Review

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Environmental assessment of bio-based chemicals in early-stage development: a review of methods and indicators

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Abstract: Climate change and fossil resource depletion are driving a transition to a bio-based economy, for which novel bio-based chemical processes need to be developed. The environmental performance of the novel bio-based chemicals should be assessed during their development, when the production process can still be adapted, although data availability is limited. Many environmental assessment methods applicable during product development ('early-stage methods') exist in the literature. The aim of this study is to provide an overview of these early-stage methods and to evaluate to what extent they are suitable for assessing bio-based chemicals in their early-stage development. The paper first describes the characteristics of early-stage chemical design and the environmental impacts of bio-based products based on published life cycle assessments. Low data requirements, the inclusion of climate change and energy indicators, and the inclusion of environmental impacts from biomass feedstock production are identified as three good-practice principles for early-stage assessment of bio-based chemicals. In the second step, 27 early-stage assessment methods are reviewed and categorized based on their scope and environmental indicators used. Finally, the reviewed methods are evaluated using the good-practice principles. A perfect early-stage method does not exist. However, choosing the most suitable method(s) based on the goal of an assessment and using complementary indicators leads to the most effective assessment for novel bio-based chemicals in development. © 2017 The Authors. *Biofuels, Bioproducts and Biorefining* published by Society of Chemical Industry and John Wiley & Sons, Ltd.

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Keywords: bio-based chemicals; environmental assessment; environmental indicators; bio-based economy

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Introduction

The concept of a bio-based economy (BBE) in which biomass resources are used for the production of energy and materials instead of fossil fuels is gaining traction, as shown for instance by the attention it receives from European policymakers.[1] The development toward using bio-based resources is driven primarily by climate change caused by greenhouse gas (GHG) emissions from fossil fuel combustion, and the depletion of fossil fuel resources. Developing a BBE entails major transformations in industry, particularly in agriculture and forestry to produce biomass feedstocks and in the chemical and petrochemical sector to convert them into chemicals. Therefore, a BBE implies establishing many new chemical processes and routes, either to create the same substances that are currently used (so-called drop-ins) or to produce entirely new chemicals. For optimal decision making, all aspects of sustainability should ideally be considered when developing these new processes, in addition to conventional economic, technical, and regulatory analyses. This paper focuses on assessing environmental performance, as bio-based chemicals are not *a priori* guaranteed to be more environmentally sustainable than conventional chemicals.

To understand the potential environmental benefits and limit trade-offs of these new production routes, there is a need for *early-stage environmental assessments* of bio-based chemicals, i.e., assessments while products are still in research and development (R&D). During product development, the freedom to adapt the production process (e.g. regarding feedstock, synthesis route, purification, by-product treatment) decreases.[2,3] It is therefore important to conduct environmental assessments at an early-stage, so that process designers can optimize new production processes for sustainability.

Defining and operationalizing early-stage environmental assessment methods is not straightforward, however. Because the production process is not yet finalized, available data are limited and subject to change. This makes it difficult and resource-intensive to apply existing comprehensive assessment methods such as life cycle assessment (LCA).[4,5] The key challenge for early-stage assessment methods is thus to provide useful sustainability guidance – ideally approaching the results of detailed assessments for commercial-scale production – with the limited information available during R&D.

Different early-stage environmental assessment methods for chemicals have already been proposed in academic literature,[6–8] most of which were not designed specifically for bio-based products. They cover different environmental impacts, use different life cycle scopes, and target different phases of product development. However, an overview of the applicable areas, the impact coverage and targeted users of these early-stage assessment methods does not exist. In addition, it is important to understand whether these methods can support sustainable decision-making when developing bio-based chemicals, by capturing potential environmental benefits as well as potential trade-offs.

This paper therefore aims to provide an overview of publicly available early-stage environmental assessment methods and to understand the implications of using them for bio-based chemicals. This is done in three steps:

- Characterization: First, the requirements for early-stage environmental assessments for novel bio-based chemical processes are characterized. The analysis focuses on understanding (i) the development process of chemicals, and (ii) the environmental impacts of bio-based products, based on published LCA studies.
- Method review: Secondly, an overview of existing (early-stage) environmental assessment methods applicable to chemicals is provided, focusing on their objectives, life cycle scopes, and indicators (e.g. covered environmental impacts). This overview helps to understand which early-stage indicators have already been proposed.
- Method evaluation: Lastly, the results of the first two steps are combined by evaluating to what extent the existing early-stage assessment methods are suitable for bio-based chemicals.

The paper concludes with a discussion of recommendations for further development of early-stage assessment methods for bio-based chemicals.

Characterization of early-stage development of chemical design and the known environmental impacts of bio-based products

Characterization of early-stage development of chemicals

The characteristics of early-stage environmental assessments for novel bio-based chemical processes must first be understood to assess the strengths and limitations of current environmental assessment methods in this context.

The development process for (bio-based) chemicals typically moves through different R&D stages before a chemical is produced at commercial scale. These stages are partly experimental and partly based on computer modeling. Each stage generates data that could be used for environmental assessments. The following subsequent R&D stages (and corresponding data outputs) can be distinguished (modified based on Sugiyama *et al.*):[9]

- In the *Concept* stage, a synthesis route to a desired chemical is developed and this concept is proven in a laboratory. In this stage, only stoichiometric information is available, as practical yields are not yet known.
- During the *Process chemistry* stage, the synthesis route is tested at laboratory scale to produce small amount of purified product. Information on the real-world performance of the main reaction(s) is gathered, such as conversion, selectivity, performance of catalysts, formation of by-products, and heat of reaction.
- *Process design* refers to using engineering tools to design, simulate, and optimize a (usually small-scale) first-of-a-kind chemical plant for the synthesis route. This goes beyond the main reaction(s) considered in the previous stages by including the design of the purification of the main product, process waste treatment, preparation of reactants, etc. This step yields data on the entire facility, for example in terms of productivity, input materials, utilities, emissions, and waste.
- In the *Piloting* stage, small-scale production facilities are established based on the process design. The real-world performance of the production process is measured and optimized to prepare for future industrial up-scaling. In piloting trials, production data simulated by the process design is validated and technological experience is gained.

