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# Principal factors affecting the yield of Dilute Acid Pretreatment of lignocellulosic biomass : a critical review

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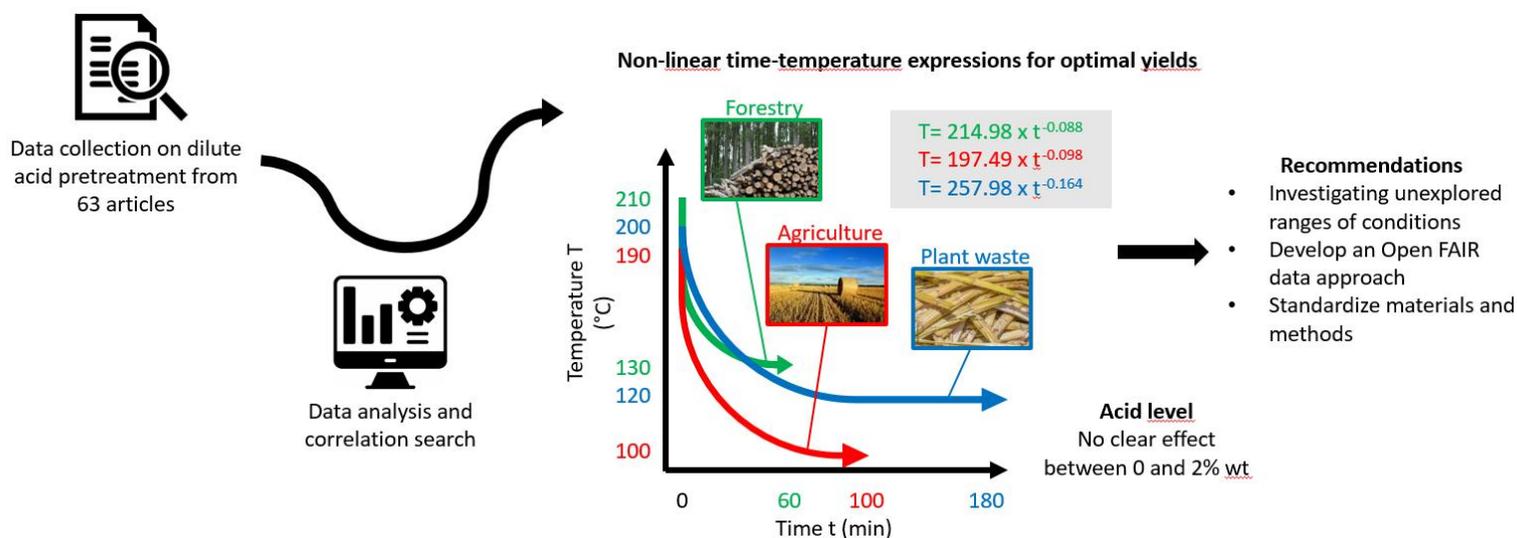
## Highlights

- Data on dilute acid pretreatment (DAP) of biomasses were aggregated from 63 papers.
- Most DAP studies are in the ranges 0–30min (70%), 100–200°C (83%) and 0%–2% (70%).
- The negative time-temperature relationship is not correlated with acid levels.
- The time-temperature equivalences are quantified by nonlinear formulas.
- Materials and methods standardization are needed to limit the variability of data.

## Abstract

This review provides a critical analysis of the state of the art of dilute acid pretreatment applied to lignocellulosic biomass. Data from 63 publications were extracted and analysed. The majority of the papers used residence times of less than 30 min, temperature ranges from 100°C to 200°C, and acid levels between 0% and 2%. Yields are quantified directly after pretreatment (xylose content) or after enzymatic hydrolysis (glucose content). Statistical analyses allowed the time-temperature equivalence to be quantified for three types of biomass: they were formulated by non-linear expressions. In further works, investigating less explored areas, for example moderate temperature levels with longer residence times, is recommended. Pretreatment material (time-temperature kinetics, reactor type) and analytical

methods should be standardized and better described. It becomes mandatory to promote the development of an open, findable, accessible, interoperable, and reusable data approach for pretreatments research.



## Keywords

Biorefinery, optimization, enzymatic hydrolysis, non-linear regression, data analysis

## 1. Introduction

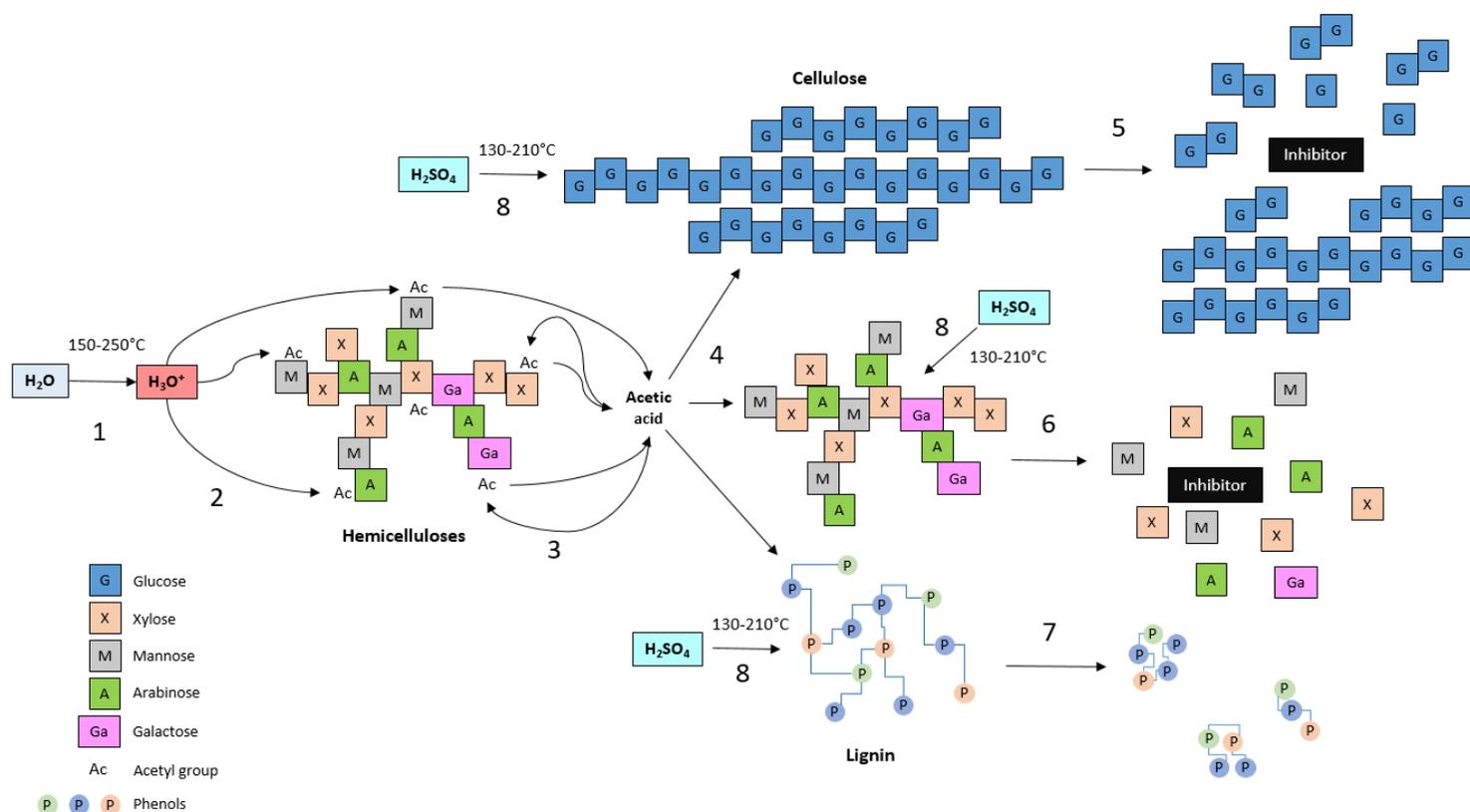
In order to tackle global warming, biomass of plant origin represents an important renewable feedstock from agriculture (dedicated crops or residues), forestry (dedicated trees, forestry operations, wood transformation plants), and other sources, such as household plant wastes. Lignocellulosic biomass (LB), the building block of plant architecture, is mainly composed of cellulose, hemicelluloses, and lignins. Cellulose consists of a linear  $\beta$ -D-(1  $\rightarrow$  4)-glucopyranosyl chain, with a variable degree of polymerization of up to

10,000 and the ability to form elongated crystalline structures, called microfibrills. Cellulose microfibrills are cast in a matrix of hemicelluloses, composed of a mixture of branched pentose and hexose units (mainly xylose and mannose). Lignins, complex arrangements of polyphenols, form heterogeneous aromatic macromolecules surrounding cellulose and hemicelluloses. Each of these bio-polymers can be valorized in chemical, materials, and energy by several transformation pathways, such as fermentation for

example (McIntosh et al., 2014; Mesa et al., 2017).

