

**General equations to estimate the CO₂ production of (bio)catalytic reactions in early
development stages.**

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SUPPLEMENTARY INFORMATION

S.1. UPSTREAM PART.

S.1.1. MASS METRICS FOR ORGANIC MEDIA.

According to the Novartis metrics, the CO₂ production by incineration of an organic mixture is estimated as 2.3 kg CO₂ · kg Solvent⁻¹.^{1,2} An average density for common solvents of 0.9 g · cm³ is assumed (see Table S1 below). Thus:

$$GWP(org) = 2.3 \cdot kg \text{ solvent}$$

$$GWP(org) = 2.3 \cdot 0.9 \cdot V = 2.1 \cdot V \cdot kg \text{ solvent}$$

The solvent volume to be treated depends on the substrate loading – to synthesize one kilogram of product –, on the actual reaction conversion, and on the proportion of solvent that is not recovered for further use, and then it is lost or incinerated (%SolventTreated). Therefore:

$$GWP(org) = \left[\frac{100 \cdot 2.1 \cdot \%SolventTreated}{Conv [SL] \cdot 100} \right]$$

$$GWP(org) = \frac{2.1 \cdot \%SolventTreated}{Conv \cdot [SL]}$$

Parameters to consider:

- [SL]: Substrate loading, in “kg L⁻¹”.
- Conv: Reaction Conversion, in “%”.
- Solvent Treated, %SolventTreated, in “%”. This corresponds to the solvent that is either not recovered and must be incinerated or is mineralized.

S.1.2. MASS METRICS FOR AQUEOUS MEDIA.

Following a similar procedure, the density of water is assumed to be 1.0 g · cm⁻³. The two general scenarios provided by Novartis are: i) mild Wastewater treatment plant (WWTP), which renders

0.073 kg CO₂ · kg wastewater⁻¹; and ii) water incineration due to recalcitrance of the effluent, which leads to 0.63 kg CO₂ · kg wastewater⁻¹. Since it is not expected that a typical biotransformation – containing chemicals, cosolvents, etc. –, could be directly accepted in the mild WWTP, it is assumed that some pre-treatment steps (e.g. pre-extraction of organics or hazardous components) are needed. Thus, a more realistic case would be something in between the two scenarios provided by Novartis, where the wastewater needs to be pre-treated before reaching the WWTP, to remove hazardous chemicals that hamper the biological treatment. An assumption is made here to be 0.35 kg CO₂ · kg wastewater⁻¹. The equations are:

$$GWP(\text{water}(\text{wwtp})) = \frac{0.073 \cdot \%WaterTreated}{Conv.[SL]}$$

$$GWP(\text{water}(\text{recommended})) = \frac{0.35 \cdot \%WaterTreated}{Conv.[SL]}$$

$$GWP(\text{water}(\text{incineration})) = \frac{0.63 \cdot \%WaterTreated}{Conv.[SL]}$$

If there are no more specific data of the process, the GWP(water(recommended)) should be the one taken for the environmental assessments. If further data are available, practitioners can easily adapt the equation to their actual cases.

S.1.3. ENERGY METRICS FOR ORGANIC MEDIA.

The reaction is set-up at a certain temperature. The energy required to heat a liquid from room temperature to the reaction temperature depends on the specific heat capacity (C_p) of the liquid, and can be calculated according to the equation:

$$Q = m C_p \Delta T$$

Table S1 summarizes densities and the Cp of commonly used (co)solvents in biocatalysis.

Table S1.

Solvent	Density (g / cm ³)	Cp (KJ / kg °C)
Water	1.00	4.184
CPME	0.86	1.84
Ethyl acetate	0.9	1.94
Toluene	0.87	1.7
2-MeTHF	0.86	2.13
Acetonitrile	0.79	1.98
Dimethyl carbonate	0.98	2.38
Heptane	0.69	2.26
Acetone	0.78	2.57
DMSO	1.1	2.20
<i>Isopropanol</i>	0.79	2.6
<i>tert</i> -butanol	0.78	2.6
Methyl- <i>tert</i> -butyl ether (MTBE)	0.74	2.12

For the calculations, it is assumed that, from the widely used organic solvents in biocatalysis (Table S1), an average Cp of 2.1 KJ/ kg °C, and an average density of 0.9 g · cm⁻³ can be taken for the generic equations.