Advancing through the R&D stages, more and higher quality (e.g. lower uncertainty, more realistic for industrial-scale production) data becomes available for environmental assessments (Fig. 1). However, as decisions are made in product development, the freedom to make changes decreases. To incorporate sustainability considerations into the decision-making, environmental assessment methods should be applied during each R&D stage and use data typically available during that stage. Ideally, early-stage methods should have low data requirements, in line with the targeted R&D stage.

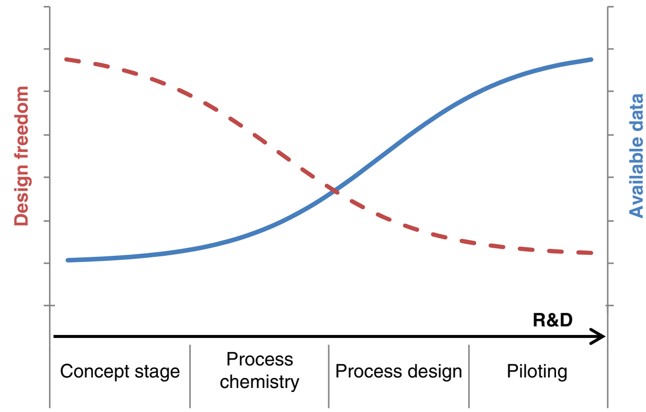

Figure 1. Conceptual model of available information and design freedom for a chemical process during different R&D stages; adapted from Ruiz-Mercado *et al.* and Tufvesson *et al.* [2,3]

Environmental impacts of bio-based chemicals

To assist companies during R&D, early-stage environmental assessments should capture the most important environmental impacts so that potential trade-offs are revealed when there is still ample design freedom. Environmental sustainability encompasses a range of different environmental impacts, however, and focusing on a particular impact may obscure important trade-offs for other impacts and bias decisions. Defining *a priori* which environmental impact types or life cycle stages are most important for bio-based products is not straightforward; they can differ from case to case, for example depending on whether fertilizers are used during biomass cultivation. Nonetheless, some general observations can be made based on LCA studies of existing bio-based products.

Figure 2 provides an overview of commonly used environmental indicators, and shows their prevalence in published LCA studies on bio-based products. There is a strong focus on climate change, which is included in all studies. Other environmental damage midpoints such as eutrophication and acidification are assessed only in about 65% or less of studies. Around 70% of studies include a resource indicator for energy, whereas only 15–25% of studies report water and land indicators. However, environmental impacts receiving much attention are not necessarily the most important ones, since impact categories may be selected based on data availability (e.g. more data might be available to assess energy demand than ecotoxicity). Prioritization of environmental impacts (for early-stage assessments of bio-based chemicals in particular) is complex and subjective. For example, political priorities may strongly differ between countries, some impacts might be critical locally but of minor importance globally, and scientific understanding of the urgency of addressing specific impacts is sometimes limited (e.g. the concept of planetary boundaries).[10] In the remainder of this chapter, we limit ourselves to determining the main environmental benefits and trade-offs for typical bio-based products based on comparisons with petrochemical products, in order to identify focus points for early-stage assessments.

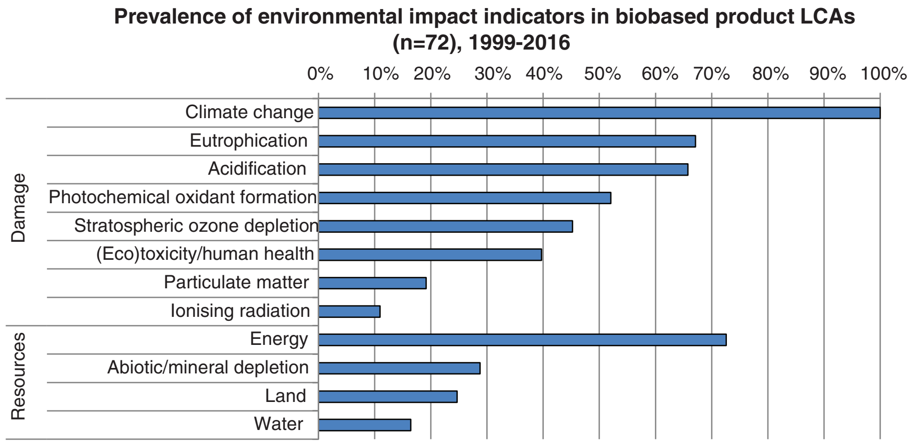

Figure 2. Prevalence of environmental impact indicators (damage or resource indicators) in 72 published LCA studies on bio-based (non-energy) products. See background information in Supporting Information A.

Many LCAs note that the feedstock production life cycle stage is important for the environmental performance of bio-based products.[11–13] For example, bio-based products contain carbon captured from the atmosphere as CO_2 during plant cultivation, reducing climate change impacts. Climate change mitigation is thus an important driving force for developing a BBE. The use of renewable resources (instead of fossil fuels) and potential climate change benefits should therefore be included in early-stage assessment methods.

However, biomass feedstock production is often also linked to intensive agriculture. The use of synthetic fertilizers in this stage can cause environmental impacts such as eutrophication, acidification, and ozone depletion.[14,15] Furthermore, biomass production requires land and water, limited resources that are closely linked to food and energy supply.[16] The importance of land and water (quality and availability) for the sustainability of bio-based products is underscored by their inclusion in the recent European EN16760 standard.[17] Land occupation and transformation are associated with issues such as biodiversity loss and soil degradation, but methods to assess these impacts are still in their infancies.[17–19] Nonetheless, simply assessing (agricultural) land occupation (e.g. in m^2yr/kg product) does not require a substantial amount of data. Given that land availability is constrained, such land occupation estimates are required to optimize the distribution of land in a BBE in general (e.g. comparing whether bioenergy or bio-based materials can achieve higher GHG emission savings per hectare),[20] and to limit agricultural land requirements for bio-based chemicals in particular. Assessments of bioenergy have also shown that land use-related issues, such as (indirect) land-use change and carbon debt, are critical in determining climate change performance.[21,22] This also applies to bio-based chemicals that are often derived from the same biomass feedstocks. Concluding, indicators assessing the environmental damage of feedstock production (e.g. eutrophication potential) or simpler indicators such as land occupation and freshwater consumption should be included in early-stage methods to identify and limit potential environmental trade-offs of bio-based chemicals.