LB thus offers an enormous potential, but a major problem, called recalcitrance, arises for some transformation routes. Recalcitrance refers to the resistance to enzymatic and microbial degradation, that results from the complex combination of chemical, physical, and ultra-structural organisation of LB (Pu et al., 2013). Consequently, the challenge of the transformation processes is to overcome recalcitrance by applying various types of treatments before the

enzymatic hydrolysis, known as pretreatments (Beig et al., 2021). Four principal types of pretreatment exist: physical, physico-chemical, chemical and biological. Each has advantages and limitations, which have been extensively described in the literature in recent years (Alvira et al., 2010; Beig et al., 2021; Mankar et al., 2021; Saravanan et al., 2022; Yoo et al., 2020; Zhou et al., 2021). The challenge however comes from the numerous parameters that must be considered to tackle recalcitrance and subsequently propose a reliable process at the industrial scale (Beig et al., 2021).



**Figure 1. Autohydrolysis and DAP of LB.** 1: dissociation of the water under high temperature; 2: attack of  $H_3O^+$  ions on acetyl groups and formation of acetic acid; 3: retroactive attack of acetic acid on remaining acetyl groups; 4: a drop in pH causes

*degradation of the components of the LB; 5: decrystallization, microfibrils swelling, and partial depolymerization of cellulose; 6: depolymerization of hemicellulose and formation of monosaccharides and inhibitor (HMF, furfural); 7: delignification and redistribution of lignin in a more condensed form; 8: Using H<sub>2</sub>SO<sub>4</sub> to avoid steps 1, 2, 3, and 4, and excessively high temperatures.*

Among the most promising pretreatments, dilute acid pretreatment (DAP) presents high efficiency at the industrial level and significant economic attractiveness (Baral & Shah, 2017; Cao et al., 2012; Herbaut et al., 2018; Hoang et al., 2021; Vasconcelos et al., 2020), which motivated the present review. DAP is an improvement of the hydrothermal pretreatment, obtained by diluting an acid in the aqueous solution, and thus directly starting the depolymerization of hemicelluloses without autohydrolysis (Mosier, 2013) (Figure 1). Lignins alteration is also observed, with a redistribution of lignin in a more condensed form (Lancha et al., 2021b; Pu et al., 2013). Then, cellulose becomes more accessible and undergoes several transformations: decrystallization, microfibrils swelling, depolymerization, and finally, formation of monosaccharides (Zhou et al., 2021). This process results in the formation of various compounds starting from oligosaccharides and monosaccharides, along with a wider range of oxygenated compounds including inhibitors such as furfural and HMF (5-hydroxymethyl-furfural) (Beig et al., 2021; Lancha et al., 2020). Formation of

pseudo-lignin can also occur through reactions between polysaccharides and lignin, which inhibits the action of enzymes even more than simple lignin (Auxenfans et al., 2017; Pu et al., 2013; Sheng et al., 2021).

Due to the interest in DAP, several companies have been involved in the development of an industrial process for the production of second-generation (2G) ethanol in recent years: NextChem in Italy, Chempolis in Finland, Ethtec in Australia, and Procethol 2G in France. Some industrial plants are already operational, for example in Brazil, a pioneer country in this field, with Raizen and GranBio (Carpio et al., 2021). However, despite the intense efforts to create industrially viable biorefinery processes, the technology is not yet consolidated and needs further studies to improve its profitability (Baral & Shah, 2017). It is recognized that a significant part of this additional cost comes from biomass feedstock and capital expenditures directly related to pretreatment (Brown et al., 2020). To improve the pretreatment step, optimization studies on DAP are necessary and have received continuous attention from many research teams (Baral

& Shah, 2017; Carpio et al., 2021; Chen et al., 2021; Vieira et al., 2020). To date, however, no comprehensive reviews have proposed a critical analysis of the scientific papers. The objective of this review is therefore to bring together these studies in order to provide an overview and key guidance, in the form of mathematical expressions, for biomass valorization under DAP conditions. To that purpose, this

review is organized in three complementary parts: (1) collecting data from literature considering process conditions and optimal yields, (2) analyzing these data to seek relationships between factors and optimal performance that can be used as guidance, (3) highlighting gaps in the literature to guide future research.

## 2. Data collection and statistical analyses

### 2.1. Data collection

The data collected for this study includes a literature analysis of 63 peer-reviewed papers on DAP. These articles were obtained on the Web of Science platform, using different keywords and their variations : dilute acid, pretreatment, biomass, lignocellulose, statistic, optimization, response surface methodology (RSM), central composite design (CCD). The exact research equation, applied to the "Topic" category of the Web of Science, takes the following form: "Dilute acid" AND \*treatment\* AND (Biomass OR Lignocellulos\*) AND (Statistic\* OR Optimi\* OR RSM OR CCD OR "Response Surface"). All were considered for the study of factors influencing DAP and 51 were examined for optimization studies (Table 1). This distinction was made as some studies use

several combined pretreatments, which biases the results of the DAP (steam explosion, alkali). Moreover, some publications do not contain an optimization study. These papers were published between 1992 and 2021: 25% before 2011, 50% before 2014, and 75% before 2017. The publication time range provides a general view of all studies carried out over the past 30 years, with an emphasis on 2011 to 2021.

Many types of LB species are investigated in these publications. The types of LB have been sorted according to three origin levels: (1) forest with trunks and branches (poplar, maple, olive tree, spruce, etc.), (2) agriculture with straw and stalk (switchgrass, rice, barley, wheat, corn, cotton), (3) industry with pulp, seed and bagasse (sugarcane, beet). The industrial category also includes all wastes

from the food and textile industries. Several criteria are used by the authors to quantify the quality of DAP. These criteria have been grouped into four types to express the yield of LB conversion after DAP. Pretreatment only (PRT) represents the content of xylose obtained in the liquid fraction after DAP relative to the content of xylan in the raw material. Enzymatic hydrolysis only (ENZ) represent the content of glucose obtained after enzymatic hydrolysis relative to the content of glucan in the pretreated material.

**Table 1: Data on DAP collected from the literature.** *nd: data not found/imprecise (optimum on a single condition considered imprecise). Bold reference : Use of DOE and/or RSM methods. PRT : Pretreatment only; ENZ : Enzymatic hydrolysis only; PRT+ENZ : Pretreatment followed by enzymatic hydrolysis; FER : Fermentation.*

Biomass	Levels of factors explored			Optimal conditions and associated yields					Year	Reference
	Time (min)	Temperature (°C)	Acid Concentration (% w/w)	Time (min)	Temperature (°C)	Acid Concentration (% w/w)	Yield	Type of yield		
Agriculture	20, 30, 40, 60, 90	150	0.69	35	150	0.69	0.63	ENZ	2018	(Santos et al., 2018)
Industry	12.72, 40, 80, 120, 147.28	62.95, 80, 105, 130, 147.05	0.90, 1.37, 2.05, 2.73, 3.17	120	130	1.37	0.86	PRT + ENZ	2021	<b>(Kamzon et al., 2021)</b>
Agriculture	20, 40, 60	121	0.92, 3.62	40	121	3.62	0.49	PRT	2021	(Li et al., 2021)
Forest	15	170, 190, 210	0.6, 1.2, 2.4, 3.6, 4.8, 6.0	15	190	4.8	0.51	ENZ	2016	(McIntosh et al., 2016)
				15	190	4.8	0.68	PRT		
Agriculture	3.5	180	1	nd	nd	nd	nd	nd	2017	(Oliva et al., 2017)
Forest	60	120, 125, 130	1.49, 2.47, 2.96, 3.44, 4.41, 4.89, 6.78, 7.25, 10.02	60	128	3.42	0.71	PRT	2020	<b>(Padilla-Rascon et al., 2020)</b>
Industry	3.3, 5, 7.5, 10, 11.7	170, 180, 195, 210, 220	0, 0.95, 1.88, 2.52	nd	nd	nd	nd	nd	2016	<b>(Pitarelo et al., 2016)</b>
Agriculture	40	121	3.62	nd	nd	nd	nd	nd	2021	(Scopel & Rezende, 2021)
Agriculture	5, 10	160, 180, 200	0.5	nd	nd	nd	nd	nd	2015	(Sharma et al., 2015)
Agriculture	30, 60, 90	60, 121	1.37, 1.82, 3.62	90	121	1.82	0.82	ENZ	2011	<b>(Vancov &amp; McIntosh, 2011)</b>
				90	121	1.37	0.88	PRT + ENZ		
				60	121	3.62	0.79	PRT		

