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REVIEW

Engineering in Life Sciences

Same but different–Scale up and numbering up in electrobiotechnology and photobiotechnology

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Facing energy problems, there is a strong demand for new technologies dealing with the replacement of fossil fuels. The emerging fields of biotechnology, photobiotechnology and electrobiotechnology, offer solutions for the production of fuels, energy, or chemicals using renewable energy sources (light or electrical current e.g. produced by wind or solar power) or organic (waste) substrates. From an engineering point of view both technologies have analogies and some similar challenges, since both light and electron transfer are primarily surface-dependent. In contrast to that, bioproduction processes are typically volume dependent. To allow large scale and industrially relevant applications of photobiotechnology and electrobiotechnology, this opinion first gives an overview over the current scales reached in these areas. We then try to point out the challenges and possible methods for the scale up or numbering up of the reactors used. It is shown that the field of photobiotechnology is by now much more advanced than electrobiotechnology and has achieved industrial applications in some cases. We argue that transferring knowledge from photobiotechnology to electrobiotechnology can speed up the development of the emerging field of electrobiotechnology. We believe that a combination of scale up and numbering up, as it has been shown for several photobiotechnological reactors, may well lead to industrially relevant scales in electrobiotechnological processes allowing an industrial application of the technology in near future.

KEYWORDS
electrobiotechnology, numbering up, photobiotechnology, reactor design, scale up

1 | INTRODUCTION

Recent developments such as an increasing world population, rise in CO_2 emissions, depletion of fossil raw materials, and the change in renewable energy production make it necessary to develop new and more flexible processes for the production of fine and bulk chemicals. There are, amongst others, two promising fields of research coping with these issues, the electrobiotechnology and the photobiotechnology. Electrobiotechnology is mainly applied to (i) use organic wastes instead of fossil fuels for the production of electricity in microbial fuel cells (MFCs) and (ii) to use (sustainable) electrical energy and abundant carbon sources (e.g. CO_2 and organic wastes) to produce fuels and chemicals in enzymatic [1–5] and microbial electrosynthesis (MES) with whole-cell biocatalyst. The latter may be even more important for industrial application; often, bulk chemicals are the desired products, but by now, it has also been shown that fine chemicals like terpenes can be produced electrobiotechnologically [6–9]. Renewable energy sources in the electric energy sector, such as photovoltaics, face temporal fluctuations and spatial separation of source and sink, which creates a demand for storage and conversion technologies. However, linking the chemical and energy sectors cannot be

Abbreviations: BES, bioelectrochemical systems; MES, microbial electrosynthesis; MFC, microbial fuel cell; TRL, technology readiness level

achieved with established technologies exclusively, but needs improved and flexible solutions. This gap can be narrowed or even closed by electrobiotechnological processes [10,11]. The field of electrobiosynthesis is still relatively new, so it is desirable to find analogous technologies, from which behavior of the new technology can be estimated. This could be photobiotechnology, which is already a little further down the road to large scale applications. The photobiotechnology uses mainly algae or photosynthetic cyanobacteria to produce fuels and other, even more valuable products [12]. Both research fields have a high potential to contribute to an energy supply and chemical production not based on fossil resources.

To become industrially relevant, it is necessary to develop the processes using these technologies in large scales. Fuels and bulk chemicals need to be produced cheap and simple using biological methods to compete with the oil industry [13]. So far, commonly applied scale up approaches in biotechnology and chemical industry appear not suitable for photobiotechnology and electrobiotechnology. In the latter technologies, the surface dependent processes of light and electron transfer have to be coupled with the 3D bioprocesses including bioreaction, mixing, substrate supply, and gas transfer in suspension culture. In terms of electrobiotechnology this means that the 2D electrode surface has to be sufficient for electron transfer between the electrodes and microorganisms in a bioreactor [13], in case of photobiotechnology light needs to access a large surface area (volume) of the culture [12]. Both process types can be referred to as "4-phase-processes", since apart from liquid medium, gaseous substrates and solid cells, a fourth phase, in case of photobiotechnology photons [14], in case of electrobiotechnology electrons, may play a process limiting role, for sure along with other limiting factors. Therefore, the reactor design challenges in both cases are comparable in certain sense. Regarding scale up of bioreactors, the challenges do even increase since the volume-to-surface ratio often increases with the working volume. One important question is, whether it is more practicable to scale the reactor up to an industrial scale by increasing the volume or might it be more useful to adopt a numbering up approach by linking several small reactors? Yet, this is not answered, especially in case of electrobiotechnology where not many scale up studies have been done. In photobiotechnology, a considerably higher number of scale-up studies have been done, especially with a numbering up approach. It should be mentioned that this opinion focuses on closed photobiotechnological systems and primary electrobiotechnological systems (in contrast to electro-assisted fermentations and hybrid systems [6]), since these two seem to show the most analogies. This opinion shall first give an overview on the latest developments of scale up and numbering up in both electrobiotechnology and photobiotechnology. The aim of this connection is to show the analogy between photobiotechnology and electrobiotechnology, which makes it possible to transfer knowledge gained during scale up in photobiotechnology to the development of larger electrobiotechnological reactors. We will show the limitations of scale up reactors in both technologies and suggest solutions to reach industrial scale in electrobiotechnology.