Beyond the feedstock production stage, the conversion of feedstocks into chemicals is generally the most energy-intensive part of the life cycle of bio-based products.[23] The environmental impacts of the subsequent use phase and end-of-life (EOL) can be significant, but are very case-specific.[13] For climate change, for example, the EOL impact depends on whether carbon in the product is fully oxidized into CO_2 or anaerobically degraded (yielding CH_4, with a 34 times higher climate change impact).[24]

Meta-analyses of LCA studies that directly compare the quantitative environmental performance of bio-based and petrochemical products found lower climate change and non-renewable energy use for bio-based products on average, whereas eutrophication and ozone depletion impacts were higher.[11,25] Results for acidification and photochemical oxidant formation are inconclusive, indicating that these impacts may be more case-specific. These findings appear to confirm the environmental importance of the feedstock production stage for bio-based products. Other impact categories are not included in these meta-analyses due to limited data. For instance, biomass production is sometimes linked to potential (eco)toxicity impacts due to pesticide use, but these impacts are case-specific (not all feedstock production uses pesticides). While only a limited amount of comparative LCA studies are available, some suggest that bio-based products can perform better than conventional products in these toxicity-related impact categories.[11] Due to this uncertainty, as of yet we cannot conclude whether bio-based products outperform petrochemical counterparts in (eco)toxicity impact categories.

To summarize, three preliminary good-practice principles are proposed for the ideal early-stage environmental assessment method for bio-based chemicals:

- **Low data requirements**. The data requirements to conduct an assessment with a method should be low, and in line with the targeted R&D stage.
- **Inclusion of climate change and energy indicators**. As a key driver for the bio-based economy, the climate change impacts of bio-based products should be assessed. The use of non-renewable primary energy sources can also be used, as it strongly correlates with climate change and other impacts,[26] and assesses non-renewable energy used in the energy-intensive conversion of feedstocks into chemicals.
- **Inclusion of environmental impacts of biomass feedstock production**. It is important to include indicators that capture the main trade-offs (on average) for bio-based products and are distinct from petrochemical reference products. Based on meta-analyses, eutrophication and ozone depletion are relevant indicators.[11,25] In addition, agricultural land occupation and water use should also be included. Such resource footprints are valuable since they are data-lean, but can still predict environmental impacts with reasonable accuracy.[27]

These principles are used later in this article to evaluate publicly available assessment methods. They are intended as a first rudimentary attempt that is open for discussion and future refinement. For example, one could argue that health and safety aspects are important enough for novel bio-based chemicals to warrant adding a principle. It should also be kept in mind that LCA meta-analyses focus on currently available products, and that future bio-based chemicals (e.g. derived from non-fertilized feedstocks or waste streams) can show different environmental performance characteristics.

Overview of environmental assessment methods for chemicals

The aim of this section is to review existing environmental assessment methods for products to understand the approaches and indicators proposed so far. We distinguish methods designed for early-stage and methods for detailed assessments of commercial products (‘full assessment’). We then describe the procedure for selecting and analyzing the methods and discuss the findings for full assessment and early-stage assessment methods.

Method selection and analysis

First, a set of environmental assessment methods is collected from the public domain (other approaches/indicators may exist in proprietary methods). We include methods proposed and/or implemented in peer-reviewed articles, research projects (e.g. Prosuite), or other reports (e.g. by companies). A method is defined here as a procedure to quantitatively measure and compare environmental sustainability. This excludes *tools*, i.e., appliances (e.g. software) that are designed to assist in using a specific method. Furthermore, only methods applicable to chemical production routes (not necessarily *bio-based* chemicals) are included, so assessment methods focusing for instance on organizations or inherent properties of chemicals (e.g. PBT profiler; www.pbtprofiler.net) are excluded.

The selected methods contain both *full assessment* and *early-stage* environmental assessment methods. The former are found to be LCA-based methods intended to be applied to commercial products. The latter early-stage group contains for instance methods who self-identify as early-stage assessment, methods targeting chemical process design, methods aiming for a simplified/quick assessment, and methods aiming to operationalize the principles of green chemistry.[28] The early-stage methods are subdivided into *single-indicator* methods and *multi-indicator* methods.

Secondly, the objective of each method is reviewed. We record the goal(s) of each method as stated by the original authors. In addition, we note whether a method was designed specifically for bio-based products, and we interpret from which R&D stage (see previous section) onwards the early-stage methods could be applied. For example, if a method requires information on the (expected) emissions of a production facility, its R&D stage is ‘Process design’, since we assume this information is not available beforehand.

Thirdly, we analyze the indicators used by the methods, i.e., the quantitative metrics used to measure and compare the environmental performance of products in the method. They are referred to differently in literature (e.g. ‘impact category’, ‘stressor’, ‘environmental damage midpoint’, ‘metric’), but all of them are called *indicators* here. Indicators that do not relate to environmental performance (but to economic or social performance, for example) are discarded for the present analysis. Furthermore, no distinction is made here between mandatory and optional indicators in a method.

The indicators are categorized into so-called LCA indicators and non-LCA indicators. LCA indicators correspond to one of the nine damage indicators (assessing a type of environmental pressure, e.g. GHG emissions) or four resource indicators (measuring use/depletion of primary resources, e.g. energy) distinguished in life cycle impact assessment (LCIA) methods as described in Supporting Information B. The non-LCA indicators include all other indicators, which are very diverse and some do not directly measure a type of environmental damage. They are therefore grouped by the broader environmental themes to which they most strongly relate. Based on the indicators encountered, we distinguish six themes: Energy, Material efficiency, Renewable resources, Water, Health and safety, and Other, a rest category. The aim of this step is to find out which non-LCA indicators have been proposed and which environmental themes receive the most attention.

For each method, we note which part of a product's life cycle is covered. Four options are distinguished: cradle-to-grave, covering the whole life cycle; cradle-to-factory gate, covering raw material extraction/biomass cultivation up to and including product manufacture; gate-to-gate, covering a single process; and mixed, when the indicators in a method have different life cycle scopes.

The indicator analysis as described here required some interpretation due to unclear descriptions in the literature sources. For instance, some methods do not provide sufficient documentation to fully understand the indicators (e.g. not indicating whether energy use is measured as final or primary energy), provide multiple variants of indicators without indicating a preference (e.g. different 'inherent safety indices'), or present aggregated indicators (e.g. 'pollutant emissions', which in turn consist of air acidification, water eutrophication, ozone depletion, freshwater acidification, and freshwater salinity). In addition to complicating this review, incomplete operationalization of indicators makes methods harder to use and reduces the reproducibility of results.