Forest	10	170, 180, 190, 200, 210	0.2, 0.6, 1, 1.4	10	210	1.4	0.77	ENZ	2008	(Cara et al., 2008)
				10	180	1.4	0.74	PRT + ENZ		
				10	170	1	0.83	PRT		
Forest	60	121	7.53	nd	nd	nd	nd	nd	2020	(Shi et al., 2020)
Forest	0, 5, 10	180, 190, 200	0.01, 0.05, 0.09	5	200	0.05	0.55	PRT + ENZ	2020	<b>(Lee &amp; Yu, 2020)</b>
Forest	2, 5, 10, 20, 60	160	1	nd	nd	nd	nd	nd	2017	(Pingali et al., 2017)
Forest	120	170	0.92	nd	nd	nd	nd	nd	2016	(Yang et al., 2016)
Forest	6, 12	180	2, 4	12	180	4	0.45	PRT + ENZ	2014	(Normark et al., 2014)
				6	180	4	0.50	PRT		
Forest	30	180	0.73	nd	nd	nd	nd	nd	2012	(Li et al., 2012)
Forest	0, 5, 10, 20, 30, 60	170, 200	1	20	170	1	0.6	ENZ	2017	(Pielhop et al., 2017)
Industry	3.9, 5.1, 14, 39 51	175, 190, 205	0.5	14	190	0.5	0.6	ENZ	2021	<b>(Ilanidis et al., 2021)</b>
				3.9	175	0.5	0.49	PRT		
				3.9	175	0.5	0.6	PRT + ENZ		
Forest	0.3, 1.1, 5.4, 8.5, 26.8	170	0.5	5.4	170	0.5	0.91	PRT	2012	(Cao et al., 2012)
Forest	10	160	1.82	nd	nd	nd	nd	nd	2010	(Jung et al., 2010)
Forest	2, 5, 10	180, 190, 200, 210, 220	0.5, 1, 2	10	180	0.5	0.88	PRT	2003	<b>(Soderstrom et al., 2003)</b>
Forest	5, 10, 60	160	1	5	160	1	0.96	PRT	2014	(Sun et al., 2014)
Agriculture	0, 2, 4, 6, 8, 10, 12, 14, 15, 16, 18, 20	130, 140, 160	1.2	8.5	160	1.2	0.87	PRT	2015	(Mittal et al., 2015)
Agriculture	3.18, 10, 20, 30, 36.82	86.36, 100, 120, 140, 153.64	0.59, 1.82, 3.62, 5.38, 6.57	36.82	121.7	4.12	0.71	PRT	2021	<b>(Yildirim et al., 2021)</b>
Agriculture	120	80	1, 3, 5, 7	nd	nd	nd	nd	nd	2020	(Wang et al.,

										2020)
Industry	30	144, 150, 165, 180, 186	0.54, 0.6, 0.75, 0.9, 0.96	30	163	0.8	0.54	PRT + ENZ	2021	<b>(Vignesh &amp; Chandraraj, 2021)</b>
				30	163	0.8	0.58	ENZ		
Forest	60	160, 180	3	60	180	3	0.41	PRT + ENZ	2021	(Ibarra et al., 2021)
				60	180	3	0.54	ENZ		
				60	160	3	0.71	PRT		
Industry	180	150, 170, 190	1.82	180	130	1.82	0.85	PRT + ENZ	2021	(Yang et al., 2021)
Agriculture	10, 20, 30	120, 125, 130	1, 2, 3	30	121	2.66	0.88	PRT	2021	<b>(Demirel et al., 2021)</b>
				16	130	1.58	0.91	PRT		
Agriculture	5, 10, 20	180	0.5, 1, 2	10	180	1	0.58	ENZ	2009	<b>(Lu et al., 2009)</b>
				10	180	1	0.68	PRT		
				10	180	1	0.72	PRT + ENZ		
Agriculture	5, 10, 20	140, 160, 180	1	10	180	1	0.96	ENZ	1992	(Schell et al., 1992)
				5	180	1	0.69	PRT		
Agriculture	10	150, 170, 190	0.5	10	170	0.5	0.49	PRT	2015	(Wang et al., 2015)
				10	170	0.5	0.74	PRT + ENZ		
Forest	10	170, 190, 210	0.5, 1, 1.49	10	210	1.49	0.86	ENZ	2015	(Martinez-Patino et al., 2015)
				10	190	0.5	0.68	PRT + ENZ		
				10	170	1.49	0.68	PRT + ENZ		
				10	170	1.49	0.70	PRT		
Agriculture	5, 20, 35, 50, 65	120, 135, 150, 165, 180	0.25, 0.69, 1.13, 1.56, 2	20	157	1.07	0.68	PRT	2016	<b>(Gaur et al., 2016)</b>
				20	157	1.07	0.85	PRT + ENZ		
				20	157	1.07	0.90	ENZ		
Agriculture	20, 40	100, 110, 120, 130	1	40	120	1	0.80	PRT + ENZ	2014	(Zu et al., 2014)
				40	120	1	0.92	PRT		
Industry	4, 8, 12, 16, 20	160, 175, 190, 205, 220	0, 0.92, 1.82, 2.73, 3.62	12	185	1.46	0.89	PRT + ENZ	2014	<b>(McIntosh et al., 2014)</b>
				23.8	150	3.44	0.87	PRT		
Forest	2.08, 3.58, 5.08	201, 216, 230	0.4	1.77	212	0.35	0.59	PRT	1998	(Nguyen et al.,

										1998)
Forest	1.66, 2, 2.33, 3	190, 205, 210, 215	0.43, 0.55, 0.99, 1.56, 1.59	1.67	215	0.43	0.50	PRT + ENZ	2000	(Nguyen et al., 2000)
				2.33	205	1.59	0.98	ENZ		
				3	190	0.55	0.80	PRT		
Forest	3, 4, 7, 9	180, 190	0.7	7	180	0.7	0.78	PRT	1999	(Nguyen et al., 1999)
Forest	6, 8, 10, 12, 14, 18, 20, 24, 29, 30, 36, 40, 45, 60, 70, 71, 72, 150.5, 160, 170, 210, 320	150, 160, 175	0.25, 0.5, 0.75	30	175	0.25	0.81	PRT + ENZ	2010	(Jensen et al., 2010)
				29	175	0.25	0.71	PRT		
20				175	0.5	0.84	PRT + ENZ			
Agriculture				60	150	0.75	0.82	PRT		
8				175	0.75	0.88	PRT			
Industry	3.18, 10, 20, 30, 36.82	143.18, 150, 160, 170, 176.82	1.32, 2, 3, 4, 4.68	10	170	4	0.59	PRT	2011	<b>(Zhang et al., 2011)</b>
Forest	2.5, 7.5, 12.5, 17.5, 22.5, 27.5, 32.5, 37.5, 57.5	160	0.5, 2	27.5	160	0.5	0.84	PRT	2013	(Zhang et al., 2013)
				22.5	160	0.5	0.82	ENZ		
				22.5	160	0.5	0.88	PRT + ENZ		
				12.5	160	2	0.88	PRT + ENZ		
Agriculture	1, 2.5, 5, 10, 20, 40, 60	140, 160, 180	0.5, 1, 2	60	140	1	0.86	PRT + ENZ	2011	(Shi et al., 2011)
				40	140	1	0.97	PRT		
				10	160	1	0.92	PRT		
				2.5	180	1	0.95	PRT		
				5	160	1	0.93	PRT + ENZ		
				1	180	1	0.89	PRT + ENZ		
Forest	2, 5, 10, 15, 20, 30, 50, 80, 120, 180	85, 95, 105	1.5, 3.1, 6.2	nd	nd	nd	nd	nd	2010	(Hu et al., 2010)
Forest	20, 70, 140	110, 120, 130	0, 1.98, 3.93	50.2	130	3.22	0.91	PRT	2015	<b>(Park &amp; Um, 2015)</b>
Agriculture	30, 60, 90	60, 121	0, 0.75, 1.0, 2.0	90	121	1	0.76	ENZ	2012	(Vancov & McIntosh,
				90	121	1	0.84	PRT + ENZ		

