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Citation	Serment-Moreno, V., Barbosa-Cánovas, G., Torres, J. A., & Welti-Chanes, J. (2014). High-pressure Processing: Kinetic Models for Microbial and Enzyme Inactivation. Food Engineering Reviews. doi:10.1007/s12393-014-9075-x
DOI	10.1007/s12393-014-9075-x
Publisher	Springer
Version	Accepted Manuscript
Terms of Use	http://cdss.library.oregonstate.edu/sa-termsofuse

High Pressure Processing: Kinetic Models for Microbial and Enzyme Inactivation

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Abstract: High pressure processing (HPP) has become the most widely accepted nonthermal food preservation technology. The pressure range for commercial processes is typically around 100-600 MPa, whereas moderate temperature (up to 65°C) may be used to increase microbial and enzymatic inactivation levels. However, these industrial processing conditions are insufficient to achieve sterilization since much higher pressure levels (>1000 MPa) would be required to inactivate bacterial endospores and enzymes of importance in food preservation. The next generation of commercial pressure processing units will operate at about 90-120°C and 600-800 MPa for treatments defined as Pressure Assisted Thermal Processing (PATP), or Pressure Assisted Thermal Sterilization (PATS) if the commercial food sterilization level required is achieved. Most published HPP kinetic studies have focused only on pressure effects on the microbial load and enzyme activity in foods and model systems. Published work on primary and secondary models to predict simultaneously the effect of pressure and temperature on microbial and enzymatic inactivation kinetics is still incomplete. Moreover, few references provide a detailed and complete analysis of theoretical, empirical, and semi-empirical basis for the kinetic models proposed to predict the level of microbial and enzyme inactivation achieved. This review organizes these published kinetic models according to the approach used, and then presents an in-depth and critical revision to define the modeling research needed to provide commercial users with the computational tools needed to develop and optimize pasteurization and sterilization pressure treatments.

KEYWORDS: High Pressure Processing, Pressure Assisted Thermal Processing, Primary and Secondary Models, Kinetics, Enzyme Inactivation, Microbial Inactivation

60 NOMENCLATURE

A	Enzyme activity; units mg^{-1}, units ml^{-1}
A_f	Accuracy factor
a	Linear temperature dependence of the activation volume under isobaric conditions, Eyring-Arrhenius secondary model; $cm^3\ mol^{-1}\ K^{-1}$
a_w	Water activity
A_0	Enzyme activity prior to thermal or pressure treatments; units mg^{-1}, units ml^{-1}
A_∞	Residual enzyme activity after long thermal or pressure treatments; units mg^{-1}, units ml^{-1}
b	Slope parameter, Weibull kinetic model; min^{-n}
b'	Slope parameter, Weibull kinetic model; min^{-1}
$c_{i;\ i=1,2,..n}$	Empirical kinetic model coefficients
C	Concentration, microbial population or enzyme activity
C_P	Specific heat capacity under isobaric conditions; $J\ mol^{-1}\ K^{-1}$
C_0	Initial concentration, microbial population or enzyme activity prior to thermal or pressure treatments
C_∞	Final concentration, microbial population or enzyme activity after long thermal or pressure treatments
D_T	Decimal reduction time describing the lethal thermal effect assuming first order kinetics; s, min
D_P	Decimal reduction time describing the lethal pressure effect assuming first order kinetics; s, min
D_{Pref}	Decimal reduction time describing the lethal pressure effect at a reference pressure and assuming first order kinetics; s, min
E_a	Arrhenius activation energy describing the temperature dependence of a process kinetics; $J\ mol^{-1}\ K^{-1}$
E_{aP}	Arrhenius activation energy at a reference pressure; $J\ mol^{-1}\ K^{-1}$
$F(t)$	System failure time predicted with the Weibull distribution function; s, min
f_P	Slope parameter when pressure is the independent Weibull kinetic model variable; MPa^{-n}
f_T	Slope parameter when temperature is the independent Weibull kinetic model variable; MPa^{-n}
g	Activation energy exponential pressure dependence under isothermal conditions, Eyring-Arrhenius secondary model; MPa^{-1}
G	Gibbs free energy; $J\ mol^{-1}$
ΔG	Gibbs free energy change; $J\ mol^{-1}$
ΔG_{ref}	Gibbs free energy change at reference pressure and temperature conditions; $J\ mol^{-1}$
h	Planck constant; 6.6260×10^{-34} J·s
H	Difference between the upper and lower asymptote, log-logistic kinetic model
HPP	High Pressure Processing

k	Reaction rate constant; min^{-1}
k_B	Boltzmann constant; $1.3806x10^{-23}$ J K^{-1}
k_{refP}	Reaction rate constant at a reference pressure; min^{-1}
k_{refT}	Reaction rate constant at a reference temperature; min^{-1}
$k^{\neq}$	Activated complex reaction rate constant; min^{-1}
K	Equilibrium constant for a reaction
$K^{\neq}$	Pseudo-equilibrium constant for a reactant to activated complex formation
L	Lethality; cfu s^{-1}, cfu min^{-1}
m	Exponent, Weibull log-logistic secondary model
n	Exponent, Weibull kinetic model
N	Microbial population; cfu g^{-1}, cfu ml^{-1}
N_0	Microbial population prior to thermal or pressure treatments; cfu g^{-1}, cfu ml^{-1}
N_∞	Microbial population surviving long thermal or high pressure treatments; cfu g^{-1}, cfu ml^{-1}
p	Scale parameter, Weibull distribution function
P	Pressure; MPa
P_c	Critical pressure parameter, Weibull log-logistic secondary model; MPa
P_{c0}	Critical pressure parameter at a reference temperature, Weibull exponential secondary model; MPa
P_{ref}	Reference pressure; MPa
$PATP$	Pressure assisted thermal processing
$PATS$	Pressure assisted thermal sterilization
q	Shape parameter, Weibull distribution function
r	Chemical reaction rate
R	Ideal gas constant; 8.314 J mol^{-1} K^{-1}, 8.30865 cm^3 MPa mol^{-1} K^{-1}
R^2	Regression coefficient
ΔS	Entropy change, thermodynamic model; J mol^{-1} K^{-1}
ΔS_{ref}	Entropy change at a reference temperature, thermodynamic model; J mol^{-1} K^{-1}
t	Time; s, min
T	Temperature; K
T_c	Critical temperature parameter, Weibull log-logistic secondary model; K
T_{c0}	Critical temperature parameter at a reference temperature, Weibull exponential secondary model; K
T_{ref}	Reference temperature; K
$\overline{V}_P$	Partial molar volume of products in a chemical reaction; cm^3 mol^{-1}

$\overline{V}_R$	Partial molar volume of reactants in a chemical reaction; $cm^3\ mol^{-1}$
$\overline{V}^{\neq}$	Partial molar volume of the active complex, transitional state theory; $cm^3\ mol^{-1}$
$\overline{V}_T^{\neq}$	Partial molar volume of the active complex at a reference temperature, transitional state theory; $cm^3\ mol^{-1}$
$\Delta\overline{V}_{reaction}$	Molar volume change of a chemical reaction; $cm^3\ mol^{-1}$
$\Delta\tilde{V}^{\neq}$	Molar volume change to reach the active complex, transitional state theory
w_P	Exponential pressure dependence of parameter *b'*, Weibull secondary model; MPa^{-1}
w_T	Exponential temperature dependence of parameter *b'*, Weibull secondary model; K^{-1}
z_P	Pressure resistant parameter under isothermal conditions, Bigelow model; MPa
z_T	Thermal resistant parameter under isobaric conditions, Bigelow model; K

GREEK SYMBOLS

α	Thermal expansivity coefficient, thermodynamic model; $cm^3\ mol^{-1}\ K^{-1}$; upper asymptote, log-logistic kinetic model
$\Delta\alpha$	Thermal expansivity coefficient change under non –isothermal and –isobaric conditions; $cm^3\ mol^{-1}\ K^{-1}$
β	Compressibility factor, thermodynamic model; $cm^6\ J^{-1}\ mol^{-1}$; lower asymptote, log-logistic kinetics model
$\Delta\beta$	Compressibility factor change under non –isothermal and –isobaric conditions, thermodynamic model; $cm^6\ J^{-1}\ mol^{-1}$
Ψ	Log fraction parameter, Weibull biphasic kinetic model
Ω	Maximum inactivation rate, log-logistic kinetic model; cfu s^{-1}, cfu min^{-1}
τ	Log time at which the maximum inactivation rate starts, log-logistic kinetic model; min
λ	Time interval in which no high pressure processing inactivation occurs , secondary quasi chemical kinetic model; min
$\upsilon^{\neq}$	Frequency at which the activated complex transforms into products, energy distribution described by the Planck equation; s^{-1}

Introduction

Food safety and high pressure processing (HPP)

High pressure processing (HPP) has successfully evolved into one of the most recurrent alternatives for thermal food processing. In the last 20 years, the number of HPP installations in the world, and processing a wide variety of foods, grew from one in 1990 to nearly 200 units with a concurrent tenfold increase in size from 25-50 L to 300-500 L (Bermúdez-Aguirre and Barbosa-Cánovas, 2011; Mújica-Paz et al., 2011). In addition, the operating pressure level increased from about 400 MPa to about 600-800 MPa reducing pressure holding times from 15-30 minutes to a few minutes. The rapidly growing number of installed units with shorter processing time and larger vessel volume has dramatically increased the installed pressure processing capacity. The high consumer acceptance of HPP-treatments reflects, in most cases, a minimal alteration of the original nutritional and sensory food characteristics while effectively inactivating pathogens, spoilage microorganisms and enzymes (Welti-Chanes et al., 2002; Barbosa-Cánovas and Juliano, 2008; López-Gómez et al., 2009; Cruz et al., 2011).

Microbial Inactivation

Microorganisms are affected by several simultaneous lethal effects with cellular membrane damage frequently reported as a dominant factor (Mañas and Pagán, 2005; Patterson, 2005; Velazquez et al., 2005; Patterson and Linton, 2009). Acyl chains of the phospholipid bilayer may experience crystallization, leading to bud formation, membrane rupture and intracellular material leakage (Mañas and Pagán, 2005; Patterson, 2005). Low-pressure treatment levels ranging from 20-180 MPa result usually in sub-lethal cellular damage. Microbial inactivation of a large variety of pathogenic and spoilage bacteria vegetative forms is achieved above 200-400 MPa, when irreversible protein/enzyme denaturation and intracellular content leakage occurs (Lado and Yousef, 2002; Mújica-Paz et al., 2011). On the other hand, HPP alone cannot inactivate bacterial spores as they can withstand pressures over 1000 MPa when temperature after compression is below 70-80°C (Mañas and Pagán, 2005; Torres and Velazquez, 2005; Patterson and Linton, 2009; Mújica-Paz et al., 2011; Reineke et al., 2011).

Enzyme inactivation

Protein denaturation effects vary depending on the protein structure and external factors such as pressure level, temperature, pH and solvent composition (Palou et al., 2007; Yaldagard et al., 2008). Irreversible changes may include dissociation of oligomeric proteins into their subunits, conformational changes of the substrate/active site, and aggregation or gelation of proteins due to a decrease in the solution volume or the association of hydrophobic molecules (Heremans, 1982; Palou et al., 2007; Yaldagard et al., 2008). Reversible protein modifications are typically observed in the 100-300 MPa range (Welti-Chanes et al., 2006) but enzyme activity may also be enhanced within this range (Palou et al., 2007; Yaldagard et al., 2008; Eisenmenger and Reyes-De-Corcuera, 2009). Some enzymes can display high baroresistance, and pressures over 500 MPa combined with moderate temperatures are required to induce significant inactivation.

Current status of high pressure processing

Commercial HPP units operate typically within a 100-600 MPa range and temperatures between 5-65°C (Balasubramaniam et al., 2008; Bermúdez-Aguirre and Barbosa-Cánovas, 2011; Mújica-Paz et al., 2011). Since these mild conditions are insufficient to achieve bacterial spore inactivation, units operating at higher pressure (600-800 MPa) and elevated temperature (90-120°C) will be necessary (Ramirez et al., 2009; Valdez-Fragoso et al., 2011). This novel procedure, known as Pressure Assisted Thermal Processing (PATP) or Pressure Assisted Thermal Sterilization (PATS) if bacterial spore inactivation attaining commercial food sterility is achieved, is under development. However, at PATP temperature and pressure conditions significant chemical changes cannot be ignored due to their potential for the breaking of covalent bonds (Torres et al., 2009; Valdez-Fragoso et al., 2011). Approval has been granted by the U.S. Food and Drug Administration for the commercial production of low-acid foods using PATS. Mashed potatoes inoculated with *Clostridium botulinum* spores were subjected to a shelf-life study under the severe conditions used when testing food supplies for the United States Army. No microbial growth was observed during storage and the sensory quality observed was superior to those possible with a conventional thermal process (NCFST, 2009).

Unlike other physical and chemical factors, pressure is delivered uniformly throughout the vessel almost immediately after being applied (Rauh et al., 2009). As a result of this compression, the food temperature increases depending on factors such as food composition, pressure level, initial food and pressurizing media temperature, pressurization media used, vessel loading factor, and equipment design. The rise in temperature per 100 MPa due to adiabatic compression heating has been reported to be ≈3°C for water and ≈8-9°C for fat and oils, while proteins and carbohydrates show intermediate values (Patazca et al., 2007; Balasubramaniam et al., 2008; Otero et al., 2010). The prediction of the temperature rise remains an area of active research.

In spite of the PATP/PATS process already approved by the FDA and suggesting the upcoming commercialization of this technology, extensive databases of predictive models, kinetic parameters, and standardized procedures similar to those developed for conventional technologies such as thermal processing are not yet available. At present, most of the kinetics information on high pressure processing of foods is disperse and obtained using relatively narrow ranges for the experimental pressure-temperature conditions tested. Even though the scientific data obtained may be sufficient for the development of a food product, it is certainly limited to evaluate the inactivation kinetics models proposed. Analysis of the fit to experimental data is frequently limited to comparing a few models. This review shows that many food scientists are still relying on linear inactivation kinetics, even though concave and sigmoidal trends are frequently observed in pressure treatments. Additionally, most of the reported HPP investigations on inactivation kinetics have focused on pressure effects, and often do not take into account the contribution of the temperature changes due to compression of the food and pressurizing fluid, and the heat exchanges involving the product and pressurization media, the vessel walls, and the equipment surroundings. When accurate temperature profiles of HPP are available, inactivation kinetics models should be paired with transport phenomena equations predicting the pressure-temperature profiles under PATP/PATS conditions when analyzing chemical reactions and the inactivation of microorganisms and enzymes in foods. Therefore, the following sections review chemical and biochemical models to

provide a concise, analytical reference for high pressure food processing kinetic models with theoretical, empirical and semi-empirical backgrounds.