As shown in Table 1, 33 environmental assessment methods are included in the final selection. Six full assessment methods are included, which are mostly generic (not sector- or product-specific). We include 27 early-stage methods which are designed for the chemical sector (e.g. for intermediate chemicals, polymers, or pharmaceuticals). Of these, 16 are single-indicator and 11 are multi-indicator methods. Table 2 provides an overview of the environmental issues covered by the indicators used in the methods. Here, an 'x' indicates that a method uses at least one indicator corresponding to the environmental impact category (LCA indicators) or the environmental theme (non-LCA indicators). The methods and their indicators are discussed in the subsequent sections.

Full assessment methods

The six full assessment methods reviewed here are all based on the LCA methodology.[4,5] The corresponding cradle-to-grave perspective means that environmental impacts occurring during feedstock production as well as during the use phase and end-of-life are accounted for (although all methods could also be applied using a cradle-to-factory gate scope). Two of the methods were developed within the chemical industry (BASF Eco-efficiency and WBCSD),[32,33] and one was developed for bio-based products in particular (S2BIOM).[34]

Table 2 shows that four out of the six methods (i.e., PEF, ILCD, Prosuite, S2BIOM) include indicators for all environmental damage categories commonly used in LCA (Supporting Information B).[29–31,34] In addition, all full assessment methods include resource indicators; mineral depletion is included in all six methods, whereas land (occupation/transformation), water and energy (use/depletion) are included in five methods.

Table C.1 in the Supporting Information lists all indicators and impact assessment models used in the full assessment methods. It reveals a large variety in terminology used, even when the same underlying impact assessment models are used. This is potentially confusing, as for example 'land transformation (PEF, S2BIOM) and 'land use' (WBCSD) could be interpreted as related yet distinct concepts, but they are assessed using the same model.[29,34,32] Overall, there seems to be consensus on the impact assessment models that should be used, since only a limited number of specific models are used for each type of environmental impact. On the other hand, many methods do not specify which impact assessment models should be used to measure an impact (though some do provide instructions themselves, see notes under Table C.1).

Some methods incorporate non-LCA indicators. BASF Eco-efficiency for instance combines LCA indicators (covering four types of environmental damage and two resource indicators) with non-LCA indicators for water emissions, toxicity potential, risks and waste produced

Table 1. Overview of selected environmental assessment methods.

		Method name/reference	Objective/description[a]	Indicators[b]	Life cycle scope	R&D phase(s)	Made for bio-based
Full assessment		PEF[29]	Product Environmental Footprint	14	Cradle-to- grave	N.a.	No
		ILCD[30]	International Life Cycle Data system handbook	13	Cradle-to- grave	N.a.	No
		Prosuite[31]	Prospective sustainability assessment of technologies	24	Cradle-to- grave	N.a.	No
		WBCSD[32]	Life cycle metrics for chemical products	22	Cradle-to- grave	N.a.	No
		BASF Eco-efficiency[33]	Eco-efficiency analysis	10	Cradle-to-grave	N.a.	No
		S2BIOM[34]	Life-cycle based environmental sustainability assessment of non-food bio-mass value chains	14	Cradle-to- grave	N.a.	Yes
Early-stage assessment	Multi-indicator	Sugiyama *et al*.[9]	Decision framework for chemical process design including environmental, health and safety assessment	4	Mixed	Concept–Process design	No
		EcoScale[6]	Semi-quantitative tool to select an organic preparation based on economic and ecological parameters	4	Gate-to-gate	Process chemistry	No
		Patel *et al*.[7]	Sustainability assessment of novel chemical processes at early stage	4	Mixed	Process chemistry	No
		GSK FLASC[35]	Fast Life Cycle Assessment of Synthetic Chemistry	8	Cradle-to-gate	Process chemistry	No
		Sheldon/Sanders[8]	Concise metrics for the production of chemicals from renewable biomass	3	Mixed	Process chemistry	Yes
		Cabezas *et al*.[36]	Pollution prevention with chemical process simulators	9	Gate-to-gate	Process design	No
		Young/Cabezas[37]	Designing sustainable processes with simulation	8	Gate-to-gate[c]	Process design	No
		Chen *et al*.[38]	Design guidance for chemical processes using environmental and economic assessments	9	Cradle-to-gate[d]	Process design	No
		Schwarz *et al*.[39]	Sustainability metrics to guide decision-making	10	Gate-to-gate	Process design	No
		Tugnoli *et al*.[40]	Quantitative sustainability assessment in the early stages of process design	16	Gate-to-gate	Process design	No
		Tabone *et al*.[41]	Sustainability metrics	11	Mixed	Process design	No
	Single-indicator	Atom economy[42]	Molecular weight of product / molecular weight of reactants	1	Gate-to-gate	Concept	No
		Reaction mass efficiency[43]	Mass of isolated product / total mass of reactants used	1	Gate-to-gate	Concept	No
		Mass intensity[44]	Total mass used in a process / mass of product	1	Gate-to-gate	Concept	No
		Environmental factor[45]	Total non-product or non-H_2O mass out of process / mass of product	1	Gate-to-gate	Concept	No
		Effective mass yield[46]	Mass of desired product / mass of all non-benign materials used in synthesis	1	Gate-to-gate	Concept	No
		Carbon efficiency[43]	Mass of carbon in product / mass of carbon in reactants	1	Gate-to-gate	Concept	No
		Specific process energy[43]	Total process energy / mass of product	1	Gate-to-gate	Process chemistry	No
		C-factor[47]	Cradle-to-gate kg CO_2 emitted / kg product	1	Cradle-to-gate	Process design	No
		Specific solvent use[43]	Total (gross) mass solvent / mass of product	1	Gate-to-gate	Process design	No
		Specific solvent recovery energy[43]	Total solvent recovery energy / mass of product	1	Gate-to-gate	Process design	No
		Persistency/bioaccumulation[43]	Total (persistent and bioaccumulative material) / mass of product	1	Gate-to-gate	Process design	No

Table 1. Continued.