				60	121	2	0.56	PRT		2012)
Agriculture	10.5, 12, 15, 18, 20.5	116, 130, 150, 170, 184	0.16, 0.5, 1, 1.5, 1.84	16.9	150	1.16	0.65	ENZ	2011	(Kim et al., 2011)
				16.9	150	1.16	0.81	PRT		
Industry	30, 45, 60, 75, 90	110, 115, 118, 120, 125, 130	1.82, 2.38, 3.62, 5.38, 5.72, 7.12, 8.83	30	130	3.37	0.88	PRT	2018	(Demirel et al., 2018)
				19	130	1.82	0.69	PRT		
Agriculture	20, 80, 140	100	1.98, 3.93, 5.84	100	100	2.37	0.78	PRT	2013	(Zhi et al., 2013)
Industry	15, 30.2, 52.5, 74.8, 90	130	0.15, 0.73, 1.58, 2.42, 3	33.8	130	2.1	0.69	PRT	2015	(Avila-Lara et al., 2015)
Agriculture	3.18, 10, 20, 30, 36.82	106.36, 120, 140, 160, 173.64	0.44, 1.37, 2.73, 4.06, 4.96	3.2	140	2.73	0.91	PRT	2012	(Baboukani et al., 2012)
Agriculture	10, 20, 30	121	1, 1.29, 1.59	27	121	1.59	0.88	PRT	2003	(Roberto et al., 2003)
Agriculture, Forest	0.5, 1, 2, 3, 5, 15, 30, 60	140, 160, 180	0.6, 0.9, 1.2	nd	nd	nd	nd	nd	1997	(Esteghlalian et al., 1997)
Agriculture	4.4	160, 170, 180	0.2, 0.5, 1	4.4	170	1	0.98	PRT + ENZ	2005	(Zhu et al., 2005)
				4.4	170	1	0.99	ENZ		
				4.4	160	1	0.87	PRT		
Agriculture	6.34, 10, 15, 20, 23.66	161.3, 165, 170, 175, 178.7	0.82, 1, 1.24, 1.49, 1.67	21	152.6	1.75	0.79	PRT	2010	(Jeong et al., 2010)
Industry	27, 40, 60, 80, 93	121	0.92, 1.37, 2.06, 2.73, 3.17	60	121	3.17	0.74	PRT	2010	(Betancur & Pereira, 2010)
				27	121	1.99	0.60	PRT		
Agriculture	5, 15, 30, 45, 55	86, 100, 120, 140, 154	1, 1.98, 3.93, 5.84, 6.78	15	140	5.84	0.48	PRT	2011	(Akpınar et al., 2011)
Industry	1, 3, 6, 8, 9, 10, 11, 15, 20, 22	170, 200	0.06, 0.1, 0.2, 0.3, 0.34	6	200	0.22	0.76	PRT	2011	(Um & Bae, 2011)
				15	170	0.24	0.79	PRT		
Industry	9.6, 30, 60, 90, 110.4	105, 110, 117.5, 125, 130	0.16, 0.5, 1, 1.5, 1.84	90	123	1	0.87	PRT	2012	(Cai et al., 2012)
				30	125	0.5	0.81	PRT + ENZ		
Agriculture	9.6, 30, 60, 90, 110.5	121	0.16, 0.5, 1.0, 1.5, 1.84	112	121	1.72	0.54	PRT + ENZ	2016	(Paniagua-Garcia et al.,

										<b>2016)</b>
Agriculture	5, 10, 15, 20	150, 170, 190, 210	0.5, 1.74, 2.96	20	190	0.5	0.68	PRT	2017	<b>(Nair et al., 2017)</b>
				15	190	0.5	0.97	PRT + ENZ		
Agriculture	10, 20, 30	150, 172.5, 195	0, 0.75, 1.49	10	195	1.49	0.72	PRT + ENZ	2017	<b>(Mesa et al., 2017)</b>
				20	173	0.75	0.94	PRT		
				25	155	1.49	0.59	PRT		

Finally Pretreatment followed by enzymatic hydrolysis (PRT+ENZ) represents the content of glucose obtained after enzymatic hydrolysis relative to the content of glucan in the raw material.

Among the 63 publications, six have used only design of experiment (DOE) methods and 24 used response surface methodology (RSM) methods to define their optimum values, which guarantees increased precision (Pereira et al., 2021) (Table 1). For the search for relationships between factors and optimal values, it was established that the yields are considered optimal when their combinations of factors make it possible to obtain yields greater than 70%, based on industrial partner experience in terms of economic impact. Using lower yields increases data scatter and decreases the accuracy of relationships.

## 2.2. Statistical analyses

The statistical techniques used varied according to the objective. All statistical analyzes were performed with *R*, using different packages: *ggplot2* and *cowplot* for graph design, *car* and *nlstools* for regression and the residues study, *FactoMineR* and *Factoshiny* for principal component analysis (PCA).

For the study of correlations between factors, different approaches were carried out: a PCA, an analysis of the scatter graph, and linear and nonlinear regressions. For regressions, several statistical indicators were considered. The first indicator considered is the *p*-value of the Fisher's exact test concerning the significance of the regression coefficients compared to 0. A *p*-value greater than 0.05 leads to the rejection of the regression. A second indicator is the residual standard error (RSE), which represents the average difference between the theoretical regression and the experimental data from the literature and allows the comparison of the precision of the regressions. RSE is expressed as a function of the degrees of freedom (DoF), which indicates the number of data used for the regression. Finally, the study of residuals obtained by the regression is conducted using various statistical tests (Durbin–Watson for

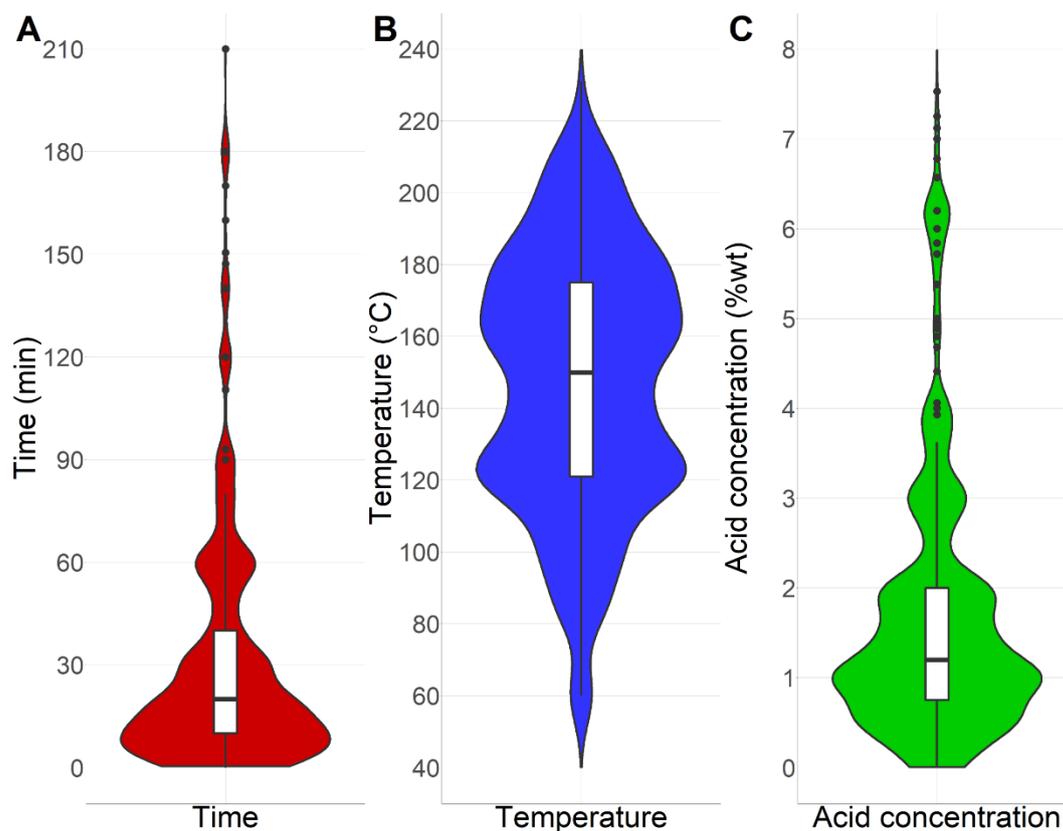
independence, NCV-test for homogeneity, and Shapiro–Wilk for normality) and graphic representations (Q-plot, residual vs. fitted plot) to select the most suitable regression formula.