Primary models

Primary modeling consists of developing mathematical expressions based on theoretical principles, empirical observations, or the combination of both, to predict changes in microbial counts, enzyme activity, or chemical concentrations as a function of the processing time. According to the shape of the kinetic behavior predicted, primary models are classified as linear, concave or sigmoidal.

Linear primary models

First order kinetics model

First order kinetics continues to be the most often model to describe microbial and enzyme inactivation, although poor estimates can be expected since non-linear trends are often observed experimentally (Peleg, 2006; Wilson et al., 2008; Corradini et al., 2009; Pilavtepe-Çelik et al., 2009). It assumes that the change in chemical changes, microbial population or enzyme activity is directly proportional to their concentration denoted as C in Eq. 1 and described by an inactivation rate constant under constant isobaric and isothermal conditions (k [=] min^{-1}).

$$-\frac{dC}{dt} = k \cdot C \tag{1}$$

By integrating from $t = 0$ through treatment time t and from C ($t = 0$) = C_0 through $C(t) = C$ the resultant model (Eq. 2) establishes that the Napierian logarithm of C/C_0 will result in a decreasing straight line that goes through the origin.

$$\ln\frac{C}{C_0} = -k \cdot t \tag{2}$$

Microbiologists frequently transform the Napierian logarithm base of Eq. 2 to decimal logarithms and report the number of decimal reductions in the microbial population (Eq. 3).

$$\log_{10}\frac{N}{N_0} = -\frac{k}{2.303}\cdot t \quad (3)$$

188

189 Therefore, a decimal reduction time (D_T) can be defined as the time required at a
190 constant lethal temperature T for a tenfold reduction in the microbial load
191 ($\log_{10} N/N_0 = \log 0.1N_0/N_0 = -1$) (Morales-Blancas and Torres, 2003a; Toledo,
192 2007). A similar parameter (D_P) can be defined for the effect of the lethal pressure
193 P (Parish, 1998; Basak et al., 2001). D_P can be calculated as the negative inverse
194 of the $\log_{10}$ linear model slope (Eq. 4).

$$\log_{10}\frac{N}{N_0} = -\frac{1}{D_P}\cdot t \quad (4)$$

195

196 The parameter D_P varies (0.01-4 min) depending on the pressure level, the
197 microorganism, and the interaction of intrinsic food product factors with the
198 microorganism (Table 1). For example, *Listeria monocytogenes* has a high
199 pressure resistance in milk (D_P = 2.43-10.99 min) and a much lower in acid media
200 such as orange juice (D_P = 0.87-2.87 min). Bacterial spores can show great
201 pressure resistance, but may be readily inactivated (D_P = 0.1-0.6 min) with a
202 combination of temperatures above 100°C and pressures over 400 MPa (Table 1).
203
204 INSERT TABLE 1
205

206 ***Fractional conversion and multiphasic models***

207 The fractional conversion model, a variation of the first order kinetics model, is
208 obtained by assuming that the thermal or pressure treatment leaves a residual
209 enzyme activity or microbial load with much higher inactivation resistance. Thus,
210 Eq. 1 is integrated from its initial conditions ($C_0 = N_0 = A_0$; at $t = 0$) to its final
211 conditions where the remaining microbial population or enzyme activity after a
212 prolonged treatment time is C_∞ ($t = \infty$), yielding the fraction conversion model
213 (Eq. 5) (Van den Broeck et al., 2000; Fachin et al., 2002; Ly-Nguyen et al., 2003;
214 Polydera et al., 2004).

$$C = C_\infty + (C_0 - C_\infty)\cdot\exp(-k\cdot t) \quad (5)$$

215

A similar approach was followed to develop the multiphasic model, for which populations with different resistance towards the pasteurization or sterilization treatment are represented by the presence of two or more isoenzymes or microbial subpopulations (Chen and Wu, 1998; Fachin et al., 2002; Peleg, 2006). The simplest form of the multiphasic model considers the presence of a labile fraction (C_L) that is inactivated more rapidly and a stable fraction (C_S) able to withstand longer treatment times. Each fraction is inactivated at a distinct rate and the concentration (C) observed represents the sum of C_L and C_S at any given time. By separating Eq. 1 into the labile and stable fractions, and by solving the integral, this form of the multiphasic model can be described by Eq. 6.

$$C = C_L \cdot \exp(-k_L \cdot t) + C_S \exp(-k_S \cdot t) \quad (6)$$

Campanella and Peleg (2001) reported major drawbacks of biphasic models. First and probably most importantly, changes in the kinetic rate constant may occur as a result of alterations in the food matrix rather than caused by populations with different pressure and/or temperature resistance. These authors questioned also the lack of generality of the model and considered it to be too specific. Peleg (2006) suggested that if enzymatic and microbial subpopulations differing in inactivation resistance do exist, they should be isolated to perform independent inactivation kinetics to validate the multiphasic model.

Concave primary models

Weibull model

Many models have been developed as alternatives to linear inactivation kinetics (van Boekel, 2008). Both mechanistic and empirical equations have led to an adequate fit to experimental data, but often they are too specific and/or complex (Mafart et al., 2002). Several authors have considered the approach of treating inactivation as the distribution of the survival microbial population/enzyme activity associated to diverse factors such as differences in the treatment intensity or due to an heterogeneous resistance (Mafart et al., 2002; van Boekel, 2002; Peleg, 2006).The Weibull distribution (Eq. 7) is used in engineering science to predict the time of failure F (t) of an electronic or mechanical system (van Boekel, 2002). Thus, the residual microbial/enzyme activity curve can be interpreted as a

cumulative function of the distribution that dictates the treatment time at which the microorganism or enzyme will fail to resist and result in inactivation.

$$F(t) = \exp\left[-\left(\frac{t}{p}\right)^{q}\right] \tag{7}$$

This function, first introduced by Peleg and Cole (1998) to model microbial survival curves, has been used to describe numerous inactivation kinetics because it is simple (only 2 parameters), flexible and theoretically sound (Peleg, 2006; Ahn et al., 2007; Buzrul et al., 2008; Corradini et al., 2009; López-Gómez et al., 2009; Pilavtepe-Çelik et al., 2009; Bermúdez-Aguirre and Barbosa-Cánovas, 2011; Carreño et al., 2011). For inactivation kinetics studies, Eq. 7 is frequently transformed to a $\log_{10}$ base of the survival fraction S (t) as in Eq. 8 (Peleg, 2006) or Eq. 9 (Corradini et al., 2005):

$$\log_{10}\frac{N}{N_0} = \log_{10} S(t) = -\frac{1}{2.303}\cdot\left(\frac{t}{b}\right)^{n} \tag{8}$$

$$\log_{10} S(t) = -b'\cdot t^{n} \tag{9}$$

The parameter n determines the shape of the survival curve (Fig. 1a), where $n < 1$ denotes upward concavity and $n > 1$ represents a downward concavity while $n = 1$ would be a *unique* case corresponding to linear or first order kinetics. Concavity can be used to interpret the population inactivation resistance: (a) homogenous ($n = 1$); (b) tailing or increasing resistance ($n < 1$); or, (c) decreasing resistance as a result of accumulated damage to the population ($n > 1$) (Peleg, 2006). Although these three resistance behaviors have been observed in modeling work, no microbial physiology studies have been conducted to confirm them experimentally. The parameter b determines the scale of the curve as observed in Fig. 1b (van Boekel, 2002), whereas the inverse of the rate coefficient b ($b' = 1 / 2.303\ b^{n}$) determines the slope steepness of the survival trend (Corradini et al., 2005). Thus Eq. 8 can be simplified and expressed as a function of b' (Eq. 9).

INSERT FIGURE 1

As shown in Eqs. 11-13, the inverse of the parameter *b'* to the -*n*th power is equivalent to the decimal reduction time (*D*) determined with the first order kinetics model (Buzrul et al., 2008):

$$\log_{10}\frac{0.1N_0}{N_0} = -1 = -b'\cdot t^n \tag{11}$$

$$1 = b'\cdot t^n \tag{12}$$

$$t = \left(\frac{1}{b'}\right)^n = D \tag{13}$$

Most studies report HPP survival curves with upward concavities yielding $n < 1$ and $b' < 1$ values for the Weibull model parameters with the latter increasing to values in the 1-3 range and a concurrent decrease in the *n* parameter for more severe pressure and/or temperature conditions (Table 2). This shows that the accumulated damage theory was fulfilled for most of the values reported in Table 2, since more severe HPP conditions sensitized the population and lowered the shape *n* parameter ($n < 1$), and higher inactivation rates were observed as the slope increased ($b' > 1$). Although this model has been often applied to predict microbial inactivation kinetics, no reports of its application to model the inactivation of enzymes, also known to display non-linear trends, were found. Finally, details on the pressure and temperature effects on the Weibull model parameter are discussed in the secondary model section.

INSERT TABLE 2

Peleg (2006) highlighted that nonlinear regression procedures for either ln $S(t)$ or $\log_{10} S(t)$ as a function of *t* can only estimate the real parameters of the Weibull distribution since deviations occur with the logarithmic transformation of Eq. 7. Furthermore, Mafart et al. (2002) claimed that *b'* and *n* are strongly correlated, consequently a poor estimation of either one will affect the other parameter.

Sigmoidal primary models

Weibull biphasic model

Guan et al. (2005) found that the single term Weibull model (Eq. 9) was not adequate to describe complex survival curves with more than one concavity change. Coroller et al. (2006) encountered this limitation when analyzing the acidic inactivation of *Listeria monocytogenes* and *Salmonella enterica*. They assumed that two bacterial subpopulations were present and thus the Weibull model was reparametrized as a function of the labile population fraction (*f*) as follows:

$$N(t) = N_0\left[f \cdot 10^{-\left(\frac{t}{b_1}\right)^{n_1}} + (1-f)\cdot 10^{-\left(\frac{t}{b_2}\right)^{n_2}} \right] \quad (13)$$

Since microbial data are frequently expressed using a decimal exponential base, the fraction (*f*) alone may not be useful. Coroller et al. (2006) transformed *f* to a decimal logarithmic base and introduced the parameter ψ in the Weibull multi population model (Eq. 14-15). An example of a survival curve for populations with different subpopulation resistance predicted with the Weibull biphasic model is shown in Fig. 2.

$$\psi = \log_{10}\left(\frac{f}{1-f}\right) \quad (14)$$

$$N(t) = \frac{N_0}{1+10^{\psi}}\left[10^{\left[\psi-\left(\frac{t}{b_1}\right)^{n_1}\right]} + 10^{-\left(\frac{t}{b_2}\right)^{n_2}} \right] \quad (15)$$

INSERT FIGURE 2

Coroller et al. (2006) simplified Eq. 15 by defining $n = n_1 = n_2$ after demonstrating statistically that the shape parameters of subpopulation 1 (n_1) and subpopulation 2 (n_2) did not differ significantly ($p_{value} < 0.05$). The model resulting from this simplification (Eq. 16) yielded a slightly more accurate fit while reducing the number of parameters for the nonlinear regression.

$$N(t) = \frac{N_0}{1+10^{\psi}}\left[10^{-\left[\psi-\left(\frac{t}{b_1'}\right)^n\right]} + 10^{-\left(\frac{t}{b_2'}\right)^n}\right] \quad (16)$$

324

325 ***Log-Logistic model***

326 Cole et al. (1993) developed a model to predict bacterial inactivation following
327 sigmoidal survival curves starting from the four parameter model shown in Eq.
328 17.

$$y = \alpha + \frac{\beta}{1+\exp(\lambda - \delta \cdot x)} \quad (17)$$

329

330 The authors attempted to confer a biological interpretation to the parameters of
331 Eq. 17 by applying the first and second derivative criterions (Eq. 18-19) to obtain
332 the maximum inactivation rate (Ω), and the time at which Ω occurs (τ).
333 Afterwards, Cole et al. (1993) defined the dependent variable as the microbial
334 population logarithm ($y = \log_{10} N$) and the independent variable as the logarithm
335 of time ($x = \log_{10} t$). Parameter ω was defined as the difference between the lower
336 and upper asymptotes ($\omega = \beta - \alpha$), and all three biological parameters (Ω, τ, ω)
337 where incorporated into Eq. 17 to obtain Eq. 20. Although the expression
338 $\log_{10}(N_{t=0})$ cannot be calculated since $\log_{10}(t = 0)$ is mathematically undefined,
339 the expression $\log_{10}(N/N_0)$ is more commonly used to describe microbial
340 inactivation kinetics than $\log_{10}(N)$. The authors gave no justification but assumed
341 that $t = 0.1$ min was a good approximation for $t = 0$ min to establish the
342 "vitalistic" log-logistic model (Eq. 21).

$$y'' = \frac{d^2 y}{dx^2} = 0 = \lambda - \delta \cdot x; \quad x = \tau = \frac{\lambda}{\delta} \quad (18)$$

$$y'\left(x = \frac{\lambda}{\delta}\right) = \frac{dy}{dx} = \frac{\delta \cdot \beta}{4}; \quad \Omega = \frac{\delta \cdot \beta}{4} \quad (19)$$

$$\log_{10} N = \alpha + \frac{\omega - \alpha}{1+\exp\left[\frac{4 \cdot \Omega}{\omega - \alpha}(\tau - \log_{10} t)\right]} \quad (20)$$

$$\log_{10} N = \frac{\omega - \alpha}{1 + \exp\left[\frac{4 \cdot \Omega}{\omega - \alpha}(\tau - \log_{10} t)\right]} - \frac{\omega - \alpha}{1 + \exp\left[\frac{4 \cdot \Omega}{\omega - \alpha}(\tau + 1)\right]} \quad (21)$$

Moreover, the application of the logarithm function to the independent variable ($x = \ln t$) should have been performed prior to the derivation of Eq. 17. The evaluation of the second derivative of Eq. 17 shown in Eq. 22 indicates that the solution presented by the authors as Eq. 18 is only valid when the parameter $\delta \rightarrow \infty$. The estimation of parameters τ and Ω depend of δ being sufficiently large ($\delta \rightarrow \infty$) as seen in Eq. 18-19. Unfortunately, we could not find if Cole et al. (1993) reported whether this condition ($\delta \rightarrow \infty$) is attained for either thermal or high pressure processing microbial inactivation. Users of this model should evaluate whether the parameter delta is sufficiently large ($\delta \rightarrow \infty$) to validate the biological interpretability of the log-logistic model parameters.

$$y'' = \frac{d^2 y}{d(\ln x)^2} = \ln\left(\frac{\delta - 1}{\delta + 1}\right) = \lambda - \delta \cdot x \quad (22)$$