	Method name/reference	Objective/description[a]	Indicators[b]	Life cycle scope	R&D phase(s)	Made for bio-based
Single-indicator	Weighted persistency/bioaccumulation[43]	Total (persistent and bioaccumulative material / (EC_{50} material / EC_{50} DDT control))[e]	1	Gate-to-gate	Process design	No
	Weighted hazard exposure[43]	Total (mass of material (kg) / permissible exposure limit for material (ppm))	1	Gate-to-gate	Process design	No
	Solvent ozone creation potential[43]	Total (mass of solvent * POCP value * vapor pressure) / (mass of product * vapor $pressure_{toluene}$ * $POCP_{toluene}$)[f]	1	Gate-to-gate	Process design	No
	Specific energy GHG emissions[43]	Mass of GHG emissions (CO_2 eq.) from energy / mass of product	1	Gate-to-gate	Process design	No
	Specific GHG emissions, excl. solvent[43]	Mass of GHG emissions (CO_2 eq.) ex. energy for solvent recovery / mass of product	1	Gate-to-gate	Process design	No

[a] For full assessment methods and multi-indicator early-stage methods, this column describes the method using (an excerpt of) the title of the original source with minor editorial changes. For early-stage single-indicator methods, a definition of the indicator is provided based on the reference with minor editorial changes for clarity.
[b] Note that this is the total number of indicators for environmental sustainability only; some methods include additional indicators for social, economic, or technical aspects. The indicators are reviewed in detail in the text.
[c] Method also accounts for the cradle-to-factory gate impacts of producing the energy consumed in a chemical process (but not of other material/utility inputs).
[d] Method focuses on gate-to-gate emissions (characterized using the EFRAT impact assessment model), but also assesses the cradle-to-entry gate environmental impacts of producing the required raw materials and equipment using the economic input–output LCA (EIOLCA) method.
[e] EC_{50}: half maximal effect concentration; DDT: Dichlorodiphenyltrichloroethane, an insecticide.
[f] POCP value: photochemical ozone creation potential, a characterization factor for the potential of a substance to cause photochemical oxidant formation

Table 2. Summary of environmental indicators in reviewed environmental assessment methods.

			LCA midpoint indicators													Non-LCA indicators					
			Environmental damage									Resource									
		Method	Climate change	Ozone depletion	Photochem. oxidation	Particulate matter	Ionizing radiation	Acidification	Eutrophication	Ecotoxicity	Human health/toxicity	Land	Water	Mineral	Energy	Health and safety-related	Material efficiency	Renewable resources	Water-related	Energy-related	Other
Full assessment		PEF[29]	x	x	x	x	x	x	x	x	x	x	x	x	x						
Full assessment		ILCD[30]	x	x	x	x	x	x	x	x	x	x	x	x	x						
Full assessment		Prosuite[31]	x	x	x	x	x	x	x	x	x	x	x	x	x	x					
Full assessment		WBCSD[32]	x	x	x	x		x	x	x	x	x	x	x	x						x
Full assessment		BASF[33]	x	x	x			x						x	x	x			x		x
Full assessment		S2BIOM[34]	x	x	x	x	x	x	x	x	x	x	x	x							
Early-stage assessment	Multi-indicator	Sugiyama *et al*.[9]													x	x	x			x	x
Early-stage assessment	Multi-indicator	EcoScale[6]															x			x	
Early-stage assessment	Multi-indicator	Patel *et al*.[7]	x												x	x				x	x
Early-stage assessment	Multi-indicator	GSK FLASC[35]	x	x				x	x						x		x		x	x	
Early-stage assessment	Multi-indicator	Sheldon/Sanders[8]									x						x			x	
Early-stage assessment	Multi-indicator	Cabezas *et al*.[36]	x	x	x			x		x	x										
Early-stage assessment	Multi-indicator	Young/Cabezas[37]	x	x	x			x		x	x										
Early-stage assessment	Multi-indicator	Chen *et al*.[38]	x	x	x			x		x	x										
Early-stage assessment	Multi-indicator	Schwarz *et al*.[39]	x	x	x			x	x			x				x	x			x	x
Early-stage assessment	Multi-indicator	Tugnoli *et al*.[40]	x	x				x	x	x	x	x				x	x	x	x	x	x
Early-stage assessment	Multi-indicator	Tabone *et al*.[41]	x	x	x					x	x			x			x	x		x	x
Early-stage assessment	Single-indicator	Atom economy[42]															x				
Early-stage assessment	Single-indicator	Reaction mass efficiency[43]															x				
Early-stage assessment	Single-indicator	Mass intensity[44]															x				
Early-stage assessment	Single-indicator	Environmental factor[45]															x				
Early-stage assessment	Single-indicator	Effective mass yield[46]															x				
Early-stage assessment	Single-indicator	Carbon efficiency[43]															x				
Early-stage assessment	Single-indicator	Specific process energy[43]																		x	
Early-stage assessment	Single-indicator	C-factor[47]	x																		
Early-stage assessment	Single-indicator	Specific solvent use[43]																			x
Early-stage assessment	Single-indicator	Specific solvent recovery energy[43]																		x	
Early-stage assessment	Single-indicator	Persistency/bioaccumulation[43]														x					
Early-stage assessment	Single-indicator	Weighted persistency/ bioaccumulation[43]														x					
Early-stage assessment	Single-indicator	Weighted hazard exposure[43]														x					
Early-stage assessment	Single-indicator	Solvent ozone creation potential[43]		x																	
Early-stage assessment	Single-indicator	Specific energy GHG emissions[43]	x																		
Early-stage assessment	Single-indicator	Specific GHG emissions, excl. solvent[43]	x																		

(Table C.1 in Supporting Information).[33] For example, no LCA midpoint for eutrophication is used. As an alternative approach, emissions which can lead to eutrophication (e.g. biological oxygen demand, chemical oxygen demand, PO_4^{3-} and NH_4^+) are compared to statutory limits. Similarly, some methods use additional indicators to capture impacts not assessed by the set of common LCA indicators. For example, the Prosuite method uses three indicators to capture *occupational* health and safety (i.e., number of non-fatal accidents at work, fatal accidents at work, and occupational diseases), which are supplementary to LCA midpoints that relate to Human health (i.e., Human toxicity and Respiratory inorganics).[31]

Early-stage assessment methods

Single-indicator methods

The single-indicator early-stage methods consist of comparatively simple indicators developed for chemical syntheses. Most single-indicator methods focus on a single conversion step and are designed to be applied in the earliest R&D stages.