## 2.3. Data description

Three main factors are involved in the optimization of the DAP: residence time, temperature and acid concentration (Hoang et al., 2021; Zhou et al., 2021). The first two factors are obviously linked because all chemical reactions are thermo-activated, so temperature and residence time pair up and influence each other to cause a total reaction unique to each DAP (Lancha et al., 2021a; Mokdad et al., 2018). All the combinations of these three factors studied in the articles collected have therefore been retrieved (Table 1). An analysis of their distribution with a violin diagram was used to show the dispersion of the data (Figure 2).

Short times are more represented than long times (Figure 2A): 75% of the publications use DAP times under 40 min, 50% consider durations under 20 min, and 35% are under 10 min. The temperature factor is described well over a wide range from 100°C to 210°C, with two more studied values around 120 and 170°C (Figure 2B), which allows a global vision. The greater

number of studies that used 120°C is likely a bias



**Figure 2: Data distribution studies of the main factors (n=1034).** A : Time factor; B : Temperature factor; C : Acid concentration factor. The box plot represents the distribution of the data according to the quartiles and the median. Black dots represent isolated data, sometimes stacked.

introduced by the use of conventional autoclaves at 121°C. Indeed, as DAP-dedicated reactors are not widespread equipment, a considerable number of publications use available materials for their studies, such as autoclaves. The distribution of acid data (Figure 2C) shows that the most represented values are the whole values: 1, 2, 3 and 4% acid. Even if the distinction is not clear on the figure, 0.5% and 1.5% values are also very studied amounts of acid. Taken together, 0.5% and 1% acid represent almost 20% of all

values. In general, studies thus focus on concentrations of less than 2%.

These three factors made it possible to define optimal conditions: the combination of these factors that gave the best yield for each study considered. As these yields can be of various types (Pretreatment only PRT, Enzymatic hydrolysis only ENZ, Pretreatment followed by enzymatic hydrolysis PRT+ENZ), a published work can have several optimal conditions. It is important

to note that these yields should be considered as local optima, just because it is impossible to test all possibilities, which

explains that the “best” yields include a wide range of actual yields (from 41.06% to 99.10%).

### 3. Correlations between factors

#### 3.1. Correlations highlighted by Principal Component Analysis

A PCA was done on the data (Table 1, column 5 to 8) with R (Figure 3). Data were centered/scaled before PCA. Dimensions 1 and 2 together explain 75.79% of the information, which allows a good overview of the correlations between variables. Dimension 3 (not shown) explains 16.49% of the information but does not provide any interesting additional data.

Dimension 1 represents the negative correlation between time and temperature: high time values imply low temperatures, and vice versa. Dimension 2 perfectly represents the yield of DAPs, and to a lesser extent the negative correlation of yield with the acid level (Figure 3A). The graphs of the individuals show two dense data clouds located at high temperatures and short times, the first with high yields (0.7-0.9) while the second depicts lower yields (0.5-0.7). The rest of the data are homogeneously dispersed across the graph, with some dots at

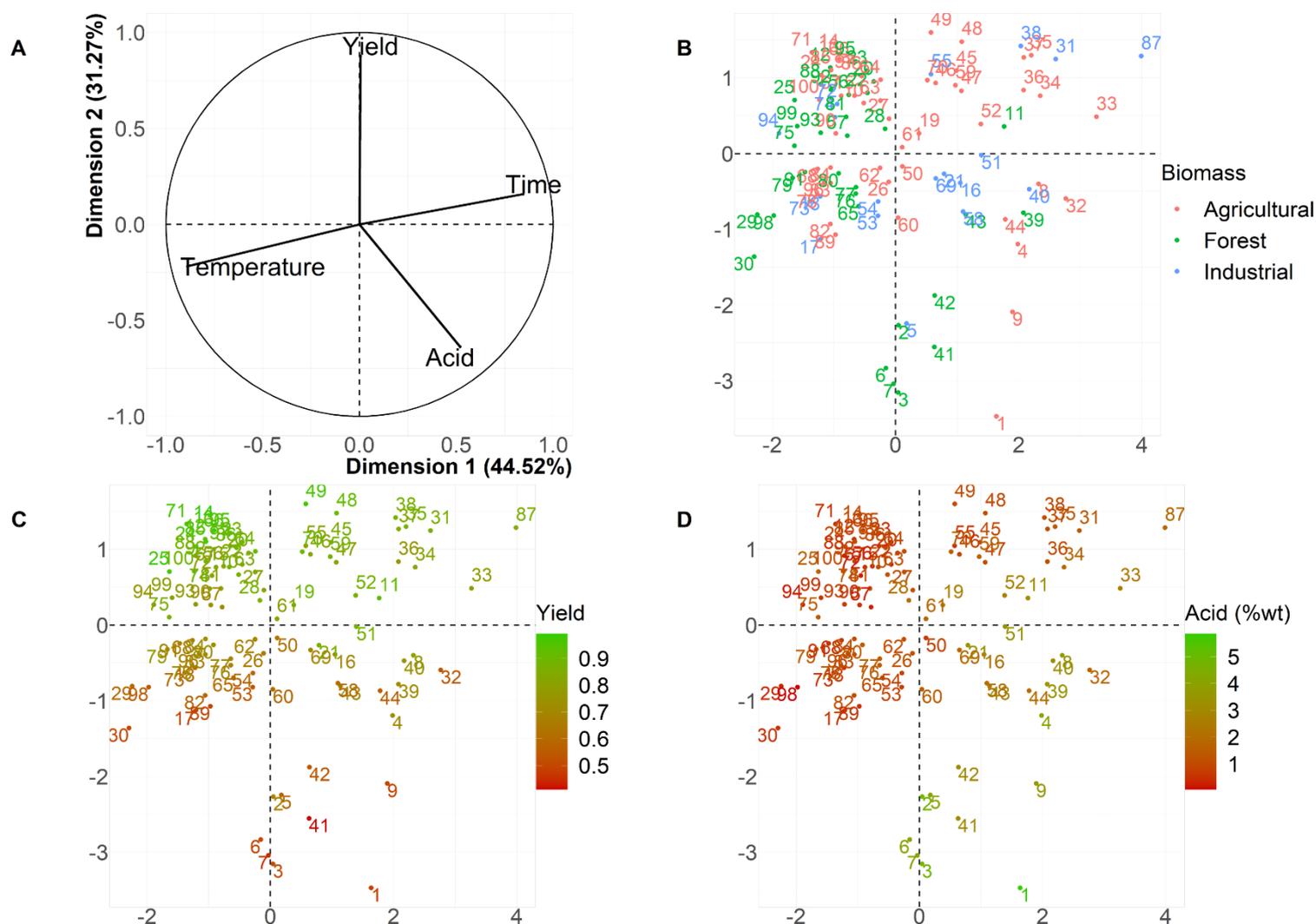
extreme acid levels (3-5%) or time (150-180min) (Figure 3B, 3C, 3D). Beyond the difference in yield, these two clouds do not show any fundamental difference in DAP condition : on average, the cloud with the lowest yield has slightly more severe conditions (1 min longer, 4°C warmer and 0.1% more acidic). The difference in yield between these two clouds must depend on another factor, not considered in this study.

The distinction of points by biomass shows a homogeneous dispersion of these parameters, except for forest biomass (Figure 3B). It is mainly located in the two data clouds mentioned above, which indicate a preference for high temperatures and short times to optimize DAPs of wood. The same trend is observed for the data defining an optimum ENZ (data not shown).