Chen and Hoover (2003a) were among the first investigators to use a slightly modified "vitalistic" log-logistic model to analyze microbial inactivation by HPP (Eq. 23). These authors defined the parameter H as the difference between the upper and lower asymptotes ($H = \alpha - \beta$) and $t \sim 0$ as $t = 10^{-6}$ min. As in the case of Cole et al. (1993), Chen and Hoover (2003b) gave no explanation for the use of this latter value. The model was evaluated for the inactivation of *Yersinia enterocolitica* in sodium potassium buffer and in UHT whole milk subjected at room temperature to pressures within the 300-500 MPa range. The experimental survival data was described using the linear, Weibull, Gompertz and log-logistic models to identify the best inactivation model. Amidst the models tested, the log-logistic equation was most consistently the best model as denoted by its regression coefficient (R^2 = 0.946-0.982) and accuracy factor (A_f = 1.047-1.144). The values reported in Table 3 for the H parameter ranged from -4.61 to -39.71, which clearly lacks a biological or physical meaning. Consequently, Chen and Hoover (2003a) decided to fix H = -14 which reduced also the number of parameters (Eq. 24). Although a clear reason for selecting this value was not provided, the reduced log-logistic model (Eq. 24) gave slightly better results than the three parameter model (Eq. 23) as shown in Fig. 3.

$$\log\frac{N}{N_0} = -\frac{H}{1+\exp\left[\frac{4\cdot\Omega\cdot(\tau-\log t)}{H}\right]} + \frac{H}{1+\exp\left[\frac{4\cdot\Omega\cdot(\tau+6)}{H}\right]} \quad (23)$$

$$\log\frac{N}{N_0} = -\frac{14}{1+\exp\left[-\frac{\sigma\cdot(\tau-\log t)}{3.5}\right]} + \frac{14}{1+\exp\left[-\frac{\sigma\cdot(\tau+6)}{3.5}\right]} \quad (24)$$

372

373 INSERT FIGURE 3

374

375 Additional Weibull and log-logistic HPP inactivation kinetic model comparisons
376 have been published for diverse pathogens and food matrixes (Buzrul and Alpas,
377 2004; Guan et al., 2005; Guan et al., 2006; Chen, 2007; Kingsley et al., 2007;
378 Wang et al., 2009) showing equally acceptable or slightly better predictions when
379 using Eq. 23. The greatest advantage of the log-logistic over the Weibull model is
380 its ability to describe sigmoidal kinetic curves without further modifications
381 (Guan et al., 2005). However, only a few values of the log-logistic model
382 parameters have been reported for HPP (Table 3) and no secondary models to
383 predict pressure and temperature effects on the parameters *H*, Ω or τ were found
384 when preparing this review.

385

386 INSERT TABLE 3

387 Other primary models

388 Other primary models commonly found for the temperature effect on microbial
389 growth and microbial/enzyme inactivation kinetics have been used to a lesser
390 extent when analyzing combined pressure and temperature effects on foods. They
391 include the Baranyi-Roberts equation (Baranyi and Roberts, 1994; Pérez et al.,
392 2007; Saucedo-Reyes et al., 2009), the Gompertz model which has consistently
393 shown poorer fit when compared to other primary models (Chen and Hoover,
394 2003a; Guan et al., 2005; Koseki and Yamamoto, 2007; Saucedo-Reyes et al.,
395 2009; Vega-Gálvez et al., 2012), and the enhanced quasi-chemical kinetic model
396 (EQCKM). Even though the latter accounts for only a few publications in the high
397 pressure kinetics area, this model was further analyzed in this review as it
398 represented a recent and very different modeling approach.

399

Enhanced Quasi-Chemical Kinetic Model (EQCKM)

Unlike most microbial predictive models which take into account only the population growth or inactivation rate kinetics, the quasi-chemical model can describe both phenomena individually or simultaneously (Ross et al., 2005). According to the quasi chemical kinetic model (QCKM), biochemical reactions occurring at the microbial level can be assumed to follow a successive four-step chemical kinetics mechanism representing: (1) transition of microbial cells from the lag phase to the growth stage; (2) multiplication of microorganisms in the growth phase on a binary exponential basis; (3) microbial death after completing the cell life cycle; and (4) microbial death by the accumulation of a non-specific hazardous metabolite.

A set of chemical reaction equations relating rate constants (k) with the microbial population or the hazardous metabolite concentration can be developed for each step and solved as a system of ordinary differential equations (Ross et al., 2005; Doona et al., 2008). The QCKM was originally developed for predictions of pathogen growth under various environmental conditions differing in pH, a_w and concentration of an added microbial inhibitor (Ross et al., 2005). The same approach has been successfully applied to model the kinetics for the pressure inactivation of *E. coli* in the 207-345 MPa and 30-50°C range (Doona et al., 2005). The quasi chemical model effectively fit sigmoidal curves for *E. coli* at 40-50°C, and shoulder formation but only under the mildest experimental conditions (Doona et al., 2005; Doona et al., 2008). Furthermore, Doona et al. (2012) reported that the QCKM failed to describe well the high pressure kinetics for the inactivation of *Listeria monocytogenes* which presented “tailing”. Therefore, the authors adapted the differential equations of the QCKM under a new set of theoretical assumptions for the complete cell cycle under high pressure and renamed it as the “enhanced” quasi-chemical kinetic model (EQCKM).

A sub-version of the EQCKM considering only microbial inactivation under high pressure is shown in Figure 4. Under the assumptions of this EQCKM sub-version, the population of microbial cells in the lag phase (M) subjected to pressure can either become metabolically active to propagate a population in the growth phase (M^*) at a very slow rate (Eq. 25), or remain in the lag phase while

displaying superior baroresistance (*BR*; Eq. 26). Finally, both *M** and *BR* undergo inactivation at different rates (*MD*, Eq. 27-28). First order kinetics was assumed to describe the change with time of all microbial populations assumed in this modified model (*M*, *M**, *BR*, *D*). Thus, each step of the EQCM (Fig. 4) corresponds to a biochemical reaction with a kinetic rate constant (k_1-k_4). Due to the presence of successive biochemical reactions, all differential equations must be solved simultaneously as shown in the analytical solution (Eq. 29a-c). However, the "true" microbial count values for *M*, *M**, and *BR* cannot not be determined experimentally. The experimental quantification of *L. monocytogenes* after each HPP treatment can describe only the total of the individual populations assumed in the model ($U=M+M^*+BR$; Eq. 29d) and not their individual values. The EQKM solution is found by minimizing the error between the experimental microbial plate counts (*U*) and sum of the predicted values.

$$M \rightarrow M^*, \ k_1 \qquad (25) \qquad \frac{dM}{dt} = -\left(k_1 + k_2\right) \cdot M \qquad (29a)$$

$$M \rightarrow BR, \ k_2 \qquad (26) \qquad \frac{dM^*}{dt} = k_1 \cdot M - k_3 \cdot M^* \qquad (29b)$$

$$M^* \rightarrow MD, \ k_3 \qquad (27) \qquad \frac{dBR}{dt} = k_2 \cdot M - k_4 \cdot BR \qquad (29c)$$

$$BR \rightarrow MD, \ k_4 \qquad (28) \qquad U = M + M^* + BR \qquad (29d)$$

INSERT FIGURE 4

Since the EQCKM describes two different inactivation rates, Doona et al. (2012) opted to validate the model by calculating the processing time (*tp*) required to deliver 6 log reductions of *L. monocytogenes* counts (*U*) for several pressure (207-414 MPa) and temperature (20-50°C) combinations. The model successfully predicted *tp* as shown by the low standard error values (0.09-0.46) in the pressure-temperature range studied. For all pressure/temperature combinations, the kinetic constants k_1 and k_3 were greater than k_2 and k_4. The differences became more evident at 414 MPa, indicating that the microbial inactivation is primarily driven by pressure in the 20-50°C temperature range. Additionally, the high pressure resistance of *L. monocytogenes* was confirmed since k_3 was only significantly higher than k_4 for pressure levels over 345 MPa, and just three of the tested PATP

treatments yielded $tp \leq 15$ min. A key disadvantage of the EQCKM is that the key variables involved (M, M^* and BR) and their relationship to experimental microbial plate counts (U; Eq. 29d) remain a theoretical construct that will be difficult to confirm experimentally.

Secondary Models

The previously reviewed primary models are useful when the processing conditions (pressure, temperature, pH, etc.) are kept constant. If any processing condition is changed, a new set of experiments must be performed to obtain new primary model parameters. To extend the application of primary models, mathematical expressions known as secondary models can be developed to estimate the pressure and/or temperature effect on the predicted primary model parameters. As in the case of primary models, secondary models can be obtained from theoretical considerations or empirical observations. Most of the secondary models here presented are non-linear, reflecting complex biological behaviors under high pressure/high temperature conditions.

Simultaneous pressure and temperature effects on first order kinetics parameters

Bigelow model

The Bigelow model was developed to obtain log-linear estimates of the decimal reduction time as a function of temperature (Bigelow, 1921; Morales-Blancas and Torres, 2003a, b). The equation became so important and broadly accepted, that even nowadays it remains the standard approach in thermal processing design (van Asselt and Zwietering, 2006; Holdsworth and Simpson, 2007; Daek and Farkas, 2012).

The Bigelow model has been adopted to model the reaction rate dependence on the applied pressure ($k(P)$) using z_P, defined as the inverse negative slope of log D_P vs. pressure level (Eq. 30). The parameter z_P determines the pressure increase

required to achieve a 10-fold increase in the inactivation rate, a constant analogous to the thermal resistance constant z_T (Parish, 1998; Lado and Yousef, 2002; Cook, 2003; Dogan and Erkmen, 2004; Van Opstal et al., 2005; Koo et al., 2006; Peleg, 2006; Ramos and Smith, 2009; Zhou et al., 2009).

$$z_p = -\frac{P - P_{ref}}{\log D_p - \log D_{P\,ref}} \quad (30)$$

Santillana Farakos and Zwietering (2011) attempted to establish a global kinetic model based on the pressure and temperature dependence of the microbial inactivation kinetics by HPP. Reported *D* values for first order kinetics (Table 4) were fitted to Eq. 30-32 and analyzed statistically. Both models for *D* (Eqs. 31-32) assume that the exponential relation of z_P and z_T was directly proportional to pressure and temperature; however, Eq. 32 includes a term describing a first order interaction between pressure and temperature. The parameter z_{PT} represents the amount that the linear term $P \cdot T$ needs to increase for a tenfold decrease in *D*.

$$\log D = \frac{1}{z_P} \cdot \left(P_{ref} - P\right) + \frac{1}{z_T} \cdot \left(T_{ref} - T\right) + \log D_{\mathrm{Pr}\,efTref} \quad (31)$$

$$\log D = \frac{1}{z_P} \cdot \left(P_{ref} - P\right) + \frac{1}{z_T} \cdot \left(T_{ref} - T\right) + \frac{1}{z_{PT}} \cdot \left[\left(T_{ref} \cdot P_{ref}\right) - \left(T \cdot P\right)\right] + \log D_{\mathrm{Pr}\,efTref} \quad (32)$$

Santillana Farakos and Zwietering (2011) showed for Eq. 30 the lowest adjusted regression coefficient (R^2_{adj} = -0.037-0.630) reflecting the large influence of temperature on HPP treatments. Both models describing the pressure-temperature effect (Eqs. 31-32) had similar prediction accuracy (R^2_{adj} = 0.30-0.87), indicating that the linear pressure-temperature interaction has no overall significance (p_{value} > 0.05). Thus, Santillana Farakos and Zwietering (2011) reported only the parameters for Eq. 31 (Table 4). Bacterial spores displayed the highest pressure resistance constant (z_P = 614-616 MPa), followed by vegetative cells (z_P = 206-385 MPa), and yeasts (z_P = 91 MPa). Conversely, under high pressure the temperature effect on yeast inactivation was less significant (z_T = 141 °C) than the observed for vegetative cells (z_T = 38-97 °C) and spores (z_T = 20-45°C), since yeasts are readily inactivated by pressure alone. The *Vibrio* species (spp.) was the only microorganism to be more readily inactivated when temperature was lowered

(z_T = -18.4±2.3). The authors highlighted the need to avoid using these models for nonlinear inactivation curves, since under- or overestimation may occur (Santillana Farakos and Zwietering, 2011).

INSERT TABLE 4

Pressure kinetics fundamentals

The Le Chatelier principle states that *under equilibrium*, a system subjected to pressure will adopt the molecular configurations, chemical interactions, and chemical reactions yielding the smallest overall volume (Farkas and Hoover, 2000; Welti-Chanes et al., 2006; Balasubramaniam et al., 2008). Mathematically, the Le Chatelier principle has been expressed with thermodynamic relations by using the partial molar volume ($\bar{V}$) concept originally defined for gas mixtures. The overall molar volume change for the reaction ($\Delta\overline{V_{reacion}}$) defined as the difference in the partial molar volumes of products and reactants (Eq. 33) can be expressed as the change of the Gibbs energy with respect to pressure at a constant temperature. Thus, $\Delta\overline{V}_{reaction}$ is related directly to the equilibrium constant (K) for the reaction (Smith et al., 1997).

$$\Delta\overline{V_{reacion}} = \sum\overline{V}_P - \sum\overline{V}_R = \left(\frac{\partial\Delta G}{\partial P}\right)_T = -RT\left(\frac{\partial \ln K}{\partial P}\right)_T \qquad (33)$$

This description is further extrapolated to biological systems under the *Transitional State Theory* by proposing the existence of a biological reactant (R) in equilibrium with an activated biological complex ($X^{\neq}$) prior to the formation of the biological reaction product P (Eq. 34). If the formation of the activated complex is in thermal equilibrium, the frequency ($\upsilon^{\neq}$) at which $X^{\neq}$ transforms into P can be calculated using quantum ($E = h\cdot\upsilon^{\neq}$) and classical physics ($E = k_B\cdot T/h$)) equations describing the internal energy distribution (Eq. 35):

$$R \xleftrightarrow{K^{\neq}} X^{\neq} \xrightarrow{\upsilon^{\neq}} P \qquad (34)$$

$$\upsilon^{\neq} = \frac{k_B \cdot T}{h} \qquad (35)$$

where h is the Planck constant (6.626 x 10^{-34} J s^{-1}), k_B is the Boltzmann constant (1.38 x 10^{-23} J K^{-1}), and T (K) is the absolute temperature at which the chemical reaction takes place (Missen et al., 1999; Leskovac, 2003). Hence, the product formation rate equation (r_P; Eq. 36) can be rewritten to yield Eq. 38 by substituting $\upsilon^{\neq}$ (Eq. 35) and the pseudo-equilibrium constant $K^{\neq}$ (Eq. 37) to obtain a theoretical definition of the kinetic rate constant k (Eq. 39).