As indicated in Table 2, 6 out of 16 methods relate to *material efficiency*, i.e., how much material is required to produce a unit of output. These methods only require mass flow information on a single conversion step, and can thus be applied to assess environmental sustainability during the Concept stage. A good score on material efficiency indicators could signal that a process does not 'waste' a lot of feedstock (since most is converted into the desired product), which limits the environmental impacts of biomass cultivation (e.g. linked to fertilizer use). Conversely, low scores can indicate substantial by-product formation, which could signal that more (potentially energy-intensive) purification is required to isolate the main product. Material efficiency indicators can thus assist in selecting synthesis routes in early R&D.

The material efficiency methods differ in which material flows are accounted for. For example, some methods focus on the inputs of a process (e.g. Mass intensity; definition in Table 1), while others focus on outputs (e.g. Environmental factor). Furthermore, some methods account for all material flows (e.g. Reaction mass efficiency), whereas others for instance ignore water (e.g. Environmental factor) or focus on 'non-benign' materials only (e.g. Effective mass yield). Their complexity also differs; some indicators are derived directly from reaction equations (e.g. Atom economy), while others also account for practical aspects like yields and molar excesses (e.g. Reaction mass efficiency).[43] Due to the lower data requirements, indicators derived from reaction equations can be used earlier in chemical R&D, but offer less detailed insights.

The ten remaining single-indicator methods are more specific than the material efficiency methods and also require more detailed data, for example on environmental emissions or on human- or ecotoxicological hazard characteristics, such as 50%-effect concentrations (EC_{50}). Due to the higher data demands, they are deemed more suitable for the Process chemistry and Process design stages. Three of these indicators relate to health and safety, by assessing the generation of hazardous substances. Two of these account for the fact that the hazard potential of substances differs, using either EC_{50} values (Weighted persistency/bioaccumulation) or permissible exposure limits (Weighted hazard exposure) to weight the substances.[43] Finally, four methods consist of LCA midpoints. Three measure climate change, but with limited coverage (e.g. focusing only on process energy, or only accounting for CO_2 and no other GHGs). The Solvent ozone creation potential method is also a midpoint, notable for using the vapour pressure to approximate the emissions of a solvent.[43]

Multi-indicator methods

The early-stage methods that use multiple indicators (Table 1) are a diverse group that have been developed from different perspectives/backgrounds. Some methods attempt to expand conventional process design (focused on economics) with environmental considerations (e.g. Tugnoli *et al*.).[40] Others try to bring detailed assessment methods for fully-developed products into R&D (e.g. GSK FLASC).[35] They are applicable to later R&D stages than single-indicator methods (Table 1) and have more information to work with, but at the same time still lack data from large-scale industrial production. After first discussing the indicators used, we review the different strategies they apply to limit data requirements.

All of the reviewed multi-indicator methods, except EcoScale,[6] use LCA indicators that are similar to those used by full assessment methods (Table 2). Key features are:

- Most methods (7 out of 11) use a set of damage indicators, although they are less complete compared to the full assessment methods. **Climate change** (7 out of 11), **acidification** (6 out of 11) are most frequently included. **Eutrophication** is only included in three of these methods as a midpoint, whereas **particulate matter formation** and **ionizing radiation** are never included.
- Six multi-indicator early-stage methods use a resource indicator, but none use more than one. Four include a type of **energy** indicator (e.g. cumulative energy

demand), but there is limited attention for **water** (one method) and **land** indicators (two methods). For the latter, Sheldon and Sanders (2015),[8] notable for being the only method developed specifically for bio-based chemicals, propose assessing the (hypothetical) amount of good agricultural soil required in Champagne, France to cultivate the biomass feedstocks required per unit of chemical produced. This approach is far simpler than assessing *actual* land use, but also nonspecific; it cannot be used to compare different feedstock sourcing locations, for example.
- None of the selected methods include **mineral** resource depletion indicators.

The methods complement these LCA indicators with up to six non-LCA indicators. In Tables 2 and 3, these are categorized according to the environmental sustainability theme that they most strongly relate to. They are for instance based on product properties (density, biodegradability), process properties (yield, energy loss index), specific inputs and outputs (organic carbon load, material efficiency) or a combination (e.g. the 'EHS method' indicator proposed by Sugiyama *et al*.).[9]

Most methods incorporate non-LCA indicators related to energy (8 out of 11 methods) and material efficiency (7 out of 11). Five methods use indicators related to health and safety, i.e., assessing the fate of substances in the environment, physical hazards and/or eco- and human toxicity damage potential. Three of these (Sugiyama *et al*.; Patel *et al*.; Tugnoli *et al*.) derive their indicators from various inherent properties of the chemical involved.[9,7,40] For example, Patel *et al.* use the flash point of chemicals to assess physical hazards such as fire or explosions.[7] The last method, EcoScale,[6] also uses hazard warning labels, assigning penalties to reactants with specific labels. This approach is simpler than the other health and safety-related indicators, but unlike the others it does not account for the likelihood that humans or ecosystems come into contact with the chemicals involved. For reference, Patel and colleagues do so by taking into account the persistency (assessed based on the half-life in water) and mobility (partial pressure, boiling point) of compounds.[7]

Water quality is considered by three methods, two of which focus on emissions of organic material, potentially causing eutrophication impacts. The last method assesses salinization potential, which is currently not included as an environmental impact in common LCIA methods.[19] Two methods contain indicators that relate to the use of renewable resources, i.e., share of renewable resources and use of renewable materials.

The multi-indicator early-stage methods employ various strategies to limit the data requirements of their environmental assessments. Three distinct but non-exclusive strategies for early-stage assessment can be distinguished:

- **Limiting the life cycle scope of the assessment**. As shown in Table 1, methods such as Tugnoli *et al*. and Cabezas *et al*. have a gate-to-gate life cycle scope, meaning that only the product manufacture stage is considered.[40,36] These are generally designed to improve the process design stage by including environmental considerations (e.g. preventing pollution caused by production facilities). They use the same midpoint indicators as full assessment methods, meaning they require full information on the (gate-to-gate) emissions of a site. Some methods acknowledge that the gate-to-gate scope is too limited to derive recommendations regarding environmental sustainability, and therefore expand it somewhat. For example, Young and Cabezas argue that final energy consumption for chemicals production is critical and therefore include the environmental impacts of energy production, assuming coal-based supply.[37] Similarly, Chen *et al*. include the cradle-to-gate environmental impacts of the input materials of a process, which are calculated using an economic input–output LCA model.[38] Both these approaches improve the life cycle coverage of an assessment.
- **Using data-lean non-LCA indicators**. This strategy is used for instance by Sheldon and Sanders, Tabone *et al*. and Sugiyama *et al*.[8,41,9] Examples of such indicators are biodegradability, feedstock transportation distance, and plastic density (Table 3). The implicit motivation for using such indicators is that they are data-lean, but have a cause-effect relationship with an environmental impact.
- **Using databases**. This strategy is practiced for instance by the GSK FLASC method,[35] and is commonly used for example when conducting screening LCAs based on the Ecoinvent life cycle inventory database.[48] It focuses on preparing datasets of key environmental indicators of commonly used material inputs. This enables fast assessments of the cradle-to-factory gate impacts of a new product. However, if an input material is not represented in the database, no assessment can be performed.