PRACTICAL APPLICATION

Most applications of electrobiotechnology are located in the field of high volume and low cost products, such as current production, methane production, or waste water treatment. Therefore, scalability is an important factor to proceed in the development. It can help scientists and engineers dealing with electrobiotechnology to find analogous fields of technology to develop and scale up new reactors for their specific task. Here, we suggest taking a look at photobiotechnology to transfer the knowledge for the development of scale up strategies for different reactors in electrobiotechnology. This opinion will show challenges in scale up and ways to overcome it by combining scale up with numbering up and will thus help to increase the industrial relevance of electrobiotechnological processes.

2 | WHAT IS THE DIFFERENCE BETWEEN SCALE UP AND NUMBERING UP?

To transfer bioprocesses from lab to pilot scale or an industrial scale, there are in general two methods [15]. The first one is to increase the volume (scale up) of the reactor used in lab scale. Here, one can differ between a rational scale up and an empirical scale up. During the rational scale up, dimensionless numbers, transport coefficients and geometrical similarities are used to construct a reactor in a larger scale [16,17]. As an example, in biotechnology many scale up calculations are done via the oxygen transfer coefficient $k_L a$, which is kept constant in the small and large scales. In contrast, an empirical scale up does not calculate dimensionless numbers but designs a reactor similar to the lab scale one rather by "try and error". This does often lead to larger reactors looking similar to the lab scale ones in terms of the overall geometry, but calculating the dimensionless numbers, major differences occur. The second method is a numbering up [15]. As the term implies, one single reactor is not necessarily larger than a lab scale reactor (but it can also be a large scale reactor already), but several reactors are linked to increase the overall working volume of

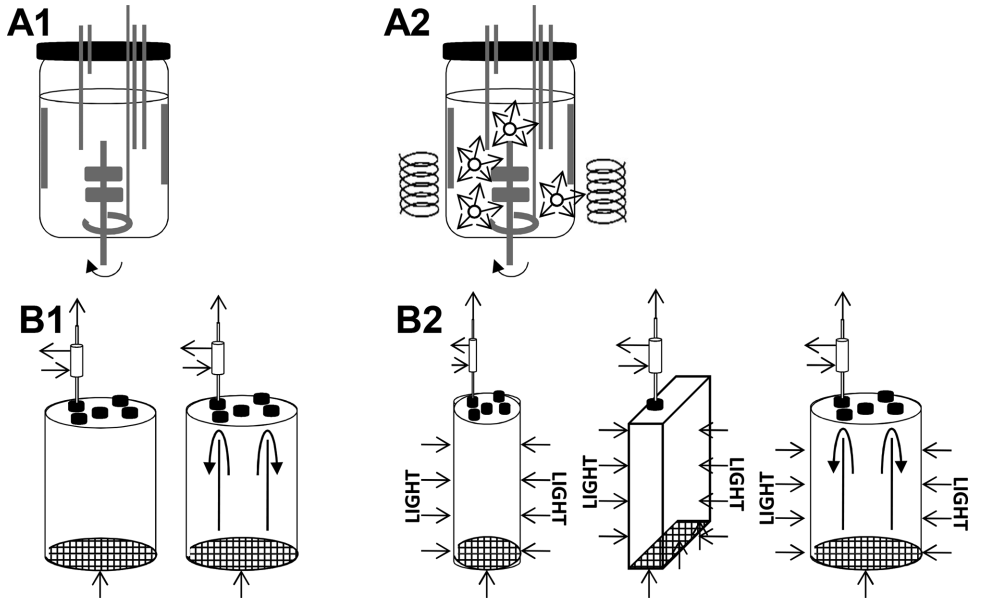

FIGURE 1 Photobioreactors adapted from classic bioreactors. (A1) Scheme of a stirred tank reactor usually used in biotechnology; (A2) Stirred tank reactor for photobiotechnology with internal LED light source operated by induction; (B1) Scheme of bubble column and airlift reactors for usual biotechnological operations; (B2) Bubble column reactors with altered geometry for the optimization of light exposed surface and airlift reactor with light exposure usable for photobiotechnology. Ting et al. (2017) show further schemes of photobioreactors [19]

the entire process. An example from the very beginnings of biotechnology is the use of a large number of small bottles for cultivation of eukaryotic cells for antibody and recombinant protein production instead of constructing one larger reactor. The big advantage here is the comparability of lab scale experiments to industrial scale applications and transfer of the safety integration level. However, major disadvantages related to the larger number of reactors are increased investment, operating costs, space requirements, and maintenance efforts.