$$r_P = \upsilon^{\neq} \cdot \left[X^{\neq}\right] \tag{36}$$

$$K^{\neq} = \frac{\left[X^{\neq}\right]}{\left[R\right]} \tag{37}$$

$$r_P = \frac{k_B \cdot T}{h} \cdot K^{\neq} \cdot \left[R\right] \tag{38}$$

$$k = \frac{k_B \cdot T}{h} \cdot K^{\neq} \tag{39}$$

To depict the effect of pressure on the kinetic rate constant for isothermal conditions, Eq. 39 can be used to substitute $K^{\neq}$ in Eq. 33. The Gibbs free energy and volume change are state functions and a reference pressure (P_{ref}) must be selected arbitrarily when quantifying these thermodynamic properties. By integrating of Eq. 40 from P_{ref} to P, and defining the kinetic constant with respect to the reference conditions (k_{ref}) yields the Eyring model (Eq. 42), where the term $h/k_B \cdot T$ is a constant and its derivative equals zero (Eq. 41).

$$\left[\frac{\partial \ln K^{\neq}}{\partial P}\right]_T = \frac{\partial}{\partial P}\left[\ln\left(\frac{k \cdot h}{k_B \cdot T}\right)\right]_T \tag{40}$$

$$\frac{\partial}{\partial P}\left[\ln k + \ln\left(\frac{h}{k_B \cdot T}\right)\right]_T = \left[\frac{\partial(\ln k)}{\partial P}\right]_T = -\frac{\Delta V^{\neq}}{R \cdot T} \tag{41}$$

$$\ln k = \ln k_{ref} - \frac{\Delta V^{\neq} \cdot \left(P - P_{ref}\right)}{R \cdot T} \tag{42}$$

According to the Eyring equation (Eq. 42), the slope of the plot ln k vs. P under isothermal conditions is an estimation of the volume change between the activated complex and the reactants ($\Delta V^{\neq}$), also known as the *activation volume.* Thus, the formation of the active complex and/or products are accelerated when the overall reaction volume is decreased ($\Delta V^{\neq} < 0$) (Heremans, 1982). Conversely, $\Delta V^{\neq} > 0$

suggests that pressure will inhibit the active complex formation and/or its subsequent transformation into products, whereas $\Delta V^{\neq} = 0$ indicates that the reaction rate is not affected by pressure. The pressure dependence of $\Delta V^{\neq}$ commonly deviates from the linear behavior dictated by the Eyring model (Eq. 42) and either theoretical or empirical approximations must be followed, as discussed in the following sections (Isaacs, 1981; Weemaes et al., 1998a; Van den Broeck et al., 2000; House, 2007; Segovia Bravo et al., 2012).

It is also important to stress that the *Transition State Theory* is an extension of the collision rate theory of gas phase kinetics. Although, the *Transition State Theory* is apparently valid to describe both gas and liquid phase kinetics in practice, a rigorous theoretical approach to liquid phase kinetics involves the determination of other critical features such as electrochemical and transport phenomena properties of all components in the solution (Atkins and de Paula, 2006), which would be very challenging, and probably impossible to determine in complex matrixes such as foods.

Eyring-Arrhenius model

A mathematical model describing the combined effects of pressure (P) and temperature (T) on the inactivation rate constant (k) developed from the exponential form of the Eyring (Eq. 43) and Arrhenius equations (Eq. 44), has been reported by several authors (Weemaes et al., 1998b; Van den Broeck et al., 2000; Polydera et al., 2004; Katsaros et al., 2010).

$$k(P) = k_{refP} \cdot \exp\left[-\frac{\Delta V^{\neq}(T)}{R} \cdot \frac{(P - P_{ref})}{T} \right] \quad (43)$$

$$k(T) = k_{refT} \cdot \exp\left[-\frac{E_a(P)}{R} \cdot \left(\frac{1}{T} - \frac{1}{T_{ref}} \right) \right] \quad (44)$$

The value of the activation energy (E_a) and activation volume ($V^{\neq}$) parameters change with the vessel pressure and temperature, respectively. For example, the inactivation rate of orange juice pectinmethylesterase (PME, 100-800 MPa, 30-

589 60°C) showed a linear dependence of $\Delta V^{\neq}$ with respect to temperature (Eq. 45),
590 whereas E_a and pressure were related exponentially (Eq. 46) (Polydera et al.,
591 2004).

$$\Delta V^{\neq}(T) = a \cdot (T - T_{ref}) + \Delta V_T^{\neq} \qquad (45)$$

$$E_a(P) = E_{aP} \cdot \exp[-g \cdot (P - P_{ref})] \qquad (46)$$

592

593 The double integration of the inactivation rate constant (k) with respect to pressure
594 and temperature yields Eq. 47:

$$k = k_{refP,T} \cdot \exp\left\{-\frac{E_{aP}}{R} \cdot \exp[-g \cdot (P - P_{ref})] \cdot \left(\frac{1}{T} - \frac{1}{T_{ref}}\right) - \frac{a \cdot (T - T_{ref}) + \Delta V_T^{\neq}}{R} \cdot \frac{P - P_{ref}}{T}\right\} \qquad (47)$$

595

596 This particular model deviated at low pressure (100-250 MPa) and moderate
597 temperature ranging from 30-40°C (Polydera et al., 2004), and therefore these
598 conditions were not taken into account for $k(P,T)$ predictions (Figure 5a).
599 However, Katsaros et al. (2010) obtained a good correlation (R^2 = 0.993) between
600 experimental and predicted values of orange PME inactivation within 100-500
601 MPa and 20-40°C when applying the same model (Fig. 5b). The different
602 outcomes obtained by Polydera et al. (2004) and Katsaros et al. (2010) may reflect
603 differences in the orange variety and experimental conditions used. Although the
604 Eyring-Arrhenius modeling of the experimental data was performed using the
605 same software, differences were observed in the estimated activation energy
606 (Table 5), i.e., E_a = 148 KJ mol^{-1} (Polydera et al., 2004) and E_a = 95 KJ mol^{-1}
607 (Katsaros et al., 2010). It should be noted that the latter authors used narrower
608 pressure and temperature ranges, and the reference conditions (P_{ref}, T_{ref}) for Eq. 47
609 were not the same. Katsaros et al. (2010) chose 300 MPa and 308 K whereas
610 Polydera et al. (2004) selected reference conditions close to the region with the
611 most significant enzymatic inactivation observed (600 MPa, 50°C). The Eyring-
612 Arrhenius parameters obtained by Polydera et al. (2004) failed to consistently
613 estimate $k(P,T)$ in the entire experimental range. Predictions of the kinetic rate
614 constant were inaccurate at 100-250 MPa, but the model fit significantly improved
615 in the proximity of the reference conditions selected (400-800 MPa, 40-60°C).
616

617 INSERT FIGURE 5

Weemaes et al. (1998b) and van den Broeck et al. (2000) encountered antagonistic pressure effects on *k*, since the enzyme was stabilized at pressures below 250-350 MPa for orange juice PME (Figure 6) and also for avocado polyphenoloxidase (PPO). The Eyring relation (Eq. 43) was not constant throughout the tested pressure range and both Weemaes et al. (1998b) and van den Broeck et al. (2000) opted to apply an empirical model to estimate pressure dependence of k_{ref} (Eq. 48). Weemaes et al. (1998b) found that the activation energy decayed exponentially as the pressure system increased (Eq. 49), whereas van den Broeck et al. (2000) reported a linear function for E_a (P) (Eq. 50).

$$\ln k_{ref}(P) = c_1 + c_2 \cdot P + c_3 \cdot P^2 + c_4 \cdot P^3 \quad (48)$$

$$E_a(P) = E_{aP} \cdot \left[\exp(-c_5 \cdot P)\right] \quad (49)$$

$$E_a(P) = c_5 - c_6 \cdot P \quad (50)$$

INSERT FIGURE 6

The substitution of E_a (P) and k_{ref} (P) in the Arrhenius equation (Eq. 44) yields two empirical models describing the effects of pressure and temperature on *k* (Eq. 51-52). Empirical parameters c_1-c_4 describe the effect of pressure on k_{ref} and the calculated values for PPO (Weemaes et al., 1998b) and PME (Van den Broeck et al., 2000) are very similar (Table 5).

$$k = \exp\left\{c_1 + c_2 \cdot P + c_3 \cdot P^2 + c_4 \cdot P^3 + \left[-\frac{E_{aP} \cdot \left[\exp(-c_5 \cdot P)\right]}{R}\left(\frac{1}{T} - \frac{1}{T_{ref}}\right)\right]\right\} \quad (51)$$

$$k = \exp\left\{c_1 + c_2 \cdot P + c_3 \cdot P^2 + c_4 \cdot P^3 + \left[-\frac{c_5 - c_6 \cdot P}{R}\left(\frac{1}{T} - \frac{1}{T_{ref}}\right)\right]\right\} \quad (52)$$

Conversely, Ludikhuyze et al. (1998b, a) found that elevating pressure increased the inactivation rates at all temperatures and therefore the Eyring model (Eq. 43) was valid for lipoxygenase (LOX) inactivation at 50-800 MPa and 10-64°C. Antagonistic effects for combined pressure-temperature treatments were again present for the low temperature (T < 40°C) and high pressure (P > 475 MPa) region and minimum values were registered between 30-40°C. In this case, the

643 Arrhenius model (Eq. 44) could not be applied as denoted by the calculated E_a
644 values, which were negative for $T < 40$°C and positive for $T > 40$°C. Therefore
645 Ludikhuyze et al. (1998a) elaborated an empirical model for $k_{ref}(T)$ (Eq. 53) and
646 $\Delta V^{\neq}(T)$ (Eq. 54). The incorporation of Eq. 53-54 into the Eyring equation resulted
647 in an Eyring-empirical secondary model (Eq. 55).

$$\ln k_{ref}(T) = c_1 + c_2 \cdot T + c_3 \cdot T^2 \quad (53)$$

$$\Delta V^{\neq}(T) = c_4 \cdot T \cdot \left[\exp(-c_5 \cdot T)\right] \quad (54)$$

$$\ln k = c_1 + c_2 \cdot T + c_3^2 \cdot T - \left\{ \frac{c_4 \cdot T \cdot \left[\exp(-c_5 \cdot T)\right]}{R \cdot T} \cdot \left(P - P_{ref}\right) \right\} \quad (55)$$

648
649 Doona et al. (2012) predicted the processing time ($tp = 1/k$) required to achieve 6
650 log reductions of *L. monocytogenes* as a function of pressure and temperature with
651 empirical models based on the Eyring and the Arrhenius equations. The pressure
652 dependence of ln k was not linear and the authors decided to include the effect of
653 pressure on $\Delta V^{\neq}$, given by the compressibility factor $\Delta\beta$ and defined through Eq.
654 56-58-56 (Morild, 1981; Van Eldik et al., 1989; Doona et al., 2012).

$$\Delta\beta = \left(\frac{\partial \Delta V^{\neq}}{\partial P}\right)_T = -R \cdot T \cdot \left(\frac{\partial^2 \ln k}{\partial P^2}\right)_T \quad (56)$$

$$\left(\frac{\partial \ln k}{\partial P}\right)_T = -\frac{1}{R \cdot T} \cdot \left[\Delta\beta \cdot \left(P - P_{ref}\right) + \Delta V^{\neq}\right] \quad (57)$$

$$\ln k = \ln k_{ref} - \frac{\Delta V^{\neq} \cdot \left(P - P_{ref}\right)}{R \cdot T} + \frac{\Delta\beta \cdot \left(P - P_{ref}\right)^2}{2 \cdot R \cdot T} \quad (58)$$

655
656 Furthermore, the extended Eyring model (Eq. 56) was reparametrized by defining
657 *tp*, γ as in Eq. (59, 60), $P_{ref} = 6.98$ MPa (≈1 kpsi), and regrouping all terms (Eq.
658 61-64) to yield a linear quadratic equation with three parameters (Eq. 63). Similar
659 modifications were performed for the Arrhenius equation (model not shown), and
660 the temperature dependence of *tp* was modeled with a non-dimensional linear first
661 order equation. Doona et al. (2012) reported that both of the secondary models
662 accurately predicted *tp* for a new set of experimental under isothermal or isobaric
663 conditions.

$$\gamma = \frac{1}{P_{ref}} \cdot \left(P - P_{ref}\right) = \frac{P}{P_{ref}} = 1 + \gamma \quad (59)$$

$$tp = \frac{1}{k} \tag{60}$$

$$k = A \cdot \exp\left(-c_1 \cdot \gamma\right) \cdot \exp\left(-c_2 \cdot \gamma^2\right) \tag{61}$$

$$A = k_{ref} \cdot \exp\left[-\left(\frac{\Delta V^{\neq} \cdot P_{ref}}{R \cdot T} - \frac{\Delta\beta \cdot P_{ref}^2}{2 \cdot R \cdot T}\right)\right]; c_0 = \ln\frac{1}{A} \tag{62}$$

$$c_1 = \frac{\Delta V^{\neq} \cdot P_{ref}}{R \cdot T} - \frac{\Delta\beta \cdot P_{ref}^2}{R \cdot T} \tag{63}$$

$$c_2 = -\frac{\Delta\beta \cdot P_{ref}^2}{2 \cdot R \cdot T} \tag{64}$$

$$\ln tp = c_0 + c_1 \cdot \gamma - c_2 \cdot \gamma^2 \tag{65}$$

For microbial inactivation Katsaros et al. (2010) modified Eq. 43-44 by defining k (T) and k (P) as a function of decimal reduction times of *Lactobacillus brevis* and *Lactobacillus plantarum* in orange juice at reference conditions (D_{Tref}, D_{Pref}) and parameters z_T and z_P as in Eq. 66-67.

$$k(T) = \frac{2.303}{D_{T_{ref}} \cdot 10^{\left(\frac{T - T_{ref}}{z}\right)}} \tag{66}$$

$$k(P) = \frac{2.303}{D_{P_{ref}} \cdot 10^{\left(\frac{P - P_{ref}}{z}\right)}} \tag{67}$$

Both k (T) and k (P) were associated by assuming an Arrhenius type relationship and an expression relating decimal reduction time (D) with the processing conditions P and T (Eq. 68).

$$D = D_{ref} \cdot \left(\exp\left\{ \begin{array}{l} -\frac{2.303 \cdot T \cdot T_{ref}}{z_T} \cdot \exp\left[-g \cdot \left(P - P_{ref}\right)\right] \cdot \left(\frac{1}{T} - \frac{1}{T_{ref}}\right) \\ +\frac{2.303 \cdot \left(P - P_{ref}\right)}{z_P \cdot R} \end{array} \right\} \right)^{-1} \tag{68}$$

Katsaros et al. (2010) reported a good fit for predicted k (P,T) of *L. brevis* and *L. plantarum* in orange juice (R^2 = 0.951 and 0.977, respectively) inactivation in the 100-500 MPa and 20-40°C range. Pressure resistance at the reference temperature

