 4.59±3.97 | 2.50±2.48 |
| G40 | 7.88±4.37 | 1.94±1.34 |
| G60 | 11.69±4.28 | 1.24±0.48 |
| G70 | 25.12±4.97 | 0.33±0.07 |

757

758 †For G10, G20, G60, 3 replicates were performed. For G0, G5, G30, G40 and G70, 6 replicates were
 759 performed

760 ‡Between 3 and 9 replicates were performed for each solution

761 For Diacetyl air/product partition coefficient (K_{ap}), the following second-degree polynomial regression
 762 curve fits the data ($R^2 = 0.94$) and was used for interpolation:

$$763 \quad K_{ap} = 8.69 \times 10^{-7} \times C_g^2 - 5.036 \times 10^{-5} \times C_g + 10.55 \times 10^{-4}$$

764 where C_g is the total carbohydrate concentration in g/100g.

765 For Diacetyl mass transfer coefficient (k_p), the following non-linear regression (exponential type) fits
 766 the data ($R^2 = 0.88$) and was used for interpolation:

$$767 \quad \log(k_p) = -6.1549 - 0.0367 \times C_g$$

768 where C_g is the total carbohydrate concentration in g/100g.

769 Error bars on the mass transfer coefficient take into account the uncertainties of the air/solution
 770 partition coefficients.

772 Table 3. Physiological parameter values

773

| | Unit | Mean value/range of variation [†] | Data source | Reference | Value from the literature |
|--------------------------------------------------|----------------------|--------------------------------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| Oral cavity Volume | cm ³ | 30-45 | Rhinopharyngometry | (Xue & Hao, 2006) | 32.95±6.10 |
| Nasal cavity volume | cm ³ | 4-14 | Rhinopharyngometry | (Cankurtaran, Celik, Coskun, Hizal & Cakmak, 2007) | 9.11±0.71 [‡] |
| Pharynx volume | cm ³ | 20-45 | Rhinopharyngometry | (Xue & Hao, 2006) | 29.65±6.10 |
| Residual product thickness in the pharynx | µm | 0.8-14.6 | Degree of freedom of the model (case of the pure product layer hypothesis) | (Wright & Hills, 2003) | 55x10 ⁻³ |
| Salivary flow rate | cm ³ /s | 3x10 ⁻² -4.7x10 ⁻² | Standard protocol (parafilm stimulation) | (Engelen, de Wijk, Prinz, van der Bilt & Bosman, 2003) (Dawes, 2008) | Less than 3.3x10 ⁻² cm ³ /s; 1.5x10 ⁻² -2.2 x10 ⁻² cm ³ /s (parafilm stimulation) |
| In-mouth saliva volume | cm ³ | 1.1 | Literature | (Dawes, 2008) | 1.1/0.8 (before/after swallowing) |
| In-mouth air/product contact area | cm ² | 81-120 | Calculated (Appendix A) | (Collins & Dawes, 1987) | 214.7±12.9 |
| Pharynx air/product contact area | cm ² | 54-81 | Calculated (Appendix A) | (Normand, Avison & Parker, 2004) | 33 |
| Tidal volume | cm ³ | 470-1460 | Spirometry | (Palsson, Hubbell & Plonsey, 2003) (Elert, 2009) (Tortora & Anagnostakos, 1990) | 390-500 |
| Respiratory frequency | Number of cycles/min | 11.5-19.5 | Ion 59 signal (PTR-MS) | (Sherwood, 2006) (Marieb & Hoehn 2008) | 12-20 |

774

775

[†] Values of parameters measured for panelists

[‡] sum of the volumes of the nasal valve, the lower and the middle turbinate

776

777 Table 4. Statistical analysis of *in vivo* diacetyl release curves

778

| Solutions | I_{NAmax}/C_{OPini} (10^5 cps/ppb) |
|------------------|---------------------------------------------------------------------|
| G0 | 1.53 A |
| G40 | 1.24 AB |
| G60 | 0.99 B |
| G70 | 0.85 B |

779

780 Each letter corresponds to a classification group performed with Bonferroni method (significance

781 level=0.05).

782

783

784 Table 5. Physicochemical characteristics of glucose syrup solutions aromatized with ethyl hexanoate

785

| Solutions | Air/product partition | Mass transfer |
|------------|-----------------------|-------------------|
| | coefficient (g/g) | coefficient (m/s) |
| | $\times 10^{-1}$ | $\times 10^{-6}$ |
| G0 | 0.82±0.17 | 8.74±1.63 |
| G5 | 1.30±0.51 | 5.46±1.84 |
| G10 | 1.22±0.30 | 4.27±0.75 |
| G20 | 1.33±0.56 | 5.29±2.07 |

786

787

788

789 **APPENDIX A**

790 Calculation of the area of the mouth and the pharynx

791 The rhinopharyngometer is an acoustic device that gives a series of cross-section areas of the upper
792 respiratory tract, at various depths, starting from the panelist's front teeth.