Considering the absence of correlation between time or temperature with yield, it seems that these parameters have no influence on the efficiency of DAP. But as mentioned before, they must be considered together. Their perfect negative correlation confirms the time-

temperature equivalence : optimal yields

require a



**Figure 3: PCA graph representing relationships between temperature, time, acid concentration, and yield (n=100).** Yield variable represents all DAP yield, whatever the optimization type and biomass origin. Each point is numbered according to its position in the data table. A : Variable Graph; B : Individuals Graph colored by Biomass origin; C : Individuals Graph colored by Yield; D : Individuals Graph colored by Acid level.

balance of these two parameters. No data show a simultaneous high or low value of these parameters. On the other hand, high yields of 0.8-0.9 can be obtained whatever the time-temperature combination (Figure 3A, 3C).

A negative correlation is also observed between yield and acid level on dimension 2. Acid-free conditions have been studied, but have not given optimal results in their studies with respect to the use of even very dilute acid. This negative

correlation is therefore probably due to the isolated data with very high acid levels (4-5%) having very low yields (0.5-0.7) (Figure 3D). An acid level of less than 4% therefore seems to be required to optimize DAP, but it depends on the temperature level. For temperatures above 150°C, only low acid levels between 0.2 and 2% can achieve very high yields, while for lower temperatures, high yields can be obtained with acid levels up to 3.5% (Figure 3C, 3D). An assumption is made that the yield is more sensitive to acid level when using high temperature. Acid would be more active at high temperatures, thus having a stronger impact on the severity of the DAP. The formula used to calculate the severity factor, which incorporates the acid level by simply subtracting the pH (Auxenfans et al., 2017), does not seem suitable for describing this phenomenon.

### 3.2. General relationship

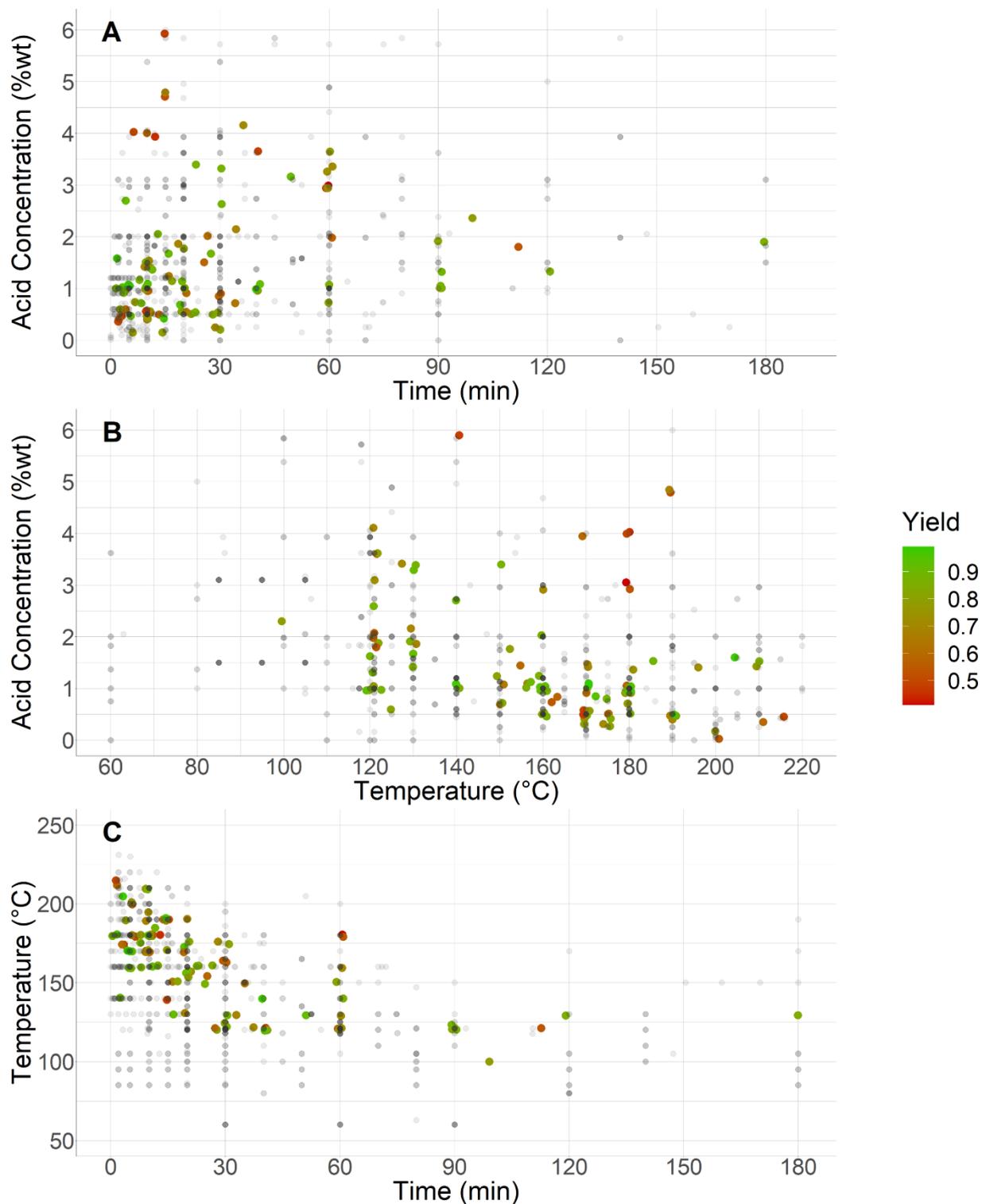
The optimal combinations were plotted for each couple of variables (Figure 4). The relationship between time and acid concentration shows that most of the optimal points (yield >0.7) are under 40 min and 2% acid (70%, 46/66) (Figure 4A). This also corresponds to the most explored area, as shown by the density and intensity of the black spots. Thus, this represents a bias, as good yields can be

obtained up to 180 min with concentrations below 2% acid. From 4% acid, the yields no longer exceed 70% (Figure 4A, 4B), which may be due to too strong DAP conditions : high concentrations of acid applied for a too long time regarding the temperature level. Note, however, that at these acid concentrations, lower temperatures have been tested without success (Figure 4B). Therefore, even lower times should be explored to exploit these temperature-acid couples. Likewise, no temperature-acid couples offer good results below 120°C except one, indicating that the time factor must be further explored, probably for times greater than 90 min. For these long periods, however, the industrial interest must be reestablished. Note also that from 150°C, only concentrations below 2% offer good yields. Above this value, the temperature-acid couple becomes too severe, which confirms the observation in PCA (Figure 3).

The last relationship to investigate is the coupled effect of time and temperature (Figure 4C). Without eliminating the lowest yields, it is already possible to see that these two factors are linked. This was expected as all kinetics are thermoactivated: a balance between residence time and temperature is therefore evident. The general trend connects points at a high temperature and short time (180–

220°C / 0–5 min) to points at lower temperature and long time (100–130°C /

90–180 min). Between 0 and 40 min, the curve decreases rapidly before



**Figure 4:** Optimal factor couples obtained by study of different couples during various DAP. A: time-acid concentration couples; B: temperature-acid concentration couples; C: time-temperature couples. Green/red dots: optimal factor couples with associated yields

( $n=102$ ); gray dots: couples tested ( $n=1034$ , the darker the point, the more the condition has been studied).

stabilizing around 125°C from 90 min, in an asymptotic way. Although the curve seems to be drawn correctly by following the optimal values, several remarks can be made on the distribution of these points. First, the couples using short times (<10 min) have been deeply investigated, but then the range of studied temperatures narrows with duration: 80–230°C for times <10 min, 80–200°C at 30 min, 100–180°C at 60 min, and 110–150°C at 90 min. Low temperatures are therefore well exploited up to 90 min, but not high temperatures. This finding represents a significant bias to the correlation: the lack of data for the behavior of DAP in the high-temperature range limits identification of the best combinations. Studies should be conducted to complete this lack of data before any attempt at general modeling. Second, not much data is available above 90 min, and the results are heterogeneously spread, which leaves significant areas without data (e.g., between 150 and 180 min, where only 150°C was studied). The asymptotic trend observed at 125°C is, therefore, unreliable. However, good yields were obtained beyond 90 min, indicating the potential of this zone.

In view of these results, no correlations could be found to relate the acid to other factors, but a correlation can be attempted on the time-temperature pair.