677 was almost the same for *L. brevis* (z_P = 94.7±7.8 MPa) and *L. plantarum* (z_P =
678 95.0±11 MPa). Nonetheless, thermal sensibility was lower for the former (z_T =
679 23.8±2.4 °C) than for the latter (z_T = 23.8±2.4°C and the decimal reduction time at
680 reference conditions was 2.1 min higher (Table 5).
681
682 Although decimal reduction times for the inactivation of enzymes are rarely
683 reported, Ludikhuyze et al. (2000) attempted to fit the Bigelow model (Eq. 28) to
684 the inactivation of raw bovine milk alkaline phosphatase (0.1-700 MPa; 25-63°C).
685 Enzyme activity kinetics followed a first order kinetics, and therefore *k* was
686 related to decimal reduction times as in Eq. (66-67). Adverse effects of PATP
687 were once again present for the low pressure/high temperature region, and the
688 pressure dependent terms (Eq. 67) were not valid in the experimental range tested.
689 Ludikhuyze et al. (2000) opted to fit experimental *D* (*T*,*P*) values to the empirical
690 model shown in Eq. 69 (Table 5), and reported that 95% of the predicted data
691 points showed less than 15% of error when compared to the experimental values.
692 Parameter c_1 could represent D_T at a reference temperature, and the calculated
693 value at T_{ref} = 50°C was D_T = 3.33 min (Table 5), implying that alkaline
694 phosphatase has an elevated thermal resistance.

$$\log_{10} D(P,T) = c_1 + c_2 \cdot P + c_3 \cdot P^2 - \frac{T - T_{ref}}{c_4 + c_5 \cdot P + c_6 \cdot P^2} \quad (69)$$

695
696 Hashizume et al. (1995) studied the effect of high pressure (120-300 MPa) and
697 sub-zero temperatures (-20 to 50°C) on *S. cerevisae* inactivation. Inactivation
698 kinetics apparently followed first order kinetics at all temperatures, whereas
699 pressures below 180 MPa and temperatures between 0-40°C caused only a minor
700 microbial inactivation. A quadratic model (Eq. 70) was utilized to predict *k* as a
701 function of both pressure and temperature. The isokinetic rate diagrams for *S.*
702 *cerevisae* inactivation presented an elliptical trend similar to a protein
703 denaturation diagram (Heremans and Smeller, 1998; Velazquez et al., 2005;
704 Meersman et al., 2006). Hashizume et al. (1995) concluded that the resemblance
705 of microbial and enzymatic isorate contours may be due to the adverse effects of
706 HPP on key enzymatic processes of microorganisms. Furthermore, Reyns et al.
707 (2000) demonstrated statistically a slightly improved prediction of decimal
708 reduction times for *Z. bailii* when the linear pressure-temperature term, denoted

by (P - P_{ref})·(T - T_{ref}) was omitted (Eq. 71). The values for the parameters of Eq. 70-71 are shown in Table 5.

$$\log_{10} k(P,T) = c_1 + c_2 \cdot (P - P_{ref}) + c_3 \cdot (T - T_{ref}) + c_4 \cdot (P - P_{ref})^2 + c_5 \cdot (P - P_{ref}) \cdot (T - T_{ref}) + c_6 \cdot (T - T_{ref})^2 \quad (70)$$

$$\log_{10} D(P,T) = c_1 + c_2 \cdot (P - P_{ref}) + c_3 \cdot (T - T_{ref}) + c_4 \cdot (P - P_{ref})^2 + c_5 \cdot (T - T_{ref})^2 \quad (71)$$

INSERT TABLE 5

Even though there are other empirical pressure-temperature secondary models, care must be taken when using them since most lack generality and have validity only for the specific inactivation study for which the equation was developed. Additionally, most of these polynomial parameters also lack a comprehensible biological or physical basis, and may include severe and numerous slope changes over a wide range leading to incorrect estimations of kinetics parameters.

Thermodynamic model

Hawley (1971) developed a purely thermodynamic model to describe ΔG for the reversible pressure-temperature denaturation of chymotrypsinogen at 0.1-700 MPa and 8.5-70°C. By integrating the general free Gibbs energy equation (Eq. 72), and including the compressibility factor (β), thermal expansivity (α) and specific heat (C_p) contribution with the Maxwell relations, the result is the model proposed by Hawley (1971) shown below (Eq. 73):

$$d(\Delta G) = -\Delta S dT + \Delta V dP \quad (72)$$

$$\Delta G = \frac{\Delta\beta}{2 \cdot R \cdot T} \cdot (P - P_{ref})^2 + \frac{\Delta\alpha}{R \cdot T} \cdot (P - P_{ref}) \cdot (T - T_{ref}) - \frac{\Delta C_p}{R \cdot T}\left[T\left(\ln\frac{T}{T_{ref}} - 1\right) + T_{ref}\right] + \frac{\Delta V_{ref}}{R \cdot T} \cdot (P - P_{ref}) - \frac{\Delta S_{ref}}{R \cdot T} \cdot (T - T_{ref}) + \Delta G_{ref} \quad (73)$$

Eq. 73 could be incorporated into the model that relates the equilibrium constant ($K^{\neq}$) between the reactants and the activated complex with the chemical reaction constant k described by the Transitional State Theory (See the *Pressure Thermodynamics Fundamentals* section) and the general ΔG equilibrium model (Eq. 72). The combination of Eq. 72-74- yields the thermodynamic kinetic model

(Eq. 75) (Morild, 1981; Weemaes et al., 1998b; Fachin et al., 2002; Ludikhuyze et al., 2002):

$$\Delta G = -R \cdot T \cdot \ln K \tag{74}$$

$$\ln k = \frac{\Delta\beta}{2 \cdot R \cdot T} \cdot \left(P - P_{ref}\right)^2 + \frac{\Delta V^{\neq}_{ref}}{R \cdot T} \cdot \left(P - P_{ref}\right) - \frac{\Delta S_{ref}}{R \cdot T} \cdot \left(T - T_{ref}\right) + \frac{\Delta\alpha}{R \cdot T}\left(P - P_{ref}\right) \cdot \left(T - T_{ref}\right) - \frac{\Delta C_p}{R \cdot T} \cdot \left\{ T \cdot \left[\ln\left(\frac{T}{T_{ref}}\right) - 1 \right] + T_{ref} \right\} + \ln k_{ref} \tag{75}$$

The thermodynamic kinetic model accurately fit experimental *k* values for the inactivation of soybean lipoxygenase (LOX) in Tris-HCl buffer (Indrawati et al., 1999), green pea juice and intact green peas (Indrawati et al., 2001) over wide pressure-temperature ranges (Table 6). Weemaes et al. (1998b) rejected this kinetic model (Eq. 75) for the case of PME inactivation because the statistical analysis showed that the residuals for *k* as a function of pressure were not randomly distributed. Weemaes et al. (1998b) stated that Eq. 75 could not be applied for avocado PPO inactivation because Hawley (1971) originally developed the thermodynamic model to describe the *reversible* inactivation of chymotrypsinogen. The authors concluded that *irreversible* enzyme inactivation mechanisms differ from those for *reversible* inactivation, and therefore a different mathematical model to estimate $k(P, T)$ should be used.

In addition, the thermodynamic model proposed by Hawley (1971) assumes that thermophysical parameters ΔC_p, $\Delta\alpha$ and $\Delta\beta$ remain constant for all pressure and temperature values, which may not always be the case (Smeller, 2002). The general ΔG equation (Eq. 70) could be approximated using a Taylor expansion series (Eq. 76) where the additional third degree terms would represent the pressure and temperature dependence of ΔC_p, $\Delta\alpha$ and $\Delta\beta$ (Clark, 1979; Heremans and Smeller, 1998; Smeller, 2002; Borda et al., 2004).

$$\Delta G = \Delta G_{ref} + \Delta V_{ref} \cdot \left(P - P_{ref}\right) - \Delta S_{ref} \cdot \left(T - T_{ref}\right) + \frac{\Delta\beta}{2} \cdot \Delta V_{ref} \cdot \left(P - P_{ref}\right)^2 + \Delta\alpha \cdot \left(P - P_{ref}\right)\left(T - T_{ref}\right) - \frac{\Delta C_p}{2 \cdot T_{ref}} \cdot \left(T - T_{ref}\right)^2 \tag{76}$$

Ly-Nguyen et al. (2003) incorporated additional polynomial degree terms given by the Taylor expansion series (Eq. 77), and the distortion of the elliptical trend of the iso-rate contour plot reported by other authors was also observed (Smeller, 2002; Borda et al., 2004).

$$\frac{\Delta\beta_2}{2\cdot R\cdot T}\cdot\left(P-P_{ref}\right)^3+\frac{\Delta C_{p\,2}}{2\cdot R\cdot T\cdot T_{ref}}\cdot\left(T-T_{ref}\right)^3+\frac{2\cdot\Delta\alpha_2}{R\cdot T}\cdot\left(P-P_{ref}\right)^2\cdot\left(T-T_{ref}\right) \quad (77)$$

The addition of these higher order terms yielded a better fit (R^2 = 0.941) than the original Hawley model (R^2 = 0.891) for carrot PME inactivation in the 100-825 MPa and 10-65°C range (Ly-Nguyen et al., 2003). Antagonistic pressure-temperature effects were observed as the value of ln *k* decreased, particularly at 50-65°C and 100-300 MPa (Figure 7). Apparently the inactivation rate values increased exponentially until reaching the high pressure (600-800 MPa), low temperature region (10-40°C), where an asymptotic trend was observed (Fig. 7a-7b). For moderate temperatures (50-65°C), the antagonistic effects were clearly noticeable in the 100-400 MPa region. The second order thermodynamic model (Eq. 76) failed to adjust to the lower experimental *k* values (Fig. 7c-7d).

INSERT FIGURE 7

Another modification of the thermodynamic model (Eq. 75) was proposed by Fachin et al. (2002) who noted that the isorate contour plots for different pressure-temperature combinations displayed no elliptical trend for the tomato PG inactivation kinetics. Consequently, the compressibility factor (β) and the specific heat capacity (C_p) from the thermodynamic model were removed (Eq. 78) because the authors stated that these terms are related to the elliptical trend. Fachin et al. (2002) found a satisfactory correlation (R^2 = 0.92) between experimental data and estimated *k* (*P*,*T*) values using the reduced thermodynamic model (Eq. 76). However, the kinetic study on the inactivation of tomato PG covered a narrower pressure-temperature range (300-600 MPa, 5-50°C) as compared to the other HPP enzyme inactivation cases presented in Table 6. Therefore, the pressure and temperature range used by these authors may have affected the shape of the isorate contour plots.

$$\ln k = \frac{\Delta V^{\neq}_{ref}}{R \cdot T} \cdot \left(P - P_{ref}\right) - \frac{\Delta S_{ref}}{R \cdot T} \cdot \left(T - T_{ref}\right) + \frac{\Delta \alpha}{R \cdot T} \cdot \left(P - P_{ref}\right) \cdot \left(T - T_{ref}\right) + \ln k_{ref} \quad (78)$$

INSERT TABLE 6

The thermodynamic model can simultaneously describe pressure and temperature effects on the inactivation rate constants with a solid theoretical background that can be interpreted physically. Most importantly, a thermodynamic model can describe experimental data with antagonistic pressure-temperature effects while still yielding accurate predictions (Indrawati et al., 1999; Indrawati et al., 2001; Ly-Nguyen et al., 2003). However, the large number of parameters involved implies an extensive experimental plan covering a wide pressure-temperature range which makes them potentially impractical to use (Morild, 1981; Indrawati et al., 1999; Ly-Nguyen et al., 2003).

Simultaneous pressure and temperature effects on Weibull model parameters

Peleg et al. (2002) questioned the application of the Arrhenius model to describe the temperature effect on inactivation kinetics, arguing the existence of temperature regions where the reaction system remains inert. The authors cited as an example oxidation and browning reactions, which become significant only when the temperature is increased. On the other hand, the parameters *b'* and *n* of the Weibull power law model are not necessarily constant and depend on the pressure and temperature condition applied (Peleg, 2006). Peleg et al. (2002) suggested a log-logistic model to simulate null reaction rates for low temperature regions, and a subsequent increase beyond a critical temperature level (T_c). Corradini et al. (2005) applied the log-logistic model to describe the Weibull rate parameter *b'* as a function of temperature (Eq. 79).

$$b'(T) = \ln\left\{1 + \exp\left[w_T\left(T - T_c\right)\right]\right\}^m \quad (79)$$

The parameter T_c denotes the temperature at which *b'* (*T*) increases linearly for *m* = 1. If $T > T_c$, the parameter *b'* (*T*) increases to the power $w_T \cdot (T - T_c)$, where w_T determines the rate at which *b'* (*T*) increases with temperature. Conversely, when

818 $T < T_c$ the exponential term tends to zero and $b'(T)$ is approximately ln (1) = 0.
819 This model may be applied also for high pressure inactivation (Eq. 80) under
820 isothermal conditions (Peleg, 2006; Corradini et al., 2009).

$$b'(P) = \ln\left\{1 + \exp\left[w_P\left(P - P_c\right)\right]\right\}^m \qquad (80)$$

821
822 Pressure and temperature increases are expected to lower parameters T_c and P_c
823 (Eq. 81-82) since inactivation should be favored by more severe treatments (Peleg
824 et al., 2005). However, these exponential-logistic models may not accurately
825 predict antagonistic pressure-temperature effects as in the case of PME.

$$P_c(T) = P_{c0} \cdot \exp(-w_1 \cdot T) \qquad (81)$$

$$T_c(P) = T_{c0} \cdot \exp(-w_2 \cdot P) \qquad (82)$$

826
827 The pressure effect on the parameter *b'* may be expressed also using the Bigelow
828 model (Eq. 83) as reported by Pilavtepe-Çelik et al. (2009) or as a simple linear
829 model as shown in Eq. 84 (Chen and Hoover, 2003a).

$$\log_{10} b' = \log_{10} b'_{ref} - \left(\frac{P - P_{ref}}{z}\right) \qquad (83)$$

$$b' = slope + intercept \qquad (84)$$

830
831 The shape parameter *n* of the Weibull inactivation model (Eq. 9) has often been
832 reported to display a slight or no temperature dependence (van Boekel, 2002;
833 Buzrul et al., 2008). This statement can sometimes be assumed for *n* (*P*) as Chen
834 and Hoover (2003a) did at certain pressure ranges for *Yersinia enterocolitica*
835 ATCC 35669 inactivation kinetics in milk and sodium phosphate buffer. No
836 significant differences were found for *n* in the 300-400 MPa and 400-500 MPa
837 regions for *Y. enterocolitica* inactivation in phosphate buffer and milk,
838 respectively, so the mean value of *n* was applied for each pressure range. However
839 the former assumption that *n* is pressure independent was not valid for the entire
840 experimental pressure range (300-500 MPa). On the contrary, Doona et al. (2008)
841 and Buzrul and Alpas (2004) observed concavity changes (Table 2), where *n*
842 tended to increase with processing pressure temperature. Therefore, a constant
843 *n*(*T*) or *n*(*P*) may not be the reflect of a non-significant pressure and/or
844 temperature effect on the kinetic model parameters, but a consequence of the

narrow pressure and temperature ranges under which the experiments were performed. The pressure-dependence of the shape parameter, $n(P)$, can be calculated empirically, e.g., using the model proposed by Pilavtepe-Çelik et al. (2009) for the inactivation of pathogens in carrot juice and peptone water (Eq. 85). The exponential model describing P_c (T) and T_c (P) (Eq. 81-82) can also be applied to the model parameter $n(T)$ or $n(P)$ (Eq. 86-87) (Doona et al., 2008).