Therefore, the equation can be developed as follows:

$$Q = \rho \cdot V \cdot Cp \cdot \Delta T$$

$$Q = V \cdot 0.9 \cdot 2.1 \cdot \Delta T$$

$$Q = 1.9 \cdot V \cdot \Delta T$$

Since the organic media volume used on the upstream can be estimated (for 1 kilogram product) as $1/[SL]$:

$$Q = \frac{1.9 \cdot \Delta T}{[SL]}$$

When adding the actual conversion of the reaction (because more solvent will be needed to produce one kilogram of product, if conversions are not complete):

$$Q = \frac{100 \cdot 1.9 \cdot \Delta T}{Conv \cdot [SL]}$$

$$Q = \frac{190 \cdot \Delta T}{Conv \cdot [SL]}$$

Assuming 15 % extra of energy for each hour of reaction to hold the requested temperature, and considering the reaction time (t), the total heat needed for the upstream would be:

$$Q = \left(\frac{190 \cdot \Delta T}{Conv \cdot [SL]} \right) + 0.15 \cdot t \cdot \left(\frac{190 \cdot \Delta T}{Conv \cdot [SL]} \right)$$

To the overall energy calculated to heat the reaction, a 25 % energy extra (x1.25) is added to assume losses, or non-ideal behaviours of the system. Aspects related to industrial heat integration – which could save some energy – are not considered. Moreover, the overall obtained value is divided by 3600 to convert KJ into kWh⁻¹, and it is multiplied by the currently assumed 0.25 kg CO₂ · kWh⁻¹ in Europe:³

$$GWP(org(energy)) = \frac{1.25 \cdot 0.25}{(3600)} \cdot \left[\left(\frac{190 \cdot \Delta T}{Conv \cdot [SL]} \right) + 0.15 \cdot t \cdot \left(\frac{190 \cdot \Delta T}{Conv \cdot [SL]} \right) \right]$$

$$GWP(org(energy)) = \frac{0.32}{(3600)} \cdot \left[\left(\frac{190 \cdot \Delta T}{Conv \cdot [SL]} \right) + 0.15 \cdot t \cdot \left(\frac{190 \cdot \Delta T}{Conv \cdot [SL]} \right) \right]$$

Simplifying:

$$GWP(org(energy)) = \left(\frac{0.017 \cdot \Delta T}{Conv \cdot [SL]} \right) + t \cdot \left(\frac{0.0025 \cdot \Delta T}{Conv \cdot [SL]} \right)$$

Therefore, the total CO₂ produced for the upstream unit in organic media is the CO₂ produced from the mass metrics, adding the energy metrics, that is: $GWP_{org} + GWP_{energ}$

Mass equation:

$$GWP(ORG) = \frac{2.3 \cdot \%SolventTreated}{Conv \cdot [SL]}$$

Energy equation:

$$GWP(energ) = \left(\frac{0.017 \cdot \Delta T}{Conv \cdot [SL]} \right) + t \cdot \left(\frac{0.0025 \cdot \Delta T}{Conv \cdot [SL]} \right)$$

Where:

- GWP is kg CO₂ · kg Product⁻¹
- %SolventTreated is the proportion of the solvent incinerated or mineralized in each reaction cycle (%).
- Conv: Conversion of the reaction (%)
- [SL] Substrate loading in kg L⁻¹
- ΔT temperature gradient, T_{reaction} – T_{initial}.
- t the reaction time (h).

S.1.4. ENERGY METRICS FOR AQUEOUS MEDIA.

If only water (or buffer) is used as reaction media, the equation of the energy is analogous to the one built for the organic media system but considering the higher heat capacity of water. Here again, an extra of energy (x1.25) is added, together with the 15% extra per reaction hour.

$$GWP(water(energy)) = \frac{0.32}{(3600)} \cdot \left[\left(\frac{419 \cdot \Delta T}{Conv \cdot [SL]} \right) + 0.15 \cdot t \cdot \left(\frac{419 \cdot \Delta T}{Conv \cdot [SL]} \right) \right]$$

Simplifying:

$$GWP(water(energy)) = \left(\frac{0.037 \cdot \Delta T}{Conv \cdot [SL]} \right) + t \cdot \left(\frac{0.0056 \cdot \Delta T}{Conv \cdot [SL]} \right)$$

S.1.5. ENERGY METRICS FOR AQUEOUS MEDIA WITH COSOLVENT.