### 3.3. Time-temperature correlation

#### 3.3.1. General correlation

Limiting the data to yield greater than 70%, a general correlation of the points has been derived with several types of models (linear, polynomial and nonlinear). Consistently with the curvature shape evidenced on Figure 4C, a polynomial model offers the best statistical results but has a severe scientific drawback: beyond 90 min, the regression starts to increase, which is unrealistic. In addition, the model still does not describe the optimum above 200°C (y-axis intercept at 183°C). To address this problem, another formula explaining the curvature of the regression is proposed (Eq. 1).

$$y = ax^b \text{ (Eq. 1)}$$

This regression works nicely over the full range of parameters values, including temperatures greater than 200°C and times greater than 90 min (asymptotic behavior over long times). With  $p$ -values

$<0.001$ , the coefficients are all statistically significant but the RSE are quite high (18.97). This RSE is consistent with the scattering of the literature data set which considers all types of biomass and optimization steps. It is however able to give the general trend of the time-temperature correlation. More precise models can be obtained by cross-referencing the optimal conditions and biomass types (Forest, Agricultural or Industrial) and the type of optimization studied (PRT, ENZ or PRT+ENZ).

### 3.3.2. *Correlations crossing biomass and optimization criterion*

Regressions were calculated with Eq 1, using optimal conditions or biomass origin to select data. The six new regressions obtained (Figure 5) show lower RSEs than for the general regression, except for the regression ENZ (Table 2). These two classifications therefore make it possible to refine the correlation between time and temperature.

Biomass regressions are the most precise, even if the RSE of agricultural biomass is still high and close to that of the general regression. As seen previously with the temperature averages, the regression for forest biomass gives temperatures systematically higher than for

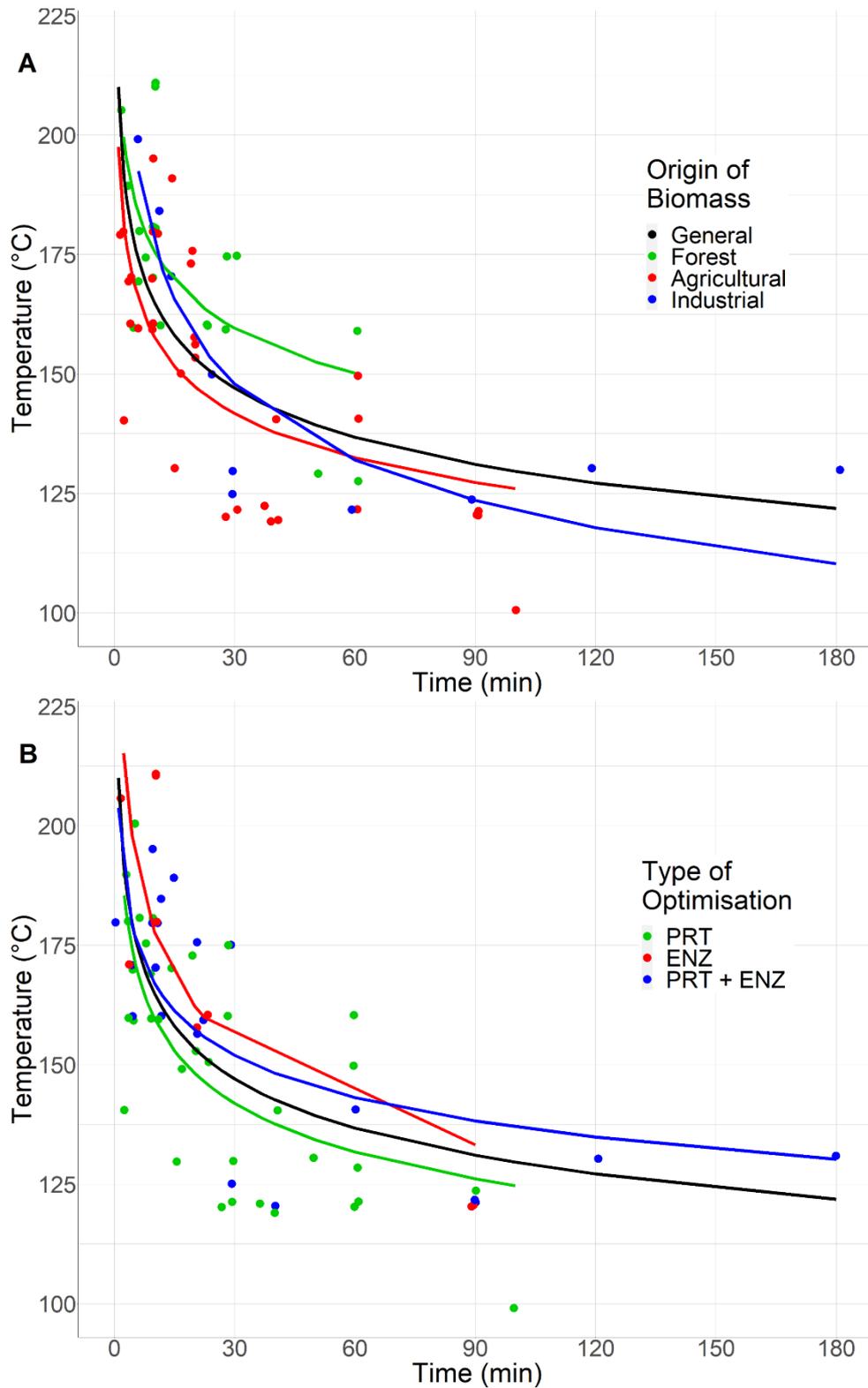
agricultural biomass, which does not reach  $200^{\circ}\text{C}$  (Figure 5A). This shows greater resistance to DAP for forest biomass. That of industrial origin is shared between the other two, closer to the forest biomass between 0 and 40 min before joining the agricultural biomass for long times. All the different biomasses are represented only up to 60 min, from which the forest biomass is no longer described. Then only 6 points are used to plot the regressions up to 180 min, three of which are merged at 90 min. The general regression is therefore only representative up to 60 min. For a longer DAP, only industrial biomass has enough data to present a reliable regression.

Optimization regressions give high RSE, especially for ENZ with an RSE above 21 and a higher  $p$ -value (Table 2) due to a sparse number of data (9 points) which is rather dispersed. The regressions allow however to validate the observations of means made previously: ENZ regression gives temperatures systematically higher than for PRT, with the higher y-axis interception at  $240^{\circ}\text{C}$ . The PRT + ENZ regression is shared between the two others: short times correspond to lower temperatures close to those of PRT, while long times imply higher temperatures as for ENZ (Figure 5B). Optimization ENZ are well represented only up to 20 min, from which the last point is at 90 min. For

a DAP longer than 60 min, only PRT+ENZ has enough data to have a reliable regression.

Finally, even if the quality of the regressions can be improved by correctly

selecting the data according to origin or purpose, the formulas remain imprecise and subject to bias when determining a reliable statistical and predictive value (wide 95%



**Figure 5: General, Biomass and Optimized Step regressions obtained for the time-temperature couples (n=67). A : General and Biomass Origin regressions ; B : General and Type of Optimization regressions. PRT : Pretreatment only; ENZ : Enzymatic hydrolysis only; PRT+ENZ : Pretreatment followed by enzymatic hydrolysis.**

**Table 2: Coefficients and statistical values for general, biomass and optimized step regression.** Eq. 1 is used for regression. PRT : Pretreatment only; ENZ : Enzymatic hydrolysis only; PRT+ENZ : Pretreatment followed by enzymatic hydrolysis; RSE : Relative Squared Error; DoF : Degrees of Freedom

Data	Coefficient A	Coefficient B	p-value	RSE	DoF
<b>General</b>	210.02	-0.105	< 0.001	18.97	64
<b>Forest</b>	214.98	-0.088	< 0.01	16.97	18
<b>Agricultural</b>	197.49	-0.098	< 0.001	18.17	34
<b>Industrial</b>	257.98	-0.164	< 0.001	14.85	8
<b>PRT</b>	204.69	-0.108	< 0.001	17.76	33
<b>ENZ</b>	240.48	-0.131	< 0.05	21.71	7
<b>PRT+ENZ</b>	203.74	-0.086	< 0.001	18.28	19

confidence intervals and high RSE). The objective is rather to provide a visual representation of the data and propose equations that can serve as tools to explore the most promising regions for optimization.

### 3.4. Origin of results variability

As seen previously, data remains scattered, which implies that the three main factors, time, temperature and acid concentration, are not enough to explain the variations of the data. First, each biomass is unique and reacts differently. Gathering them into three groups (forestry, agricultural and industrial) limits these variations, but some differences remain between species in the same group. For example, when grouping forest biomass together, hardwood, tropical hardwood, and softwood are included, whereas they display well-known variations in cell wall structure and composition, typically in the

proportion and nature of lignin (Ralph et al., 2019).