$$n(P) = n_{ref} + a \cdot \left(\frac{1}{P} - \frac{1}{P_{ref}} \right) \quad (85)$$

$$n(P) = d_{0P}(T) \cdot \exp\left[- d_{1P}(T) \cdot P \right] \quad (86)$$

$$n(T) = d_{0T}(P) \cdot \exp\left[- d_{1T}(P) \cdot T \right] \quad (87)$$

Recently Carreño et al. (2011) proposed an alternative Weibull secondary model for the survival fraction ($\log_{10} S$) under isothermal and isobaric conditions by inferring that the pressure and temperature resistance of microorganisms followed a Weibull distribution. Pressure and temperature substituted the independent variable time (t) in Eq. 9 and resulted in Eq. 88-89.

$$S(P) = -\left(\frac{P}{f_P} \right)^n \quad (88)$$

$$S(T) = -\left(\frac{T}{f_T} \right)^n \quad (89)$$

The parameters f_P and f_T represent the pressure and temperature for the first decimal reduction of the microbial population. The use of the isothermal model to describe the inactivation of *L. plantarum* at 0-400 MPa for 10-60 s in tangerine juice with an initial temperature of 15-45°C yielded R^2 =0.952-0.990 and A_f =1.021-1.066 (Carreño et al., 2011). Although no sigmoidal curves were observed, Carreño et al. (2011) also investigated the kinetics of *L. plantarum* HPP inactivation combined with mild heat treatments (45-90°C, 10 s). The survival curves presented concavity changes and the single Weibull model with pressure and temperature as independent variables (Eq. 88-89) had an inaccurate fit (36% prediction error). As a result, a biphasic Weibull model (Eq. 90) combining Eq. 15 and Eq. 88 was applied and yielded a 9% prediction error with A_f = 1.009.

$$N(T) = \frac{N_0}{1+10^{\Psi}}\left[10^{\left[\Psi-\left(\frac{T}{f_{T_1}}\right)^{n_1}\right]}+10^{-\left(\frac{T}{f_{T_2}}\right)^{n_2}}\right] \quad (90)$$

869

870 For isothermal conditions, Eq. 79 can also be expressed as a function of the
871 pressure applied (Eq. 91)

$$N(P) = \frac{N_0}{1+10^{\Psi}}\left[10^{\left[\Psi-\left(\frac{P}{f_{P_1}}\right)^{n_1}\right]}+10^{-\left(\frac{P}{f_{P_2}}\right)^{n_1}}\right] \quad (91)$$

872

873 Finally, it is important to note that information concerning any of the Weibull
874 HPP secondary models here presented is scarce (Table 7).

875

876 INSERT TABLE 7

877 Simultaneous pressure and temperature effects on quasi-chemical
878 kinetic model parameters

879 Only Doona et al. (2008) have reported secondary inactivation expressions for the
880 quasi-chemical kinetic model. This includes a general inactivation rate constant
881 (μ) for *E. coli* (207-345 MPa, 30-50°C) as the minimum slope of the process
882 lethality $L(t)$ (Eq. 93). The time at which μ occurs can be defined as t_μ ($t = t_\mu$),
883 thus $L_\mu = L(t_\mu)$, and the initial phase of the HPP for which no microbial
884 inactivation occurs is defined as the "lag time" ($L_0 = 0$; $t = \lambda$). A straight line of
885 $L(t)$ with slope μ can be observed from L_0 to L_μ as in Eq. 93, and the lag time can
886 be obtained by solving for λ, which is a function of the total microbial plate counts
887 (U) determined experimentally as shown in Eq. 92 .

$$\mu = \frac{L_\mu - L_0}{t_\mu - \lambda} \quad (92)$$

$$L(t) = \frac{d\log_{10}(U(t))}{dt} \quad (93)$$
$$U(t) = M^{*} + M^{**}$$

$$\mu = \frac{L_\mu - L_0}{t_\mu - \lambda} \quad (93)$$

888

The pressure dependence of the inactivation rate μ for *E. coli* under isothermal conditions (30-50°C) showed a log-linear relationship. Furthermore, Doona et al. (2008) fitted the experimental data to Eq. 94 to describe the pressure-temperature effect on the kinetic constant $\mu(P,T)$. The coefficient values C_0 = 4.496±0.2007, C_T = -0.0416±0.0038, and C_P = -0.0417±0.0028 are valid only when pressure is expressed in *psi* units, but the model behavior was acceptable in the entire experimental range as observed in Fig. 8a (R^2 = 0.956).

$$-\log_{10}\mu(P,T) = C_0 + C_T \cdot T + C_P \cdot P \qquad (94)$$

The application of this secondary model was extended to predict the time (t_P) required for 6 decimal reductions in *E. coli* counts for various pressure and temperature combinations. The extended model (Eq. 95) also included the lag time (λ), and the predicted processing times to achieve log N/N_0 = -6 (t_p) were consistent with a new set of experimental conditions that were selected for validation (Fig. 8b).

$$t_P = \lambda + \frac{6}{\mu(P,T)} \qquad (95)$$

Secondary models for the enhanced quasi chemical kinetic model (EQCKM) were semi-empirical equations based on the Eyring and Arrhenius model, which were discussed in the section describing the EQCKM model.

INSERT FIGURE 8

Simultaneous pressure and temperature effects on kinetics models under dynamic conditions

During PATP, the difference in thermophysical and transport properties, and several PATP design variables (inlet fluid, vessel design, location of food samples in the pressure chamber, food product composition and geometry, etc.) affect temperature, leading to heat transfer between the food, pressurizing fluid, vessel walls and equipment surroundings (Denys et al., 2000; Hartmann and Delgado, 2002, 2003; Otero et al., 2007; Barbosa-Cánovas and Juliano, 2008; Infante et al., 2009; Knoerzer et al., 2011). Therefore, isothermal conditions are difficult to achieve even for lab-scale PATP units, influencing the interpretation and validity

of experimental observations. Experimental practices to approach quasi-adiabatic PATP conditions include: (a) isolate the sample and pressurizing fluid in a carrier with low thermal conductivity (de Heij et al., 2003; Van Scepdael et al., 2004; Wang et al., 2009; Grauwet et al., 2010; Ramaswamy et al., 2010; Shao et al., 2010; Daryaei and Balasubramaniam, 2013); (b) reduce the pressurization rate allowing more time to dissipate adiabatic heating; (c) start the kinetic study after thermal equilibrium is achieved (Ly-Nguyen et al., 2003; Van Opstal et al., 2005; Verlinde et al., 2009; Ghawi et al., 2012); and, (d) use dynamic kinetics modeling techniques to interpret the data (Ludikhuyze et al., 1997a; Ludikhuyze et al., 1998a; Peleg et al., 2012). However, these experimental approaches do not solve the need to incorporate the dynamic temperature conditions in the design of PATP process meeting desired safety and quality objectives. Therefore, fluid dynamics simulation under PATP conditions *is a must* and numerous authors had made important contributions in this field. However, an in depth coverage of studies also is beyond the scope of the current review, thus just a few examples will be examined next.

Dynamic Eyring-Arrhenius model

Ludikhuyze et al. (1997a) demonstrated that non-isobaric and non-isothermal conditions affected the predicted values of *Bacillus subtilis* α-amylase inactivation in Tris-HCl buffer (0.01 M, pH 8.6) and in a buffer-water-glycerol (15% w/w) mix. A secondary model that described the pressure and temperature dependence of the first order kinetics rate constant (k) was previously obtained under uniform pressure-temperature conditions (Eq. 96) and tested for dynamic PATP treatments (Eq. 97) (Ludikhuyze et al., 1997b). The secondary inactivation model developed under static pressure-temperature conditions clearly underestimated dynamic P-T effects and Eq. 96 parameters had to be recalculated. A new set of secondary model parameters was obtained by coupling residual activity with the corresponding pressure-temperature profiles, accurately predicting α-amylase inactivation for both static and dynamic PATP conditions (R^2 = 0.95-0.98). Additionally, the authors attempted to obtain a model combining both static and dynamic enzymatic kinetic data although the predictions registered an error between 5% and over 100% (Ludikhuyze et al., 1997a). Likewise, Ludikhuyze et

al. (1998a) came upon the same situation when validating another empirical secondary model (Eq. 55) for soybean lipoxygenase (LOX) inactivation at 0.1-650 MPa, 10-64°C).

$$k(P,T) = k_0 \cdot \exp\left\{-\left[B \cdot \left(\frac{1}{T} - \frac{1}{T_0}\right) + C \cdot (P - P_0)\right]\right\} \quad (96)$$

$$\ln \frac{A}{A_0} = \int_0^t k(P,T) \cdot dt \quad (97)$$

3-Endpoints Method

Envisioning PATP inactivation kinetics as a purely dynamic thermal process based on the 3-Endpoints method was recently proposed by Peleg et al. (2012). Measuring microbial counts and other intrinsic properties without interrupting the food treatment is not always possible. For example, a multiple vessel system run, or multiple runs with various holding times when using a single vessel system, are required to determine the kinetic effects of HPP treatments. In the case of thermal treatments, the capillary method cannot be applied for solid food matrixes and the withdrawal of samples is practically impossible (Corradini et al., 2009; Peleg et al., 2012). The 3-Endpoints method allows the estimation of inactivation model parameters using the final survival ratios ($\log_{10} S$) and their respective temperature profiles (Corradini et al., 2009). A dynamic Weibull model $\log S[T(t)]$ (Eq. 98) can be obtained as described in the following paragraphs (Peleg et al., 2005; Peleg, 2006).

$$\frac{d \log_{10} S(t)}{dt} = -b'[T(t)] \cdot n[T(t)] \cdot \left\{-\frac{\log_{10} S(t)}{b'[T(t)]}\right\}^{\frac{n[T(t)]-1}{n[T(t)]}} \quad (98)$$

An equation describing the dynamic changes in the microbial population ($S = \log N/N_0$) can be obtained by calculating the derivative of the Weibull kinetic model (Eq. 9). The process temperature can briefly assumed to remain constant at $t = t^*$ (Eq. 99-100). Thus, the slope at $t = t^*$ is equal to the instantaneous surviving population (Fig. 9), and by substituting Eq. 100 in Eq. 99 the dynamic Weibull kinetic model is obtained (Eq. 98).

$$\left|\frac{d\log_{10} S(t)}{dt}\right|_T = -b'(T)\cdot n(T)\cdot t^{n(T)-1} \qquad (99)$$

$$t^* = \left\{-\frac{\log_{10} S(t)}{b[T(t)]}\right\}^{\frac{1}{n(T)}} \qquad (100)$$

INSERT FIGURE 9

The logistic model for *b'* (*T*) described by Eq. 79 was incorporated in the dynamic Weibull model (Eq. 98) by Peleg (2012). If temperature has no effect on the shape parameter *n*, three final survival ratios (S_1, S_2, S_3) and three temperature profiles (T_1, T_2, T_3) are needed (Fig. 10) to formulate a 3 x 3 differential equation system whose solution will yield the dynamic Weibull model parameters *n*, w_c and T_c (Corradini et al., 2009). However, Peleg et al. (2012) highlighted the model impracticality when the pressure dependence of *b'* is incorporated (Eq. 80), and the difficulties to numerically solve the differential equation system when *n* can no longer be considered constant in the temperature and pressure range of interest.

INSERT FIGURE 10

Final Remarks

At present, the availability of kinetics model and data for the pressure processing of foods is still very limiting, inconsistent, and lagging behind the standardized information available for food pasteurization and sterilization by conventional thermal treatments. Parameters describing the microbial inactivation kinetics have been determined mostly only for the primary models most frequently utilized in thermal food processing, i.e., first order kinetics, Weibull and log-logistic models, whereas the Bigelow model is still the only one generally used for secondary modeling. Applications of non-linear models such as the Weibull and log-logistic equations, frequently used to describe the non-linear behavior observed typically in the pressure inactivation of enzymes, were not found.

Although a large number of empirical and phenomenological secondary models predicting pressure and temperature effects on the inactivation rate constant for

the pressure-inactivation of enzymes and microorganisms were found and are presented in this review, no general model has been developed. This may reflect the complexity of the kinetics of inactivation by pressure and the insufficiency of good-quality experimental data. Since narrow experimental ranges were consistently observed in the literature reviewed, extreme caution is recommended. The limited number of experimental conditions considered in these experiments may lead to the misinterpretation of results. Thus, kinetic studies covering 600 MPa pressure and 50°C temperature intervals, respectively, appear sufficient when evaluating the inactivation kinetics of most moderate- and high-pressure/temperature resistant microorganisms and enzymes. Moreover, the increasing availability of mathematical tools, computer software and high pressure equipment instrumentation has motivated researchers to increase the amount of dynamic kinetic model data since knowledge of the temperature gradients generated within the vessel is crucial for the assessment of PATP/PATS applications.

ACKNOWLEDGEMENT

The authors acknowledge the support from the Tecnológico de Monterrey (Research chair funds CAT 200), México's CONACYT Scholarship Program, and Formula Grants no. 2011-31200-06041 and 2012-31200-06041 from the USDA National Institute of Food and Agriculture.