3 | SCALE UP AND NUMBERING UP IN PHOTOBIOTECHNOLOGY

Currently, large scale algae cultivation is often done in open ponds, especially if biomass is the main product. This is not suitable for more valuable products, since contaminations, low yields and difficult product separation might occur [12]. Therefore, this article will focus on closed photobioreactorsonly, which, in contrast to open ponds, allows monoseptical cultivation and defined process conditions, and on the scale up to a pilot scale. Five different types of closed photobioreactors are mainly used in photobiotechnology, which are stirred tank reactors, bubble column reactors, tubular reactors, airlift reactors and flat panels, whereby flat panels can also be seen as bubble column or airlift reactor in terms of aeration with a geometry optimized for light exposure. Apart from that, plastic bag reactors can be used as cheap cultivation systems for biomass production with phototrophic organisms, which are a further development of a bubble column reactor [18]. Some of these reactor types are developed from reactor forms usually used in biotechnology (Figure 1).

There are already studies with direct comparison of the different systems available [20]. Scale up to pilot and industrial scale in photobiotechnology is strongly limited by the penetration depth of light into the liquid medium. As an example, for tubular reactors, rational scale up via tube diameter and mixing time was proposed. A study showed that this would lead to a maximum tube diameter of 10 cm to allow similar conditions as in smaller scale [21]. This, for sure, only holds true for reactors with an external illumination. During the last years, there have been developments of internal light sources within the photobioreactors, e.g. via small LEDs working via induction from the outside, or via optical fibers [22]. This allows more complex reactor geometries and larger diameters, as needed for stirred tank reactors, but adds additional costs in comparison to the use of external light sources. Another limiting factor is the gas concentration gradient within the reactor. If a gas stream enriched in CO_2, which is the main carbon source for algae under auxotrophic conditions, enters the reactor from one side, the CO_2 concentration decreases with increasing way length due to the consumption by the algae, while the O_2 concentration increases. Photosynthesis can be limited by an increased O_2 concentration [23]. The CO_2 concentration does also affect the pH, leading to different growth conditions within the reactor [24]. Here, it is important to consider the changing solubility of CO_2, which is also dependent on the system pressure and may therefore be increased in large scale systems with higher

TABLE 1 Examples of scale up and numbering up in photobiotechnology

Working volume and light exposed surface	Reactor type	Results (Product concentration)	Source
400 L with 148 m^2 light exposed surface	Tubular, winded	1.43 $g_{Dry\ Biomass}$/L∗d	[25]
15 L	Stirred tank reactor	9.16 $\mu g_{Yessotoxin}$/L*d	[26]
6*20.5 L with 3.4 m^2 light exposed surface each	Flat plate	0.85 $g_{Dry\ Biomass}$/L*d	[27]
20 L *16	Plastic bag	17.37 $mg_{Fatty\ acids}$/L*d	[28]
6 L *50	Airlift	1.56 $g_{Dry\ biomass}$/L (final concentration)	[29]

hydraulic pressure in the lower parts of the reactor. Table 1 shows examples for scaled up and numbered up photobioreactors: most of these examples are for the production of biomass, but also higher value products were produced (see Table 1).

The tubular reactor studied in [25] and the flat plate reactor shown in [27] can be seen as an empirical scale up in combination with numbering up for the cultivation of algae; although the same type of microalgae was used, the tubular reactor performed better, maybe because the light exposed surface per volume was higher. The stirred tank reactor was scaled up based on a 2 L reactor based on similarities according the maximum shear stress, the flow regime and the impeller tip speed. In contrast, the aspect ratio increased for the larger reactor to allow a larger light exposed surface per volume. It was reported, that yields in the 15 L reactors are comparable to those obtained in a 2 L stirred tank reactor and higher than yields in shake flasks [26]. The plastic bag reactor again is an empirical scaled up system, numbered up to a larger plant size. The airlift photobioreactor started from an empirical scale up but was further optimized and characterized in terms of flow regime; a further scale up is considered to be easily possible by numbering up and by comparing it to photo bubble column reactors in smaller scales, the growth rate is reported to be higher [29].