The energy to heat both the water fraction and the cosolvent fraction need to be considered separately ($\text{heat}_{\text{water}} + \text{heat}_{\text{cosolvent}}$). It is assumed that ideal cases are followed, and x1.25 will be added to the final value to counter on loss of ideal behaviours. GWP would be:

$$\begin{aligned} GWP(\text{water}/\text{cosolv}(\text{energy})) &= \frac{0.32}{(3600)} \cdot [[(4.184 \cdot V_{\text{water}} \cdot \Delta T) + (1.9 \cdot V_{\text{cosolv}} \cdot \Delta T)] + 0.15 \cdot t \cdot [(4.184 \cdot V_{\text{water}} \cdot \Delta T) \\ &+ (1.9 \cdot V_{\text{cosolv}} \cdot \Delta T)] \end{aligned}$$

The total volume (V_t) needed to produce one kilogram of product, considering conversion and substrate loading, is: $V_t = 100 / (\text{Conv} \cdot [\text{SL}])$. And V_{water} and V_{cosolv} are:

$$V_{\text{water}} = (V_t \cdot \% \text{water}) / 100; \quad V_{\text{cosolv}} = (V_t \cdot \% \text{cosolv}) / 100$$

Substituting and simplifying, the equation for the energy of a water-cosolvent system is:

$$\begin{aligned} GWP(\text{water} - \text{cosolv}(\text{energy})) &= \left[\left(\frac{0.00037 \cdot \% \text{water} \cdot \Delta T}{\text{Conv} \cdot [\text{SL}]} \right) + \left(\frac{0.00017 \cdot \% \text{cosolv} \cdot \Delta T}{\text{Conv} \cdot [\text{SL}]} \right) \right] + t \cdot \left[\left(\frac{0.000056 \cdot \% \text{water} \cdot \Delta T}{\text{Conv} \cdot [\text{SL}]} \right) + \right. \\ &\left. \left(\frac{0.000025 \cdot \% \text{cosolv} \cdot \Delta T}{\text{Conv} \cdot [\text{SL}]} \right) \right] \end{aligned}$$

S.2. DOWNSTREAM FOR ORGANIC MEDIA. DISTILLATION AND (PARTIAL) RECOVERY.

If the reaction is conducted in organic media, during the downstream the solvent needs to be heated up to its boiling point and then distilled, based on its enthalpy of vaporization. Later on the recovered solvent can be reused or incinerated, following the equations depicted previously. Therefore, the overall equation for the GWP of the downstream (distillation) of a reaction in organic media would be:

$$GWP(org(dsp)) = GWP(reactemp - bp) + GWP(dist) + GWP(incineration)$$

Following equations (1) and (5) from the upstream part, the GWP for increasing the temperature to the boiling point of the solvent (and assuming 1 hour at that temperature for the distillation), plus the GWP of the solvent incineration for the proportion that is not recovered would be:

$$GWP(org(dsp)) = Eq (5) + Eq (1) + GWP(dist)$$

That is, GWP contribution of heating the solvent from the temperature of the reaction to the boiling point, plus incinerating the proportion of the solvent.

$$GWP(org(dsp)) = \left[\left(\frac{0.017 \cdot \Delta T}{Conv \cdot [SL]} \right) + t \cdot \left(\frac{0.0025 \cdot \Delta T}{Conv \cdot [SL]} \right) + \frac{(2.1 \cdot \%SolventTreated)}{Conv \cdot [SL]} \right] + GWPdist$$

Since the time to hold the solvent at distillation temperature can be considered 1 h, the equation would be:

$$GWP(org(dsp)) = \left[\left(\frac{0.02 \cdot \Delta T}{Conv \cdot [SL]} \right) + \frac{(2.1 \cdot \%SolventTreated)}{Conv \cdot [SL]} \right] + GWP(dist)$$

$$GWP(org(dsp)) = \left(\frac{(0.02 \cdot \Delta T) + (2.1 \cdot \%SolventTreated)}{Conv \cdot [SL]} \right) + GWP(dist)$$

The heat for the distillation would be:

$$Q_{dist} = m \Delta H$$

Assuming an average density of $0.9 \text{ g} \cdot \text{cm}^{-3}$:

$$Q_{dist} = 0.9 \cdot V \cdot \Delta H$$

Relating the volume to the conversion and the substrate loading:

$$Q_{dist} = (0.9 \cdot 100 \cdot \Delta H) / (Conv \cdot [SL])$$

Adding 1.25 extra, passing from KJ to kWh⁻¹, and adding the European contribution from electricity:

$$GWP(dist) = \frac{0.9 \cdot 100 \cdot 1.25 \cdot 0.25 \cdot \Delta H}{Conv \cdot [SL] \cdot 3600}$$

$$GWP(dist) = \frac{0.008 \cdot \Delta H}{Conv \cdot [SL]}$$

And therefore, the equation for the downstream of an organic media would be (equation (8)):

$$GWP(org(dsp)) = \left(\frac{(0.02 \cdot \Delta T) + (0.008 \cdot \Delta H) + (2.1 \cdot \%SolventTreated)}{Conv \cdot [SL]} \right)$$

Where ΔH is given in KJ / Kg, SL in Kg/L, and %SolventTreated in %.