Table 1. Reported values for the first order inactivation related kinetics and related models

Target	Medium	Pressure Come Up Time Holding time Depressurization Temperature	Kinetic model	Model parameters	Regression software	Reference
Aerobic bacteria	Fresh, whole, raw milk pH 6.64 7.68 x 10^7 cfu ml^{-1} inoculum	300, 400, 600 MPa 100-200 MPa s^{-1} 0-105 min NR 25°C	First order (Eq. 3) *D* value (Eq. 4)	k = 0.1643-0.7576 min^{-1} D_P = 3.04-14.03 min	SigmaPlot 8.0	(Dogan and Erkmen, 2004)
Aerobic bacteria	Fresh, filtered orange juice pH 3.35 5.71 x 10^7 cfu ml^{-1} inoculum	300, 400, 600 MPa 100-200 MPa s^{-1} 0-30 min NR 25°C	First order (Eq. 3) *D* value (Eq. 4)	k = 0.5152-1.8573 min^{-1} D_P = 1.24-4.47 min	SigmaPlot 8.0	(Dogan and Erkmen, 2004)
Aerobic bacteria	Fresh, filtered peach juice pH 5.21 5.75 x 10^7 cfu ml^{-1} inoculum	300, 400, 600 MPa 100-200 MPa s^{-1} 0-70 min NR 25°C	First order (Eq. 3) *D* value (Eq. 4)	k = 0.2357-1.0812 min^{-1} D_P = 2.13-9.77 min	SigmaPlot 8.0	(Dogan and Erkmen, 2004)

Aerobic bacterial spores	Deionized water *B. amyloliquefaciens* TMW 2.479 Fad 82 *B. amyloliquefaciens* TMW 2.482 Fad 11/2 *B. sphaericus* NZ 14 *B. amyloliquefaciens* ATCC 49763	700 MPa 0.58 min 0-5 min NR 105, 121°C	*D* value (Eq. 4)	D_P = 0.30-0.60 min (105°C) D_P = 0.10-0.50 min (121°C)	Microcal Origin 7.5	(Ahn et al., 2007)
Anaerobic bacterial spores	Deionized water *C. sporogenes* ATCC 7955 *C. tyrobutylicum* ATCC 27384 *T. thermosaccharolyticum* ATCC 27384	700 MPa 0.58 min 0-5 min NR 105, 121°C	*D* value (Eq. 4)	D_P = 0.20-0.60 min (105°C) D_P = 0.30 min (121°C)	Microcal Origin 7.5	(Ahn et al., 2007)
Bacillus stearothermophilus spores	Egg Defrosted egg patties 10^6 spores g^{-1} inoculum	400, 600, 700 MPa 1.9-2.4 min 0-16 min NR 105.8±0.6°C	*D* value (Eq. 4)	D_P = 0.41-0.72 min	SAS	(Rajan et al., 2006)
Escherichia coli	Fresh extracted carrot juice pH 6.6 K-12 strain MG1655 10^9 cfu ml^{-1} inoculum	200, 250, 300, 350, 400, 450, 500, 550, 600 MPa 100 MPa min^{-1} 0-60 min NR 5-45°C	*D* value (Eq. 4)	D_P = 2.00-188.00 min	SAS online DOC 8.01	(Van Opstal et al., 2005)

Listeria monocytogenes	Fresh, whole, raw milk pH 6.64 7.48 x 10^7 cfu ml^{-1} inoculum	300, 400, 600 MPa 100-200 MPa s^{-1} 0-105 min NR 25°C	First order (Eq. 3) *D* value (Eq. 4)	k = 0.2096-0.9477 min^{-1} D_P = 2.43-10.99 min	SigmaPlot 8.0	(Dogan and Erkmen, 2004)
Listeria monocytogenes	Fresh, filtered orange juice pH 3.35 2.93 x 10^7 cfu ml^{-1} inoculum	300, 400, 600 MPa 100-200 MPa s^{-1} 0-30 min NR 25°C	First order (Eq. 3) *D* value (Eq. 4)	k = 0.8024-2.6471 min^{-1} D_P = 0.87-2.87 min	SigmaPlot 8.0	(Dogan and Erkmen, 2004)
Listeria monocytogenes	Fresh, filtered peach juice pH 5.21 2.95 x 10^7 cfu ml^{-1} inoculum	300, 400, 600 MPa 100-200 MPa s^{-1} 0-70 min NR 25°C	First order (Eq. 3) *D* value (Eq. 4)	k = 0.3733-1.5151 min^{-1} D_P = 1.52-6.17 min	SigmaPlot 8.0	(Dogan and Erkmen, 2004)
Native microflora	Unpasteurized Hamlin variety orange juice pH 3.7, 10.7°Brix	350, 400, 450, 500 MPa 45-60 s 1-300 s NR 25±5°C	First order (Eq. 3) *D* value (Eq. 4)	k = 0.0002-0.0064 min^{-1} D_P = 0.05-1.32 min	NR	(Parish, 1998)

Saccharomyces cerevisae ascospores	Commercial pasteurized orange juice 10^5 cfu ml^{-1} inoculum	350, 400, 450, 500 MPa 45-60 s 1-300 s NR 25±5°C	First order (Eq. 3) *D* value (Eq. 4)	k = 0.0002-0.041 min^{-1} D_P = 0.07-1.27 min	NR	(Parish, 1998)
Saccharomyces cerevisae vegetative cells	Commercial pasteurized orange juice 10^5 cfu ml^{-1} inoculum Several strains	350, 400, 450, 500 MPa 45-60 s 1-300 s NR 25±5°C	First order (Eq. 3) *D* value (Eq. 4)	k = 0.0005-0.0137 min^{-1} D_P = 0.02-0.63 min	NR	(Parish, 1998)
Vibrio cholerae	Phosphate-buffered saline 10^8 cfu ml^{-1} inoculum Several strains	200-250 MPa 55-80 s 0-240 s <2 s 8-10°C (initial)	*D* value (Eq. 4)	D_P = 2.10-3.38 min (200 MPa) D_P = 0.60-0.82 min (250 MPa)	Microsoft Excel	(Cook, 2003)
Vibrio parahaemolyticus	Phosphate-buffered saline 10^8 cfu ml^{-1} inoculum Several strains	200-250 MPa 55-80 s 0-240 s <2 s 8-10°C (initial)	*D* value (Eq. 4)	D_P = 0.88-2.78 min (200 MPa) D_P = 0.26-0.60 min (250 MPa)	Microsoft Excel	(Cook, 2003)

Vibrio vulnificus	Phosphate-buffered saline 10^8 cfu ml^{-1} inoculum Several strains	200-250 MPa 55-80 s 0-240 s <2 s 8-10°C (initial)	*D* value (Eq. 4)	D_P = 0.28-0.62 min (200 MPa)	Microsoft Excel	(Cook, 2003)

Table 2. Reported parameters for the primary Weibull model describing HPP inactivation kinetics.

Target	**Medium**	**Pressure** **Come Up Time** **Holding time** **Depressurization** **Temperature**	**Model parameters**	**Regression software**	**Reference**
Aerobic bacterial spores	Deionized water *B. amyloliquefaciens* TMW 2.479 Fad 82 *B. amyloliquefaciens* TMW 2.482 Fad 11/2 *B. sphaericus* NZ 14 *B. amyloliquefaciens* ATCC 49763	700 MPa 0.58 min 0-5 min NR 105, 121°C	b' = 1.5-3.1 (105°C); 2.1-6.5 (121°C) n = 0.2-0.5 (105°C); 0.3-1.0 (121°C)	Microcal Origin 7.5	(Ahn et al., 2007)
Anaerobic bacterial spores	Deionized water *C. sporogenes* ATCC 7955 *C. tyrobutylicum* ATCC 27384 *T. thermosaccharolyticum* ATCC 27384	700 MPa 0.58 min 0-5 min NR 105, 121°C	b' = 1.5-3.2 (105°C); 1.7-2.8 (121°C) n = 0.2-0.5 (105°C); 0.5-0.7 (121°C)	Microcal Origin 7.5	(Ahn et al., 2007)
Bacillus coagulans spores	Phosphate buffer (100 mM, pH 6.7) 10^6 cfu ml^{-1} inoculum IFFI 10144 strain	400-600MPa 3.1-4.6 min 0-30 min NR 70-80°C (initial temperature)	b' = 1.977-2.622 (70°C); 1.553-3.447 (80°C) n = 0.160-0.207 (70°C); 0.124-0.260 (80°C)	SPSS 13.0	(Wang et al., 2009)

Bacillus stearothermophilus spores	Egg Defrost egg patties 10^6 spores g^{-1} inoculum	400, 600, 700 MPa 1.9-2.4 min 0-16 min NR 105.8±0.6°C	*b′* = 1.30-1.96 *n* = 0.30-0.54	SAS	(Rajan et al., 2006)
Escherichia coli	Whey protein surrogate food system ATCC 11229 strain	207-439 MPa NR 0-300 min NR 30, 40, 50 °C	*b′* = $2.7x10^{-8}$-0.482 (30°C); $4.0x10^{-4}$-2.161 (40°C); $3.0x10^{-3}$-2.653 (50°C) *n* = 0.70-3.37 (30°C); 0.36-2.24 (40°C); 0.48-1.81 (50°C)	NR	(Doona et al., 2008)
Escherichia coli	UHT whole milk pH 6.64 10^8 cfu ml^{-1} inoculum ATCC 11775 strain	400, 450, 500, 550, 600 MPa 300 MPa min^{-1} 0-80 min 300 MPa min^{-1} 22°C	*b′* = 1.2-10.5 *n* = 0.78	SigmaPlot 2000 6.0	(Buzrul et al., 2008)
Listeria innocua	UHT whole milk pH 6.64 10^8 cfu ml^{-1} inoculum ATCC 33090 strain	400, 450, 500, 550, 600 MPa 300 MPa min^{-1} 0-80 min 300 MPa min^{-1} 22°C	*b′* = 1.1-12.2 *n* = 0.79	SigmaPlot 2000 6.0	(Buzrul et al., 2008)

Listeria innocua	Peptone solution 0.1% CDW47 strain 10^8-10^9 cfu ml^{-1} inoculum	138, 207, 276, 345 MPa 300 MPa min^{-1} 0-30 min <1 min 25, 35, 45, 50°C	*b'* = 0.09-0.21 (25°C); 0.01-0.03 (35°C); 0.002-2.12 (45°C); 0.19-4.38 (50°C) *n* = 0.45-0.79 (25°C); 0.64-1.26 (35°C); 0.35-1.87 (45°C); 0.23-1.14 (50°C)	SigmaPlot 2000 6.0	(Buzrul and Alpas, 2004)
Yersinia enterocolitica	UHT whole milk pH 6.70 5 x 10^8 cfu ml^{-1} inoculum ATCC 35669 strain	400-500 MPa	*b'* = 0.66 (400 MPa); 1.13 (500 MPa) *Calculated from linear approach *n* = 0.583	SAS 8.2	(Chen and Hoover, 2003a)

Table 3. Reported parameters for the primary log-logistic model describing HPP inactivation kinetics.

Target	Medium	Pressure Come Up Time Holding time Depressurization Temperature	Kinetic model	Model parameters	Regression software	Reference
Bacillus coagulans spores	Phosphate buffer 100 mM, pH 6.7 10^6 cfu ml^{-1} inoculum IFFI 10144 strain	400-600MPa 3.1-4.6 min 0-30 min NR 70-80°C (initial temperature)	3 parameter (Eq. 23)	H = -(4.611-18.848) 70°C H = -(4.754-5.938) 80°C Ω = -(1.871-2.074) 70°C Ω = -(1.726-2.953) 80°C τ = 0.449-3.956 (70°C) τ = 0.011-1.049 (80°C)	SPSS 13.0	(Wang et al., 2009)
Listeria innocua	Peptone solution 0.1% CDW47 strain 10^8-10^9 cfu ml^{-1} inoculum	138, 207, 276, 345 MPa 300 MPa min^{-1} 0-30 min <1 min 25, 35, 45, 50°C	3 parameter (Eq. 23)	H = -(4.92-23.39) 25°C H = -(2.89-15.08) 35°C H = -(1.26-56.24) 45°C H = -(1.37-39.71) 50°C Ω = NR τ = NR	SigmaPlot 2000 6.0	(Buzrul and Alpas, 2004)

Yersinia enterocolitica	UHT whole milk pH 6.70 5 x 10^8 cfu ml^{-1} inoculum ATCC 35669 strain	350-500 MPa	3 parameter (Eq. 23)	H = -(9.878-27.884) Ω = -(7.748-11.199) τ = 1.478-2.100	SAS 8.2	(Chen and Hoover, 2003a)
Yersinia enterocolitica	UHT whole milk pH 6.70 5 x 10^8 cfu ml^{-1} inoculum ATCC 35669 strain	350-500 MPa	2 parameter (Eq. 24)	H = -14 Ω = -(6.944-10.324) τ = 1.380-1.989	SAS 8.2	(Chen and Hoover, 2003a)

Table 4. Reported parameters for an attempted global Bigelow secondary model. Modified from Santillana Farakos and Zwietering (2011).

Microorganism	***D samples***	***P range (MPa)***	***T range (°C)***	R^2_{adj}	z_P	z_T	**log** $D_{PrefTref}$	P_{ref} **(MPa)**	T_{ref} **(°C)**
Bacillus spp. spores	48	100-700	45-121	0.86	614.7±122.9	45.2±6.5	0.27±0.25	400	100
Clostridium spp. spores	54	600-900	80-121	0.88	616.3±106.3	20.4±1.1	0.85±0.36	400	100
Cronobacter spp.	24	200-600	22-25	0.78	368.2±39.4	NR	-0.19±0.13	400	NR
Escherichia coli	117	100-700	2-50	0.30	385.6±53.2	97.5±45.2	0.88±0.23	400	30
Listeria spp.	74	200-700	2-50	0.61	298.9±34.6	38.6±7.5	0.56±0.18	400	30
Vibrio spp.	80	69-345	10-25	0.61	206.9±32.0	-18.4±2.3	0.06±0.20	400	30
Zygosaccharomyces bailii	48	100-400	-5-45	0.71	91.0±8.4	141-7±58.6	-0.84±0.24	400	30

Table 5, Reported parameters for the secondary Eyring-Arrhenius related models and its variants.