A further design as a flat panel and especially reactor characterization strategies were proposed by [30]. Although the reactor design itself was based on empirical scale up, the characterization may well help to compare, optimize and scale up photobioreactors [30]. A possibility to overcome the limitation of reactor size by the penetration depth of light is the introduction of light into the reactor, via fibers, LED balls or light sticks [31]. This technology is smart and may be very beneficial for the production of high value products, but for cheap base chemicals it is desirable to use sun light as main light source to minimize the production costs. To allow a rational scale up, more sophisticated systems are required. These may be stirred tank reactors with internal light sources or airlift reactors. Numbering up can be done with several reactors in parallel, which do then face the same environmental conditions (light intensity, temperature). For numbering up, flat plate reactors, plastic bag reactors and tubular systems are often used, which can be placed next to each other with little space demand. Using several reactors in parallel, it is important to bear in mind shading effects if the reactors are close to each other in order to minimize the surface to footprint area [14]. This can happen especially with flat plat reactors [32]. In general it seems that "easy" reactor designs without stirring and complicated inner installations might be more suitable for a numbering up, since the single units are cheap, easy to construct and operate. On the contrary, scale up of these simple systems is limited because of increasing gradients within one unit. More sophisticated systems, like stirred tank and airlift reactors, might perform better during rational scale up, but the costs of building and operation (power input by gassing etc.) are only reasonable if high value products are desired.

4 | SCALE UP IN ELECTROBIOTECHNOLOGY

In electrobiotechnology, two main setups of bioelectrochemical systems or reactors (BES) have been frequently used: a single-chamber reactor and a two-chamber system [33]. In case of the single-chamber system, the working and counter electrodes are placed within one and the same reactor chamber, and the reaction of interest takes place without a separation from the counter electrode reaction. The reaction of interest can be, in general, either current generation at the anode from organic substrates (MFC), hydrogen evolution at the cathode via an additionally applied potential (microbial electrolysis cell), or the production of compounds out of CO_2 or organic substrates and electrical current at the cathode (MES). In two-chamber reactors, the reaction of interest is separated from the counter reaction usually by an ion exchange membrane to shelter sensitive organisms from toxic product of the counter reaction, to avoid further conversion of the desired product and to maintain concentration gradients (e.g. pH, oxygen) [33]. Examples for the scale up of different systems are summarized in Table 2.

Concerning the production of current and methane or hydrogen from wastewater, pilot plant studies up to 1000 L have been conducted [34].

The reactor design of the two single chamber systems found was rather empirically, shaped as a rectangular tank

TABLE 2 Scale up examples in bioelectrotechnology (MEC)

Working volume and electrode area	Reactor type	Current generation	Source
1100 L, 16.5 m^2 geometrical cathode area	Single chamber rectangular tank	0.41 A/m^2	[34]
88 L, 1.44 m^2 anode area	Single chamber rectangular tank	0.8 L_{H2}/d over ½ year	[35]
30 L, 0.58 m^2 anode area	Two chamber flat plate	0.72 A/m^2	[36]

with several electrode modules [34,35]. Cusick et al. also used the same substrate (winery wastewater) for MFC in a 30 mL MFC in the lab, generating up to 0.72 A/m^2 of current. Apart from that, single chamber-reactors larger than 10 L have not been studied so far as single reactors, but several studies used single units larger than 10 L in a numbering up approach of even larger sizes [37,38]. For two-chamber systems, also empirical scale up strategies have been followed to reach pilot scale, mainly based on increasing the electrode area in a flat plate electrobioreactor. For example, a 30 L working volume flat plate reactor was used for the production of current from waste water [36]. Here, an additional 120 L tank was used to recycle the wastewater in order to simulate a continuous flux. Yet, only MFCs and MEC were scaled up to pilot or industrial scale, but not MES processes; this is not surprising since yet, most MES processes still have to undergo optimizations to be ready for scale up in an economical point of view.

During empirical scale up studies, it has been observed that current densities and performance were often lower in the larger systems compared to smaller ones [34,39]. Brown et al. (2014) concluded that it is not enough to focus simply on the electrode surface area. On the contrary, it is necessary to also maintain the flow regime within the cell, giving reason for the use of rational scale up methods [36]. Rational scale up in electrobiotechnology to a larger scale has not been shown so far, but several suggestions for scale up parameters have been made, including the calculation of dimensionless numbers, geometrical similarity, model-based approaches such as computational fluid dynamics and electrode surface area [40–43].