Beyond the biomass origin, variations might come from the materials and methods through the use of non-standardized equipment that is specific to each laboratory. The use of acid requires suitable reactors to prevent corrosion of the equipment. Since the reactors dedicated to DAP are not standardized, laboratories and industries develop their own reactors and processes. Out of 63 DAP studies, 11 used Parr reactors (300 mL, 1 L, and 2 L), 17 used autoclaves, and 6 designed their own reactors. Other studies operated reactors from other suppliers (5) or without providing a supplier (13). Different devices were also used, such as oil bath systems (4), fluidized sand baths (3), glassware (2), or a kettle (1). For two studies, there was no information on the materials used (Yang et al., 2016; Zhi et al., 2013). This large variability in methods poses

problems of repeatability and harmonization of results. Studies have shown that the type of reactors used strongly influences the production of glucose by modifying the kinetic reactions of polymer formation and decomposition (Hoang et al., 2021). In two-thirds of the studies, the heating and cooling rates or the type of materials used are not described. The target temperature can be reached in 2 min for the oil baths (Shi et al., 2011; Zhang et al., 2013), 9 to 12 min for some Parr reactors (Pielhop et al., 2017), and 30 min for others (Jung et al., 2010; Pingali et al., 2017). The other types of reactors—lab-made or commercial devices—have heating times of approximately 20 min (Gaur et al., 2016; Zu et al., 2014). As DAP occurs before and after the plateau when close to the set temperature, the accuracy of a small residence time remains questionable.

## 4. Recommended conditions for optimizing DAPs

The overall evolution of the three factors studied in this review is summarized in the graphical abstract, which gathers all DAP conditions reported to obtain yields greater than 70%, organized according to biomass origin. Simple equations and their corresponding ranges of validity are proposed to represent

The observed responses also present limitations because of their variety: DAP is a highly complex phenomenon impacting many intricate features that are quite difficult to characterize as a whole. The use of non-standardized analytical methods that are not always sufficiently detailed also invites reproducibility problems that likely contribute to large data variations.

Despite these variations, the regressions obtained in this review must be considered regarding the origin of the data. This work assembles varied data from more than 60 papers, which have been aggregated using reliable statistical tools. The distribution of the data over the ranges of treatment conditions is the result of the variability of published studies rather than a distribution chosen by experimental design. Accordingly, the results presented here are as accurate as they can be given the lack of control over the data.

the negative correlation between residence time and temperature (Eq 1). Following this recommended conditions does not ensure reaching the optimal yield but defines the time-temperature pathway for which the optimum can be reasonably found.

In addition to these recommended conditions, domains to avoid (1 and 2) or to favor (3) have been defined: (1) temperature/acid couples above 150°C and 2% acid seem too severe to give good yields, whatever the DAP time (2) the use of temperature below 120°C under 60 min, or below 140°C under 15 min does not seem severe enough to bring good yield, (3) below 2% acid, it seems possible to always find a time-temperature couple to obtain a good yield (on the range studied) if the time-temperature equivalence is considered. In order to imagine new processes likely to save energy or to use fatal energy, moderate temperature levels with sufficient residence times are promising.

Another important finding is that the optimal conditions depend on the biomass used or the desired optimization criterion: (1) forest biomass has an average DAP temperature 20–25°C higher than other biomasses, especially between 30

and 60 min (p-value < 0.005), (2) beyond 60 min, only industrial biomass and PRT+ENZ optimization seems to react well to long times pretreatment, and (3) the use of residence time between 0 and 20 min is recommended for optimizing ENZ, with temperatures on average 20°C higher than for the other optimizations (p value <0.05).

Since no correlations linking the acid concentration to the other factors could be found, it should be studied separately. As stated before, below 2% acid, it seems that an optimal time-temperature couple can be identified. Some publications have used higher concentrations with success using temperature levels below 150°C, but only for PRT optimization. In the context of an industrial use which is not limited to a pretreatment step, it is preferable to limit the acid to 2% to promote a good yield for the ENZ and PRT+ENZ optimizations.

## 5. Research needs and future direction

### 5.1. Gaps in knowledge

Further explorations of DAP intended to refine the optimal conditions can be recommended: (1) short times, under 15 min, should be explored at high acid concentrations (>4%) and low

temperature (120–150°C), (2) time-temperatures combinations 170–220°C / 20–60 min and 150–175°C / 60–90 min for acid concentrations <3% seem too severe, but no study proves it, (3) beyond 90 min, studies are rare and any additional information on the DAP but also on

industrial viability would be interesting, for example between 100 and 120°C, and (4) studies on acid levels between 2 and 4% should be conducted with the same time-temperature combinations to overcome the reported lack of correlation.

In optimizing an entire processing line, the selection of an appropriate acid content must be seen as a trade-off between time gain, yield loss, energy and chemical consumption, which can impact on the cost and sustainability of engineering elements throughout the process. Finally, to improve the DAP conditions and adapt them to the industrial plants, a new severity factor is needed. An ideal severity factor should be able to better integrate the acid level, including acid-free treatment, and to take into account the actual evolution of temperature over time.

## 5.2. Data quality

In addition to the choice of the levels of time, temperature, and acid concentration factors, other recommendations can be suggested to improve the quality of the information provided by research on DAP. The suggestions derive from the problems of variability encountered during the aggregation of DAP data. Recommendations can be considered as

general recommendations and also include other types of pretreatment, not only DAP. Following these recommendations will speed up future research on pretreatments, making it easier to compare and reuse quality results with a detailed description.

Besides, it is essential to consider only one biomass feedstock at a time. Indeed, as indicated several times in this review, each biomass is unique and reacts differently to pretreatment. For the same biomass, different parts are affected by these variations (leaf, branch, trunk) and it is even possible to observe variability in the same part (tissues differ in their composition and structure depending on their location). In all cases, adapted and precise sampling are strongly recommended.

To favor the development of an open findable, accessible, interoperable, and reusable (FAIR) data approach, an effort must be made in the transmission of the DAP parameters used (time =  $f(\text{temperature})$ , reactor model, fraction of biomass used, etc.) as well as in the detailed description of the analytical methods. All the data will thus be standardized to be shared and reused.

To move from an analysis of separate factors to a global consideration of their non-linear interactions, as

proposed in this review, a kinetic model able to account for the whole time-temperature pathway would be a major step forward. For this purpose, the DAEM formulation, which has proven effective for poplar (Lancha et al., 2021a), offers a relevant framework. The development of such models for different kinds of biomass would be very useful tools, not only to define the best conditions but also to consider the heating and cooling phases in the treatment characterization.

An effort should also be made to enlarge the domains studied during each DAP. Large descriptive studies should be conducted rather than small optimization studies. The results obtained would thus be more comprehensive, with less local

optima and would be more representative of the entire field of applications. The methodology associating DOE and RSM is ideal to meet this need and should be systematically employed as a standardized method. Such investigations will be useful in designing innovative processes that meet new sustainability standards. For example, to consider the economic and ecological dimension of the DAP, the amount of acid should be limited. This restriction reduces the cost of substrates, reactor corrosion, an additional neutralization step, and potential environmental degradation. These constraints are also applicable for the time-temperature couple: a fair balance must be found to optimize the cost related to the heating and pressure levels as well as residence time.

## Conclusions

Among the 63 publications on dilute acid pretreatment, most studies were done with short residence times, high temperatures and low acid content. This leads to appropriate conversion yields, but the critical analysis shows that long times and moderate temperatures can also produce similar yields. Mathematical expressions of the time-temperature equivalence were derived for contrasted biomass families. Overall, this review proposes two important recommendations: investigating unexplored ranges of dilute acid pretreatment (acid concentration  $> 4\%$  or  $< 0.2\%$ , residence time  $>90$  min, temperature  $< 120^{\circ}\text{C}$ ) and best practice rules to limit data variability, structuring data and meta-data to promote open science.

### **CRedit authorship contribution statement**

Julien du Pasquier: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization.

Gabriel Paës: Conceptualization, Writing - review & editing, Visualization, Project administration, Funding acquisition.

Patrick Perré: Conceptualization, Writing - review & editing, Visualization, Project administration, Funding acquisition.

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