Evaluation of the assessment methods for bio-based chemicals in development

Previous sections derived three general 'principles' for early-stage assessment of bio-based products: low data requirements, including climate change/primary

Table 3. Non-LCA indicators in multi-indicator early-stage methods per environmental theme (used in addition to LCA indicators as shown in Table 2).

Method	Indicator (name as found in method)	Details	Environmental theme: Health and safety-related	Material efficiency	Renewable resources	Water-related	Energy-related	Other
Sugiyama *et al.*[9]	EHS method	Based on inherent properties of chemicals (alternatively: risk phrases). Includes physical hazards (e.g. fire/explosions), toxicity (e.g. acute toxicity) and environmental fate (e.g. mobility, persistency, bioaccumulation).	x					
	Energy loss index	Based on presence of water, product concentration, minimum difference of boiling point, inherent waste amount, reaction energy. Used to assess gate-to-gate costs/environmental impacts using reaction information only.					x	x
	Mass loss index	Total non-product mass out of process or process step / mass of product		x				
EcoScale[6]	Safety	Based on hazard warning labels. Covers physical hazards and toxicity.	x					
	Yield	After purification. Used to assess optimal use of resources and ease of purification.		x				
	Temperature/time	Based on process properties, i.e., reaction temperature, heating requirements, cooling requirements					x	
	Workup and purification	Based on process properties, for example need for distillation, liquid-liquid extraction, classical chromatography, etc.					x	
Patel *et al.*[7]	EHS index	Minor adaptation of indicator used by Sugiyama *et al.*, 2008	x					
	Energy loss index	Minor adaptation of indicator used by Sugiyama *et al.*, 2008					x	x
GSK FLASC[35]	Net mass of materials used	No details provided		x				
	Total Organic Carbon load before waste treatment	Represents the pre-treatment carbon load				x		
	Energy required	Not clear whether indicator represents final or primary energy. If primary energy is used, this is an energy resource LCA indicator					x	
Sheldon/Sanders[8]	Material efficiency	Total weight of useful products / total weight of useful products + waste		x				
	Overall energy efficiency	Calorific value of the end product and useful side products / sum of all energy inputs including all agricultural inputs for fertilisers, tractor, transport, and the chemical processes and downstream processing.					x	

Table 3. Continued.

Schwarz *et al.*[39]	Material intensity	Mass not converted into desired product per unit output		x				
	Salinity in freshwater	Total mass of released Na^+, Cl^-, SO_4^{2-}, Mg^{2+}, Ca^{2+}, K^+ / mass of product				x		
	Energy intensity	Net fuel energy consumed per unit output. Electricity and steam use are expressed in fuel energy using fixed efficiencies.					x	
	Toxic emissions	Mass of toxic material emitted per unit output. Assessed based on lists of toxic substances by U.S. EPA.	x					
Tugnoli *et al.*[40]	Inherent safety index	Method indicates that various indices can be used and does not indicate a preference.	x					
	Nonrenewable materials	No details provided		x				
	Renewable materials	No details provided			x			
	Organic load	No details provided				x		
	Electrical power	No details provided					x	
	Solid waste disposal	Ratio of disposal cost of process waste over disposal cost of municipal waste.						x
Tabone *et al.*[41]	Density	Density of final product (plastics). Used to assess the 'material efficiency' theme		x				
	Atom economy	Molecular weight of product / molecular weight of reactants. Used to assess the 'avoid waste' theme		x				
	Percent from renewable sources	Used to assess the 'use renewable feedstocks' theme			x			
	Feedstock distance	Used to assess the 'use local resources' theme						x
	Biodegradability	Used to assess the 'design to degrade' theme						x
	Percent recycled	Used to assess the 'design products for recycle' theme		x				

energy indicators, and covering the typical environmental impacts of feedstock production. Furthermore, we reviewed environmental assessment methods from the public domain for all development stages. We now combine these perspectives to evaluate the available methods.

All full assessment methods meet the good-practice principles derived here, apart from having low data requirements. Their cradle-to-grave scope and wide range of LCA indicators enable comprehensive assessments for bio-based chemicals in line with the state-of-the-art of the LCA framework. As soon as data allows (which could be during advanced stages of Process design already), it is recommended to use these methods when developing bio-based chemicals.

The early-stage single-indicator methods (section on *Single-indicator methods*) all focus on a particular issue. Due to their minimal data requirements, they can easily bring environmental considerations into the earliest R&D stages. However, because of this simplicity, the methods cannot meet all the good-practice principles set out here, although they are also not intended to be comprehensive.

For the multi-indicator early-stage methods (section on *Multi-indicator methods*), Table 4 indicates to what extent they adhere to the good-practice principles.

Some general findings for multi-indicator early-stage methods are derived from Table 4 and method overview presented here. First, a perfect method does not exist. Table 4 shows that GSK FLASC scores highest on the good-practice principles,[35] followed by Chen *et al*., Sugiyama *et al*. and Patel *et al*.[38,9,7] All methods have lower data requirements than full assessment methods, and can be applied during R&D (principle 1). They also all include indicators for climate change and/or energy (principle 2), though some only partially cover these issues (EcoScale; Sheldon and Sanders).[6,8] Most variation between methods is seen for the third principle. While some methods have a comprehensive set of indicators (e.g. Tugnoli *et al*.),[40] they use a gate-to-gate scope that cannot account for impacts occurring during feedstock production. Others do use cradle-to-gate indicators, but do not capture the typical environmental downsides of bio-based products (e.g. Patel *et al*., GSK FLASC and Chen *et al;* Table 4).[7,35,38] The shortcomings encountered for the third principle are consequences of the objectives of the methods (e.g. not specifically targeting bio-based chemicals) and targeted R&D stage.