As for photobiotechnology, it might be useful to adapt reactor designs known from usual bioprocesses to the requirements of electrobiotechnology. A suitable BES design for scale up might be a stirred tank reactor with an "upgrade kit" to allow bioelectrochemical processes within the reactor. This has been shown for the production of para-hydroxybenzoate in a single chamber reactor with up to 2.5 L working volume [44], for current production in a single chamber system with 2.5 L [43], for current production in a two chamber electro-stirred tank reactor with up to two liter [42,43] and for the production of organic acids in a two chamber reactor with up to 2 l [43]. It has also been shown that CFD (Computational Fluid Dynamics) studies for the "upgraded" bioreactors reveal the mixing conditions within the reactor, so it might be possible to use the knowledge gained from CFD simulations for the scale up of the systems [43]. Recently, [45] developed a single-chamber BES with a rode-shaped "All-in-One" electrolysis electrode which can be easily inserted into typical bioreactors (e.g. stirred tank and bubble column). This system has been successfully used for in situ generation of H_2 and O_2, control of redox potential and recharge of electron mediator for electricity-aided production of 1,3-propanediol and *n*-butanolin laboratory scales (0.5 and 2.5 L) [46]. Another design which may be suitable for a rational scale up is an electrochemical bubble column reactor. It has been shown that this design is suitable for current generation as well as for fuel production [40]. These studies show that modified design of typical bioreactors from biotechnology can be suitable for electrobiotechnology aiming at production of fuels and chemicals. Yet, a scale-up of such systems to a pilot scale has not yet been shown. Figure 2 illustrates the design of these potentially scalable reactors in contrast to the similar types of bioreactors for other processes.

5 | NUMBERING UP IN ELECTROBIOTECHNOLOGY

In electrobiotechnology, MFCs and microbial electrolysis cells have already been numbered up successfully by stacking several fuel cells together (examples of different stacked reactor types in Table 3). Numbering up studies on BES for the production of chemicals have not been published so far to a pilot scale of more than 10 L.

As in photobiotechnology, flat plate and tubular reactors seem to be suitable for numbering up to a pilot plant scale. It seems that for tubular reactors, smaller units are used, but the number of units stacked together can be higher. Several other studies showed the possibility to stack fuel cells in lab scale. A remaining question is how to connect the single modules in the stacks, parallel or serial [53–55]. For parallel connection, it seems that a slightly higher power production can be obtained, but more research is needed here to allow a final conclusion which method should be used for numbering up. There is another special case for electrobiotechnology, which has been shown in literature; Apart from building several units and putting them together in a stack, it is also possible to use one unit and just enlarge the electrode surface area within this unit. This is not really a numbering up or a scale up, but rather a kind of optimization of one unit. As an example, the

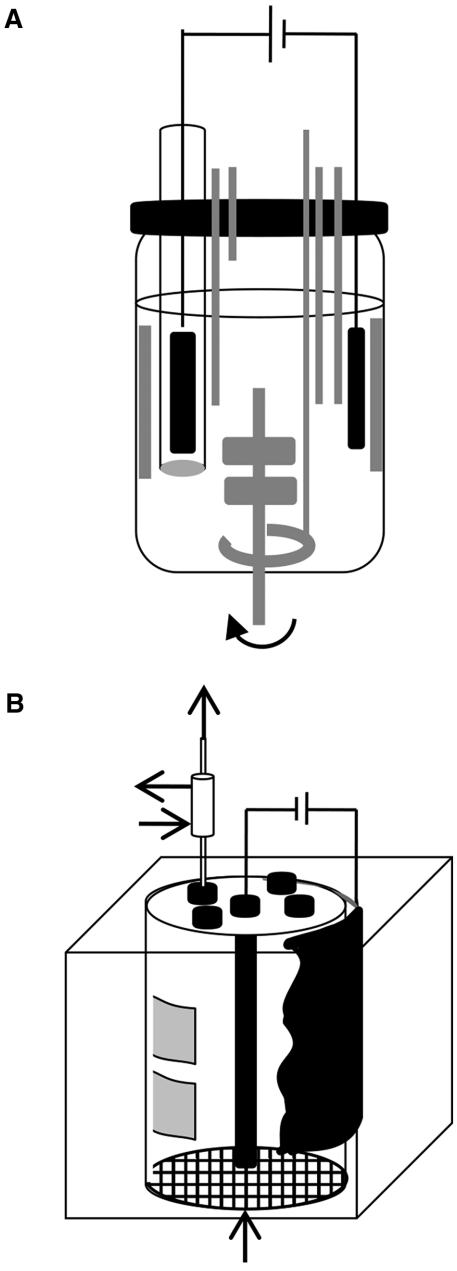

FIGURE 2 Development of electrobioreactors based on designs known from biotechnology. (A) Stirred tank reactor for electrobiotechnology with electrodes and a second chamber within the reactor; (B) Bubble column reactor with internal electrode and surrounding counter chamber for electrobiotechnology [40]. Further reactor designs for electrobiotechnological reactors have been described by Krieg et al (2018) [33]

"All-in-One" electrode mentioned above could be used to place multiple electrodes into the same bioreactor [45].