793 The value of interest here is the lateral area of the respiratory tract. It was calculated by assuming that
794 cross-sections are ellipses with a known eccentricity. The eccentricity was graphically estimated from
795 a study of the measurements of airway dimensions of the human oral passage done by Cheng, Cheng,
796 Yeh & Swift (1997).

797

$$798 \quad \text{Area} = \sum \text{Perimeter}(h)\Delta h \quad (\text{A.1})$$

799 where dh is the distance between two successive measurements of cross-sectional areas with the
800 rhinopharyngometer (0.43 cm).

801 and:

$$802 \quad \text{Perimeter}(h) = \pi \times [3 \times (a + b) - \sqrt{(3a + b) \times (a + 3b)}] \quad (\text{A.2})$$

$$803 \quad S = \pi \times a \times b \quad (\text{A.3})$$

804 where S is the cross-sectional area measured at a given distance, a the major radius and b the minor
805 radius.

806 Given $k = \frac{a}{b}$ as the ratio between the two radii, we obtain:

$$807 \quad a = \sqrt{\frac{S \times k}{\pi}} \quad (\text{A.4})$$

808 where $k = 7.4$ for the mouth, 1.25 for the oropharynx and 1 for the hypopharynx.

809 The total area of a compartment is therefore the sum of all intermediate areas that have been calculated
810 within the limit of the compartment considered.

811

812

813 **APPENDIX B**814 **Model for the determination of the Mass Transfer Coefficient**

815 In the Volatile Air Stripping Kinetic (VASK) method (Lauverjat, de Loubens, Deleris, Trelea &
 816 Souchon, 2009), the product containing the volatile compound is equilibrated with the headspace air in
 817 a closed flask. At time $t=0$, the headspace is stripped with a constant airflow, and the volatile
 818 compound concentration in the outlet air is continuously measured by PTR-MS.

819 The volatile concentrations in the product and in the headspace are given by:

$$820 \quad V_p \times \frac{dC_p}{dt} = -A \times k_p \times \left(C_p - \frac{C_a}{K_{ap}} \right) \quad (\text{B.1})$$

$$821 \quad V_a \times \frac{dC_a}{dt} = A \times k_p \times \left(C_p - \frac{C_a}{K_{ap}} \right) - C_a \times Q \quad (\text{B.2})$$

822 where:

823 V_p and V_a are the volume of the liquid product and of the air, respectively.

824 A is the contact area between the air and the product.

825 Q is the air flow rate stripping the headspace.

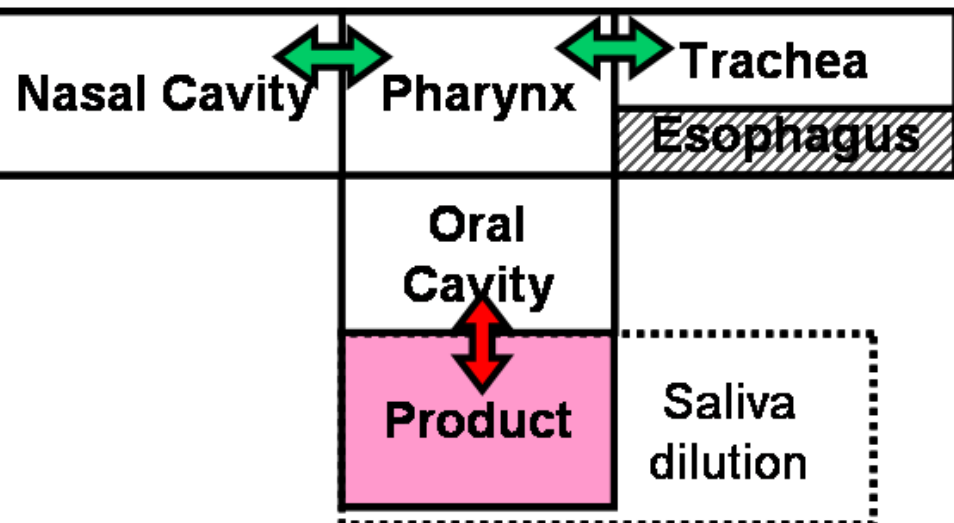
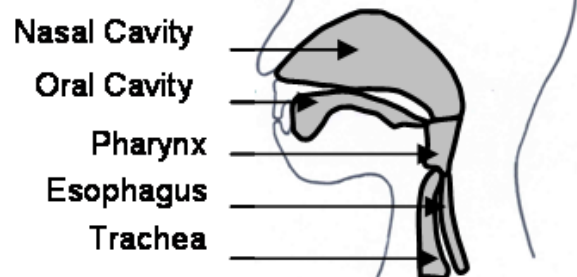
826 C_p and C_a are the concentration of aroma in the product and in the air, respectively.

827 The mass transfer coefficient (k_p) is determined by fitting the air concentration predicted by
 828 the model to the PTR-MS measurements.

829

830

A



B

Step 1

Step 2

Step 3



Contraction

Relaxation

Product residence in
mouth t_0 t_{deg-} t_{deg} t_{deg+}