It should be kept in mind that Table 4 shows a generic assessment which reflects neither the objectives nor the limitations of a method. For example, methods may deliberately prioritize their aim of having a quick assessment over having a full set of indicators covering all important impacts. Furthermore, methods such as GSK FLASC and Chen *et al*. rely on databases,[35,38] which also has drawbacks. For example, while assessments with GSK FLASC can be carried out quickly, the underlying database is derived from data-intensive LCA work. If a product is made from exotic materials not present in the database, it cannot be (fully) assessed. Assessing such limitations in detail is beyond the scope of the present work, but they should be kept in mind when selecting or developing methods.

Secondly, most early-stage methods include indicators related to health and safety, either using LCA indicators for human health or ecotoxicity (Table C.1 in Supporting Information), or using non-LCA indicators ('non-LCA indicators; in Table 3). The former assess the environmental impacts associated with all emissions occurring at a chemical production facility (and, if a cradle-to-gate scope is used, with all emissions associated with producing all process inputs as well). Some non-LCA indicators consider physical hazards (e.g. risk of fire or other occupational health and safety issues), thereby expanding beyond the scope of the LCA indicators for human health and ecotoxicity (which are only based on emissions to the environment). Nevertheless, all LCA and non-LCA indicators related to health and safety that are reviewed here are *retrospective*, i.e., based on hazard information (e.g. median lethal doses, risk phrases) that is already known. As an alternative, technology developers can consider using prospective indicators (e.g. quantitative structure-activity relationships to predict biological activity based on chemical structures using regression),[49] or bringing *in vivo* passive sampling models (e.g. zebrafish) to early stages of sustainable chemical design (Tan L, unpublished).[50]

Lastly, all reviewed early-stage methods are designed for cradle-to-gate or gate-to-gate assessments. While the use and EOL phases could be relevant for novel chemicals that offer new functionality, the myriad applications of intermediate chemicals complicate cradle-to-grave assessments. For early-stage assessments, it may not be realistic to quantify the impacts of these life cycle phases.

Conclusions

The paper first described the characteristics of early-stage chemical design and the environmental impacts of bio-based products based on published LCAs. Low data requirements, the inclusion of climate change and energy

Table 4. Evaluation of multi-indicator early-stage environmental assessment methods based on preliminary good-practice principles for bio-based chemicals.

Methods	Principles: 1. Low data requirements for assessments[a]	2. Climate change/energy indicators[b]	3. Environmental impacts of feedstock production[c]
Sugiyama *et al*.[9]	++	++	+
EcoScale[6]	+++	+	-
Patel *et al*.[7]	++	++	+
GSK FLASC[35]	++	+++	++
Sheldon/Sanders[8]	++	+	+
Cabezas *et al*.[36]	+	++	-
Young/Cabezas[37]	+	++	+
Chen *et al*.[38]	+	++	++
Schwarz *et al*.[39]	+	+++	-
Tugnoli *et al*.[40]	+	+++	-
Tabone *et al*.[41]	+	++	+

[a] +++: low data requirements (e.g. reaction information only); ++: medium data requirements (e.g. information on material inputs of production plant); +: high data requirements (e.g. production plant emissions)

[b] +++: multiple indicators covering both climate change and energy; ++: single indicator covering one issue; +: issues partially or indirectly covered by indicators

[c] +++: captures most of the important environmental issues of feedstock production (eutrophication, ozone depletion, land use, water use); ++: captures some of the important environmental issues of feedstock production; +: some indicators include feedstock production, but they do not capture the important environmental issues (e.g. only including cradle-to-gate GHG emissions; or unspecific indicators); –: feedstock production stage not included

indicators, and the inclusion of environmental impacts from biomass feedstock production are identified as three good-practice principles for early-stage methods.

The review showed that a perfect method does not exist. Full assessment methods have broad coverage of environmental issues, but are data-intensive and thus difficult to apply during R&D. A wide variety of early-stage methods has been proposed, ranging from single-indicator approaches to complicated methods with 16 indicators. Early-stage methods have lower data requirements than full assessment methods, but also assess fewer environmental impact categories and have limited life cycle scopes. However, some proposed indicators in early-stage methods assess environmental issues not typically covered in LCAs (e.g. occupational health and safety, salinization).

Out of the multi-indicator early-stage methods, GSK FLASC, Chen *et al*., Sugiyama *et al*. and Patel *et al*. scored highest on the good-practice principles,[35,38,9,7] although improvements are possible. Most importantly, none of the methods fully implements the third good-practice principle, capturing the environmental impact types (e.g. eutrophication) that are likely to represent a trade-off for bio-based chemicals. Improvements can be made here for instance by combining gate-to-gate assessments with (already available) information on the environmental impacts of biomass feedstock production. For the latter, life cycle inventory databases (e.g. Ecoinvent and Agri-footprint) can provide quantitative environmental impact data for various bio-based feedstocks. Alternatively, feedstock certification schemes may provide qualitative information on the sustainability of a specific feedstock, if quantitative information is not available.

Improvements are also possible for the first principle, low data requirements. The review revealed a range of non-LCA indicators that are promising for early-stage assessments due to their low data requirements. However, their accuracy and reliability are typically not discussed. This may not be problematic for indicators with a strong cause-effect relationship with a particular impact, but others may need to be validated. Future research could therefore focus on identifying the strongest data-lean non-LCA indicators for bio-based chemicals, for example by comparing them to full assessment indicators over a range of case studies.

The results from early-stage assessments of chemicals can be very uncertain, since production processes can change dramatically throughout R&D. However, it should also be borne in mind that the primary goals of early-stage environmental assessments should be to identify critical issues early-on and steer the development process in the right direction, rather than providing accurate results in an absolute sense. Choosing the most suitable method(s) based on the goal of an assessment and using complementary indicators leads to the most effective assessment for novel bio-based chemicals in development.

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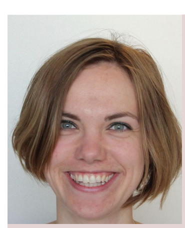

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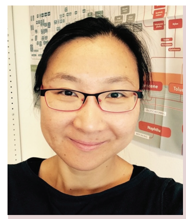

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