6 | COMBINATION: ALGAE IN MFC

There are attempts to use microalgae in MFCs and create a kind of biological solar cell, reviewed in [56]. In this

TABLE 3 Numbering up to pilot scale in electrobiotechnology

Product/ Process	Working volume or surface area	Reactor type	Number of units	Performance	Source
Current from acetate	20 L, 1.5 m^2 electrode surface	Flat plate	4* 5 L	11 W/m^3; 0.3 A/m^2; after improvement of cathode 144 W/m^3 at 2.8 A/m^2	[47]
Current from wastewater	96 L	Tubular, serial connection	48*2 L	1.35 W/m^3; 93 mA	[48]
Current from wastewater	10 L, 0.57 m^2 electrode surface	Tubular, serial and parallel connection	40*0.25 L	4.1 W/m^3 (serial connection) 6 W/m^3 (parallel connection); 0.11 A/m^2	[49]
Current from acetate	72 L	Flat plate, parallel connection	6*12 L	50.9 W/m^3; 1.8 A	[38]
Current from wastewater and H_2	10 L; 0.005 m^2 electrode surface	Flat plate	2 *5 L	up to 400 A/m^3; up to 50 mL H_2/L*d	[50]
Current from wastewater	45 L	Flat plate	4*11.2 L	0.012 kWh_{el}/m^3	[37]
Current from wastewater	1000 L	Flat plate	50*20 L	up to 125 W/m^3	[51]
Current form waste water	65 L	Flat plate, serial connection	6*10.8 L	2-4 W/m^3	[52]

combination, algae may grow as phototrophic biofilm on the cathode producing oxygen as electron acceptor, while the current is produced from wastewater at the anode side [57]. Another possibility is to introduce algae to the anode side as electron donor from sunlight [58]. A third idea is to grow algae on both sides and combine the effect of electron donation by algae and oxygen production as electron acceptor separated from each other. Yet, no experiments have been conducted in pilot scale, although first lab scale tests with stacked MFCs have been carried out [59]. This is an interesting field of research in terms of reactor design, since it combines the difficulties of electrobiotechnology and photobiotechnology, and the development of scalable reactors will remain a challenge during the next years.

7 | SAME BUT DIFFERENT–COMPARISON OF PHOTOBIOTECHNOLOGY AND ELECTROBIOTECHNOLOGY

To gain knowledge from photobiotechnology for the development and optimization of electrobiotechnological systems, several analog limitations of the processes can be found (Table 4). Examining the techniques to overcome these limitations in both photobiotechnology and electrobiotechnology one may find similar strategies. It is to mention that this is certainly not a complete list of all limitations in these processes. Especially in electrobiotechnology, the influences of electrode type, membrane and electrical field distribution occur which are not considered in this opinion, since they do not necessarily find their analogy in photobiotechnology. To evaluate the performance of scaled up designs, performance parameters can be found in both technologies

An important factor electrobiotechnology can learn from photobiotechnology is the "penetration depth" of the "4th dimension". In photobiotechnology, it can be observed that the reactor diameter is limited by the penetration of light into the reactor. In electrobiotechnology, this might be somehow similar, depending on the type of electron transfer mechanism; the maximum distance of electron transfer between electrode and microorganism, so e.g. the maximum length of conductive pili, the maximum thickness of a biofilm on a cathode or the effective diffusion way of mediator molecules, could be compared to this penetration depth, limiting the maximum effective diameter of the reactor. It would be interesting to learn more about the "penetration depth" of electrons in different BES to allow conclusions about maximum reactor diameters or maximum electrode distances. This certainly depends on the electron transfer mechanism of the electroactive culture. The availability of light or, electrons, is also dependent on the illuminated surface area or the electrode area, respectively. Recently, 3D-electrodes and fluidized bed electrodes allow new designs for reactors in electrobiotechnology, similar to the invention of internal light sources in photobiotechnology. Depending on the mixing conditions, the penetration depth and the surface area also influence the "contact time" of each cell with the "4th dimension", which leads to light/dark cycles [60] of each cell in photobiotechnology and a limited contact time of cells and electrode for electron uptake in electrobiotechnology. Also, algae biotechnology reminds the electrobiotechnolgy of limited reactor heights if CO_2 is used as substrate and consumed rapidly by the microorganisms, which might be the case in optimized processes; also, changing solubility of CO_2 in high reactors with increased hydraulic pressure might be limiting. In many electrobiotechnological processes, valuable chemicals shall be produced from CO_2 using electrical current. All in all, these limitations make it obvious that scale up does only work up to a certain volume, it still has to be tested what the maximum volume in electrobiotechnology could be. A further comparison to photobiotechnology can be made by using the technology readiness level (TRL) [61]. This index shows on which step between the research idea (or concept) and the industrial application a technology or process stands, starting with TRL 1 (basic principle reported) and leading to TRL 9 (technology operates in industrial scale). Based on the current research, the TRL of electrobiotechnology is still lower than that of photobiotechnology. We suggest to place electrobiotechnology at most in TRL 5 (Technology validated in relevant environment (industrially relevant environment in the case of key enabling technologies)) and photobiotechnology in TRL 9, since some processes are already working since several years in industrial scale [62] (Table 5). It must be mentioned that the TRLs of the most electrobiotechnology and photobiotechnology process are lower [63].