S.3. DOWNSTREAM FOR AQUEOUS MEDIA BY EXTRACTION WITH AN ORGANIC SOLVENT.

If the biotransformation is conducted in aqueous media, the extraction with an excess of organic solvent is typically the applied downstream. Herein, a certain volume of organic media is added to the aqueous solution (V_{ext}), which is then decanted. Then the organic solvent is distilled to obtain the product, and eventually the solvent is recovered. The different GWP impacts would be: i) energy needed to bring the solvent mixture from the extraction temperature to its boiling point (and hold it there for 1 h); ii) energy for distillation, based on vaporization enthalpy of the solvent; iii) waste produced from organic solvent incineration, based on the %SolventTreated; iv) waste generated by treating the wastewater of the reaction, assuming “recommended” scenario, equation (2). Thus:

$$GWP(water(dsp)) = GWP(reactemp - bp) + GWP(orgdist) + GWP(inc(org)) + GWP(water(rec))$$

The energy to heat the extractive solvent from the reaction temperature to its boiling point would be:

$$Q = m C_p \Delta T$$

Following an analogous procedure as in the upstream part, an average density of $0.9 \text{ g} \cdot \text{cm}^{-3}$ is taken, as well as an average C_p of $2.1 \text{ KJ} / \text{kg} \text{ } ^\circ\text{C}$ (see Table S1):

$$Q = 1.9 \cdot V_{ext} \cdot \Delta T$$

Converting it in $GWP(reacttemp-bp)$:

$$GWP(reactemp - bp) = (1.9 \cdot V_{ext} \cdot 1.25 \cdot 0.25 \cdot \Delta T) / (3600)$$

$$GWP(reactemp - bp) = 0.00017 \cdot V_{ext} \cdot \Delta T$$

To that equation, the 15 % contribution for holding the extractive solvent for ca. 1 hour at that temperature for distillation must be added:

$$Q = 0.15 \cdot 1 \cdot 0.9 \cdot 2.1 \cdot V_{ext} \cdot \Delta T$$

$$GWP_{15\%extra} = 0.000025 \cdot V_{ext} \cdot \Delta T$$

And therefore, the GWP contribution of heating the extractive solvent from the reaction temperature to the boiling point, and assuming 1 hour at that temperature would be:

$$GWP(reactemp - bp) = 0.0002 \cdot V_{ext} \cdot \Delta T$$

Where V_{ext} is the total volume used in the extraction, and ΔT the difference between the temperature of the reaction and the boiling point of the solvent.

With respect to the distillation of the solvent:

$$Q = 0.9 \cdot V_{ext} \cdot \Delta H$$

Converting it to GWP:

$$GWP(dist) = (1.25 \cdot 0.25 \cdot 0.9 \cdot V_{ext} \cdot \Delta H) / (3600)$$

$$GWP(dist) = 0.00008 \cdot V_{ext} \cdot \Delta H$$

With respect to solvent incineration, the solvent recovery must be considered, analogous to the development depicted above for upstream, and connect it to equation (1):

$$V(treated) = (V_{total} \cdot \%SolventTreated) / (100)$$

$$GWP(inc(org)) = 0.021 \cdot V_{tot} \cdot \%SolventTreated$$

And finally, the water of the reaction is treated according to equation (4), assuming the recommended scenario:

$$GWP(water(recommended)) = \frac{0.35 \cdot \%WaterTreated}{Conv \cdot [SL]}$$

If other scenarios for wastewater treatment should be considered, namely mild conditions or incineration, the last part of the equation can be replaced by the respective equations.

Therefore, the GWP for the extractive downstream would be the equation (9):

$$GWP(\text{extraction}(dsp)) = \frac{(0.0002 \cdot V_{ext} \cdot \Delta T) + (0.00008 \cdot V_{ext} \cdot \Delta H) + (0.021 \cdot V_{ext} \cdot \%SolventTreated) + (0.35 \cdot \%WaterTreated)}{Conv \cdot [SL]}$$

References

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