Target	**Medium**	**Pressure** **Come Up Time** **Holding time** **Depressurization** **Temperature**	**Kinetic model**	**Model parameters**	**Regression software**	**Reference**
Alkaline phosphatase	Bovine milk	0.1-725 MPa 100 MPa min^{-1} 14-300 min NR 25-63°C	Decimal reduction time empirical model (Eq. 72)	c_1 = 3.33±0.16 c_2 = (3.88±0.77)*10^{-3} c_3 = (-1.05±0.09)*10^{-5} c_4 = 4.88±0.02 c_5 = (5.3±0.90) *10^{-2} c_6 = (-2.7±0.7) *10^{-8} T_{ref} = 323 K	SAS	(Ludikhuyze et al., 2000)
Lactobacillus brevis	Orange juice Greek Valencia variety pH 3.8, 11.6°Brix	100-500 MPa NR 0-30 min NR 20-40°C	Eyring-Arrhenius decimal reduction times (Eq. 68)	$D_{refP,T}$ = 3.42±0.51 min^{-1} P_{ref} = 300 MPa T_{ref} = 303 K z_T = 23.8±1.4 °C z_P = 94.7±7.8 MPa a = -0.009±0.001 MPa^{-1}	SYSTAT 8.0 Least squares regression analysis	(Katsaros et al., 2010)

Lactobacillus plantarum	Orange juice Greek Valencia variety pH 3.8, 11.6°Brix	100-500 MPa NR 0-30 min NR 20-40°C	Eyring-Arrhenius decimal reduction times (Eq. 68)	$D_{refP,T}$ = 1.32±0.11 min^{-1} P_{ref} = 300 MPa T_{ref} = 303 K z_T = 18.8±1.3 °C z_P = 95.0±11 MPa a = -0.013±0.002 MPa^{-1}	SYSTAT 8.0 Least squares regression analysis	(Katsaros et al., 2010)
Lipoxygenase (LOX)	Tris-HCl buffer (0.01 M, pH 9) Commercial lyophilized soybean type B LOX	50-650 MPa 100 MPa min^{-1} NR NR 10-64°C	Empirical Eyring Arrhenius (Eq. 55)	c_1 = -3.12±0.28 c_2 = (-1.39±0.18)*10^{-1} c_3 = (2.66±0.27)*10^{-3} c_4 = -15.6±1.4 c_5 = (7.1±0.28) *10^{-2}	SAS	(Ludikhuyze et al., 1998b, a)
Pectinmethylesterase (PME)	Orange juice Greek Valencia variety pH 3.8, 11.6°Brix	100-500 MPa NR 0-30 min NR 20-40°C	Eyring-Arrhenius (Eq. 47)	$k_{refP,T}$ = 0.582±0.048 min^{-1} P_{ref} = 300 MPa T_{ref} = 308 K E_{aP} = 95±11 KJ mol^{-1} $V_T^{\neq}$ =-30±5 cm^3 mol^{-1} a = 0.64±0.07 cm^3 mol^{-1} K^{-1} g = -0.002±0.0003 MPa^{-1}	SYSTAT 8.0 Least squares regression analysis	(Katsaros et al., 2010)

Pectinmethylesterase (PME)	Orange juice Navel variety (*Citrus sinesis*)	100-800 MPa NR 0-30 min NR 30-60°C	Eyring-Arrhenius (Eq. 47)	$k_{refP,T}$ = 1.76 min^{-1} P_{ref} = 600 MPa T_{ref} = 323 K E_{aP} = 148 KJ/mol $V_T^{\neq}$ =-25.1 cm^3mol^{-1} a = 0.703 $cm^3\ mol^{-1}\ K^{-1}$ g = 8.374 x 10^{-4} MPa^{-1} * Valid in 40-60°C range only due to enzyme reactivation at T < 40°C	SYSTAT	(Polydera et al., 2004)
Pectinmethylesterase (PME)	Deionized water (pH 4.5) Commercial orange peel PME 0.4 mg PME powder per ml of buffer	50-900 MPa NR 20-220 min NR 15-82°C	Empirical Eyring Arrhenius (Eq. 52)	c_1 = -1.88±0.10 c_2 = (-17.55±1.09)*10^{-3} c_3 = (53.27±3.26)*10^{-6} c_4 = (-35.95±2.79) *10^{-9} c_5 = 352.12±18.55 c_6 = 0.348±0.027	NR	(Van den Broeck et al., 2000)
Pectinmethylesterase (PME)	Citric acid buffer 5 mM, pH 3.7 Lyophilized orange pulp PME extract Navel variety 2.0 mg PME powder per ml of buffer	50-900 MPa NR 20-220 min NR 15-82°C	Empirical Eyring Arrhenius (Eq. 52)	c_1 = -2.39±0.17 c_2 = (-19.00±1.83)*10^{-3} c_3 = (55.20±5.94)*10^{-6} c_4 = (-38.50±5.35) *10^{-9} c_5 = 193.44±22.89 c_6 = 0.248±0.036	NR	(Van den Broeck et al., 2000)

Polyphenoloxidase (PPO)	Phosphate buffer (pH 7; 0.1 M) Lyophilized avocado PPO powder 0.5 mg PPO powder per ml of buffer	0.1-900 MPa NR 35-180 min NR 25-77.5°C	Empirical Eyring Arrhenius (Eq. 51)	c_1 = -2.42±0.07 c_2 = (-17.2±0.7)*10^{-3} c_3 = (41.1±1.8)*10^{-6} c_4 = (-23.3±1.3) *10^{-9} c_5 = (-16.8±0.6) *10^{-4} E_{aP} = 342.30±11.63 KJ mol^{-1}	NR	(Weemaes et al., 1998b)
Saccharomyces cerevisae	0.85% NaCl solution 8.0 x 10^6-1.0 x 10^7 cfu ml^{-1} inoculum at stationary phase IFO 0234 strain	120-300 MPa 2 min 0-40 min 30 s (-20)-50°C	Quadratic model (Eq. 70)	c_1 = -4.26 c_2 = 1.25*10^{-2} c_3 = -3.37*10^{-2} c_4 = 8.55*10^{-6} c_5 = -7.55*10^{-5} c_6 = 1.42*10^{-3} P_{ref} = 0.1 MPa T_{ref} = 273 K	NR	(Hashizume et al., 1995)
Zygosaccharomyces bailii	Tris-HCl buffer 40mM, pH 6.5 CBS 109	120-320 MPa 100 MPa min^{-1} 0-60 min NR (-5)-45°C	Reduced Quadratic model (Eq. 71)	c_1 = 1.55±0.04 c_2 = -(15.05±0.49)*10^{-3} c_3 = -(24.05±1.53) *10^{-3} c_4 = (23.52±6.63) *10^{-6} c_5 = -(16.42±1.01)*10^{-4} P_{ref} = 220 MPa T_{ref} = 293 K	SAS	(Reyns et al., 2000)

Table 6. Reported parameters for the secondary Hawley thermodynamic model and its variants.

Target	Medium	Pressure Come Up Time Holding time Depressurization Temperature	Kinetic model	Model parameters	Regression software	Reference
Chymotrypsinogen	Aqueous solution, pH 2.07	0.1-700 MPa NR NR NR 8.5-70°C	Thermodynamic model (Eq. 73)	$\Delta\beta$ = -0.296 cm^6 J^{-1} mol^{-1} $\Delta V^{\neq}_{ref}$ = -14.3 cm^3 mol^{-1} ΔS_{ref} = 950 J mol^{-1} K^{-1} $\Delta\alpha$ = 1.32 cm^3 mol^{-1} K^{-1} ΔC_p = 15,900 J mol^{-1} *ln k_{ref} = -4.66 P_{ref} = 0.1 MPa T_{ref} = 273 K *Calculated from reported ΔG^0	NR	(Hawley, 1971)

Lipoxygenase (LOX)	Green pea juice	0.1-625 MPa 100-125 MPa min^{-1} 0.1-625 MPa NR (-15)-70°C	Thermodynamic model (Eq. 75)	$\Delta\beta$ = -(0.0937±0.0192) cm^6 J^{-1} mol^{-1} $\Delta V^{\neq}_{ref}$ = -(38.18±3.37) cm^3 mol^{-1} ΔS_{ref} = 13.79±11.78 J $mol^{-1}K^{-1}$ $\Delta\alpha$ = -(0.12±0.09) cm^3 $mol^{-1}K^{-1}$ ΔC_p = 1,837.4±244.0 J mol^{-1} ln k_{ref} = -3.71 P_{ref} = 500 MPa T_{ref} = 298 K	SAS	(Indrawati et al., 2001)
Lipoxygenase (LOX)	Green pea	0.1-625 MPa 100-125 MPa min^{-1} 0.1-625 MPa NR (-10)-70°C	Thermodynamic model (Eq. 75)	$\Delta\beta$ = -(0.1382±0.0406) cm^6 J^{-1} mol^{-1} $\Delta V^{\neq}_{ref}$ = -(50-76±7.37) cm^3 mol^{-1} ΔS_{ref} = 21.19±25.69 J mol^{-1} K^{-1} $\Delta\alpha$ = -(0.23±0.20) cm^3 mol^{-1} K^{-1} ΔC_p = 1,058.6±375.0 J mol^{-1} ln k_{ref} = -2.85 P_{ref} = 500 MPa T_{ref} = 298 K	SAS	(Indrawati et al., 2001)

Lipoxygenase (LOX)	Tris-HCl buffer 0.1 M, pH 9 Lyophilized soybean LOX powder 0.4 mg enzyme powder per ml of buffer	0.1-625 MPa 100-125 MPa min^{-1} 0.1-625 MPa NR (-10)-70°C	Thermodynamic model (Eq. 75)	$\Delta\beta$ = -(0.1382±0.0406) $cm^6\ J^{-1}\ mol^{-1}$ $\Delta V^{\neq}_{ref}$ = -(50-76±7.37) $cm^3\ mol^{-1}$ ΔS_{ref} = 21.19±25.69 J $mol^{-1}\ K^{-1}$ $\Delta\alpha$ = -(0.23±0.20) $cm^3\ mol^{-1}\ K^{-1}$ ΔC_p = 1,058.6±375.0 J mol^{-1} ln k_{ref} = -2.85 P_{ref} = 0.5 MPa T_{ref} = 298 K	SAS	(Indrawati et al., 1999)
Pectinmethylesterase (PME)	Tris-HCl buffer 20 mM, pH 7.0 Carrot PME extract	100-825 MPa 100 MPa min^{-1} 0-250 min NR 10-65°C	Thermodynamic model (Eq. 75)	$\Delta\beta$ = -(1.40±1.06) $cm^6\ J^{-1}\ mol^{-1}$ $\Delta V^{\neq}_{ref}$ = -(341.95±22.21) $cm^3\ mol^{-1}$ ΔS_{ref} = -20.65±7.20 J $mol^{-1}\ K^{-1}$ $\Delta\alpha$ = 3.20±0.26) $cm^3\ mol^{-1}\ K^{-1}$ ΔC_p = 3,046.6±207.2 J mol^{-1} ln k_{ref} = -4.36 P_{ref} = 700 MPa T_{ref} = 323 K	NR	(Ly-Nguyen et al., 2003)

Pectinmethylesterase (PME)	Tris-HCl buffer 20 mM, pH 7.0 Carrot PME extract	100-825 MPa 100 MPa min^{-1} 0-250 min NR 10-65°C	Extended thermodynamic model (Eq. 76-77)	$\Delta\beta$ = -(0.0307±0.03467) cm^6 J^{-1} mol^{-1} $\Delta V^{\neq}_{ref}$ = -(41.64±2.70) cm^3 mol^{-1} ΔS_{ref} = 148.3±24.01 J mol^{-1} K^{-1} $\Delta\alpha$ = -(0.0415±0.0967) cm^3 mol^{-1} K^{-1} ΔC_p = 4,573.9±1306.7 J mol^{-1} ln k_{ref} = -2.70 $\Delta\beta_2$ = -(0.00012±0.00004) [cm^6 J^{-1} mol^{-1}]^2 $\Delta\alpha_2$ = 0.00026±0.00015 [cm^3 mol^{-1} K^{-1}]^2 ΔC_{p2} = 88.02±28.94[J mol^{-1}]^2 P_{ref} = 700 MPa T_{ref} = 323 K	NR	(Ly-Nguyen et al., 2003)
Polygalacturonase (PG)	Sodium acetate buffer 40 mM, pH 4.4 Tomato PG extract	300-600 MPa 100 MPa min^{-1} 0-200 min NR 5-50°C	Reduced thermodynamic model (Eq. 78)	$\Delta V^{\neq}_{ref}$ = -(55.69±2.95) cm^3 mol^{-1} ΔS_{ref} = 265.28±18.14 J mol^{-1} K^{-1} $\Delta\alpha$ = -(1.029±0.15) cm^3 mol^{-1} K^{-1} ln k_{ref} = -3.26 P_{ref} = 400 MPa T_{ref} = 298 K	SAS	(Fachin et al., 2002)

Table 7 Reported simultaneous effect of pressure and temperature on the Weibull model parameters that describe PATP kinetics.

Target	Medium	**Pressure** **Come Up Time** **Holding time** **Depressurization** **Temperature**	Kinetic model	Model parameters	Regression software	Reference
Escherichia coli	Peptone water 0.1%, pH 6.95 10^7 cfu ml^{-1} O157:H7 933 strain Stationary phase	200-400 MPa 400 MPa min^{-1} 5-40 min >20 s 40°C	Weibull parameter *n* inverse (Eq. 85)	n_{ref} = 0.4±0.08 a = 125.5±10.2 MPa	SigmaPlot 2000 v. 6.00	(Pilavtepe-Çelik et al., 2009)
Escherichia coli	Whey protein surrogate food system ATCC 11229 strain	207-439 MPa NR 0-300 min NR 30, 40, 50 °C	Weibull (Eq. 80, 86)	P_c = 357-458 MPa (30-50°C) w_P = 0.026-0.042 1/MPa (30-50°C) d_{0P} = 5.7-43.3 (30-50°C) d_{1P} = 0.00039-0.00077 (30-50°C)	NR	(Doona et al., 2008)
Lactobacillus plantarum	Fresh clementine mandarin (*Citrus reticula*, variety *Nules*) juice $2x10^8$ cfu ml^{-1} inoculum	0-450 MPa 90 sec 10-60 sec 15 sec 15, 30, 45°C (initial)	Pressure dependent Weibull biphasic model (Eq. 91)	f_P = 128-335 MPa (15-45°C) n = 2.41-7.55 (15-45°C)	Statgraphics Centurion XV	(Carreño et al., 2011)

Lactobacillus plantarum	Mandarin juice Clementine mandarin (*Citrus reticula*, commercial variety *Nules*) Fresh juice $2x10^8$ cfu ml^{-1} inoculum	0-450 MPa 90 s 10-60 s 15 s 15, 30, 45°C (initial)	Pressure dependent Weibull biphasic model (Eq. 91)	Ψ = 2.56-3.08 (15-45°C) f_{P1} = 128-335 MPa (15-45°C) f_{P2} = 445-668 MPa (15-45°C) n = 3.28-6.00 (15-45°C)	Statgraphics Centurion XV	(Carreño et al., 2011)
Staphylococcus aureus	Carrot juice (pH 6.22) Fresh, squeezed juice 10^7 cfu ml^{-1} 485 strain Stationary phase	200-400 MPa 400 MPa min^{-1} 5-40 min >20 s 40°C	Weibull parameter n inverse (Eq. 85)	n_{ref} = 0.6±0.1 a = 230.4±65.4 MPa	SigmaPlot 2000 6.00	(Pilavtepe-Çelik et al., 2009)
Staphylococcus aureus	Peptone water 0.1%, pH 6.95 10^7 cfu ml^{-1} 485 strain Stationary phase	200-400 MPa 400 MPa min^{-1} 5-40 min >20 s 40°C	Weibull parameter n inverse (Eq. 85)	n_{ref} = 0.6±0.06 a = 332.5±50.1 MPa	SigmaPlot 2000 6.00	(Pilavtepe-Çelik et al., 2009)

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