Numbering up seems to be the main method in photobiotechnology to allow large scale applications. Although the working volumes shown here in photobiotechnology are lower compared to the largest systems in electrobiotechnology, the TRL of the technology is higher; one has to keep in mind that industrial applications are often done in open ponds of more than 25000 L [62], which have not been discussed here since open reactor designs are not yet suitable for electrobiotechnology. In electrobiotechnology, little scale up to pilot plant or industrial scale has been done at all and empirical scale up predominates in the production of chemicals and fuels, while numbering up is often used for MFCs. Since the effective size of a bioelectrochemical system is limited, as the size of a photobiosystem, numbering up will surely be necessary to allow large production plants for electrobiochemically produced chemicals. In electrobiotechnology, more studies should therefore be done concerning numbering up of BES and the development of new, scalable reactors for the production of chemicals. In contrast to photobioreactors, knowledge should be gained here about the electrical connection, e.g. whether

TABLE 4 Analog limitations in photobiotechnology and electrobiotechnology

	Photobiotechnology	Electrobiotechnology
Limiting "4th dimension"	Light penetration depth	"Electron penetration depth"
Surface limitation	Illuminated surface area	Electrode surface area
Limitation on cell level	Light /dark cycle of each cell	Contact time to electrode (if direct electron transfer occurs)
Substrate supply	CO_2 transfer	CO_2/substrate transfer
Efficiency parameter	Photon efficiency [60]	Coulombic efficiency [40]

TABLE 5 Photobiotechnologyand electrobiotechnology on the way to industrial application

	Photobiotechnology	Electrobiotechnology
Mainly used reactor type	Flat plate, Tubular, bubble column	Flat plate
Maximum size reached by scale up	400 L	1100 L [34]
Maximum size reached by numbering up	320 L	1000 L [51]
Highest TRL	9	5

parallel or serial connection is suitable for the different approaches. In both fields, rational scale up of lab scale reactors is rather rare. For a better comparison and optimization, it is desirable to have more studies dealing with rational scale up of the reactor units, which can then be linked to large production plants by numbering up. By now, it seems that especially well mixed reactors like stirred tanks and airlift/bubble column reactors are suitable for scale up to industrial scale, while flat plate reactors and tubular reactors should rather be numbered up to avoid bad mixing conditions in large scale.

8 | WHERE TO GO: LARGE SCALE PROCESSES IN ABIOTIC ELECTROCHEMISTRY

In contrast to electrobiochemical technologies the electrochemical production of a variety of chemicals is already an established industrial process. Two of the most prominent examples are the fused-salt electrolysis (mainly applied for aluminum production) and the chlorine-alkali electrolysis. In both industrial processes the single reactor size is increased to a certain range followed by a numbering up to increase the amount of product [64]. So, the electrode surface of every single unit is rather small (2.7 m^2), but compared to the BES, the current density of these electrodes is very high (up to 4 kA/m^2) [64]. From this example it can be learned that simultaneous to scale up, electrode optimization should be done in electrobiotechnology to reach higher current densities.

In general, the scale up of electrochemical systems is thereby mainly limited by the increasing space between the working and the counter electrode. With an increasing distance between both electrodes the ohmic resistance of the electrolysis cell is increased proportional leading to a higher cell voltage and consequently a higher energy demand. This challenge is even greater in the field of electrobiotechnology, where the use of electrolytes with high conductivity is often forbidden due limitations in the stability of the biocatalysts [65].

However, a direct transmission from abiotic electrochemical systems towards bioelectrochemical technologies might not be feasible. One of the main problems when combining biological and electrochemical methods is the different reaction speed. Electrochemical reactions at the electrode surface are generally faster compared to the metabolic activity of bacterial cells, which is one of the reasons that current densities in biological systems are rather low compared to abiotic electrochemical systems. One elegant option to overcome the gap in different reaction speed is the use of capacitive electrodes and systems, such as fluidized bed electrodes [66]. In this type of reactors capacitive electrode particles such as granular activated carbon serve as fluidized charge buffer whereby the charge transfer is realized physical contact to a current collector. This is, however, also limited by the type of organisms used, which may be shear sensitive, and the power input by gassing to fluidize the granulate.

9 | CONCLUDING REMARKS

Some reactor types, like flat panel reactors and airlift reactors, show similar geometries in photobiotechnology and electrobiotechnology, and in both cases the designs may be based on reactors used in classical biotechnological processes. The electrobiotechnology can for sure learn from photobiotechnology in terms of design and optimization of the used reactors to speed up the development of systems in industrial scale.

So, our suggestion (Figure 3) for rational process development in electrobiotechnology would be to do first tests in H-cells to verify the potential of the process. Afterwards, different reactor types from photobiotechnology,

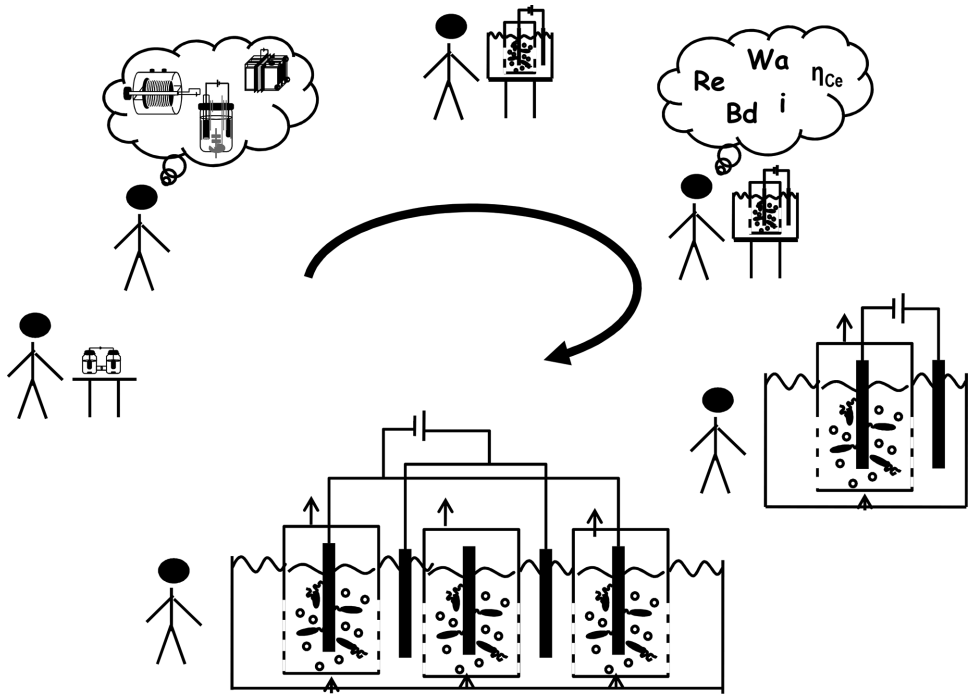

FIGURE 3 Steps to an industrial bioelectrochemical process. First studies in H-cells as feasibility study, then choice of appropriate reactordesign based on literature; small scale experiments with process characterization and optimization followed by rational scale up to a pilot scale up to 100 L, afterwards numbering up to final industrial scale

electrobiotechnology and electrochemistry should be assessed for their suitability in the desired process. A small scale reactor should then be constructed and used for process optimization; Here, the development of electrode materials with three dimensional structures and therefore enlarged surface areas, which are biocompatible and extremely conductive at the same time, will remain a challenge. During these lab scale experiments, researchers should start to conduct the experiments with an eye towards application and therefore characterize the performance of their processes far better to allow optimization, comparison and scale up. We suggest to calculate dimensionless numbers such as Wagner number, Reynolds number, Bond number or Weber number and note ratios like the specific electrode surface, anode to cathode ratio and gassing rates. If possible, a CFD analysis of the small scale reactor can help to better understand mixing conditions in the reactor. After the optimization in lab scale, a rational scale up to a reactor of 10 to 100 L working volume should be conducted; looking at the current scale up attempts in electrobiotechnology, this seems to be a realistic size for a single unit. To create larger processes, several of these units shall now be connected, resulting in a final numbering up of the process. The large scale application has to be verified using different performance parameters to allow an evaluation of the scale up method.

When looking at the large number of studies dealing with scale up and numbering up in both, electrobiotechnology and photobiotechnology, it is obvious that more work has to be done during the next years to allow competition with the standard production procedures of fuels, chemicals and energy. Both technologies are important to industry and will certainly remain in the focus of research during the next years, and by now it looks as if processes using electrobiotechnology are already thinkable from an economic point of view [67]. At the moment there is a discrepancy of a bright future for electrobiotechnology at the horizon [63]. Nevertheless, there is a risk that electrobiotechnology is running into the "valley of death", like other promising technologies in the past. The "valley of death" is characterized by the fact that excellent research and development results with a probably high societal, economic and ecological impact will not be transferred into innovative commercial products and ready to use technologies. Knowledge based scale up and/or numbering up concepts are needed to avoid the risk that electrobiotechnology will not be applied in the future.

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CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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