Space Biomanufacturing of Lactic Acid: Conceptual Design and Techno-Economic Analysis

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Abstract

Space biomanufacturing is an emerging paradigm to support long-term missions by generating products on-site and thereby reducing the high cost of resupply. This is done by creating circular manufacturing systems based on biological processes that are capable of recycling waste to minimize the need for make-up resources. This paradigm is motivated by the fact that deployment cost of a space system depends strongly on the cost of transportation of system components and resources, which is directly proportional to their mass. The total system mass is thus a critical factor that dictates its design; specifically, mass constraints require tight system integration and restricts the type of resources and equipment used (e.g., for production, heating/cooling, and storage). In this work, we present a computational framework to conduct design and techno-economic analysis of space biomanufacturing systems for lactic acid. Lactic acid (LA) is a platform chemical that can be converted into polylactic acid (PLA) for habitat construction. The framework is used to inform the selection of the best organisms and their preservation methods. We use the Equivalent System Mass (ESM) metric as the key design metric that maps system components (e.g., energy, resources, equipment) to a common mass basis. Our analysis reveals that the preservation modality plays a key role in overall system mass due to primarily to energy use. We also found that lyophilized cultures can reduce storage energy use by up to 99%. By leveraging in situ resource utilization, a 8 ton system could produce the sufficient PLA for fabricating a lunar habitat, with nearly a 90% reduction in logistical cost. In addition, we find that radiation-induced reductions

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in microbial yield can increase system mass by up to 28%. These findings highlight how a system mass centered approach can guide the design of modular, resource-efficient biomanufacturing systems for future space habitats.

Keywords: manufacturing, space, mass, design, circularity.

1 Introduction

Space exploration has been driven by the growing need to deploy and monitor critical infrastructure (e.g., satellite communications) and to gain scientific understanding.[1] As space missions become more frequent and longer, it is necessary to develop support systems that can recycle resources and waste and with this minimize the need for resupply missions.[2,3]

The International Space Station (ISS) is a notable example that illustrates the importance and challenges of properly designing support systems. The ISS is a research laboratory that has provided significant technological and social benefits,[4] advancing our understanding of human health,[5,6] materials science,[7,8] and biological processes.[9,10] However, a major challenge in executing new research projects in the ISS is the associated high maintenance costs. To give some perspective, approximately 60% ($1.8 billion) of the total ISS annual budget ($3 billion) is devoted to the *transportation* of crew and resources.[11] This is mainly due to the high cost of fuel, which is the dominant cost in space missions.[12] The need to minimize fuel imposes strict mass limitations, making it essential to manage resources and equipment in an effective manner. For context, the cost of shipping just *one kilogram of resources* to low-Earth orbit is approximately $10,000.[13] On-site resource utilization is thus key to enable the on-demand production of chemicals/materials while minimizing resupply.[14] These materials can then be used for the construction, maintenance, and repair of mission systems,[15] which is particularly important in long-term missions.[16]

Biomanufacturing is a promising approach to support circular systems for space exploration.[17] This relies on the use of biological processes that are engineered to produce and manufacture products and materials on-demand.[18] Space biomanufacturing has diverse applications; for example, microorganisms can be used for regenerative medicine applications (e.g., tissue engineering and disease modeling),[5] as well as for pharmaceutical synthesis to produce drugs and chemicals,[19,20] food production[21,22] and waste recycling.[11,23] In addition, biomanufacturing can be employed in regolith bioremediation and biomining,[24] allowing the extraction of useful materials from lunar soil. Another important application is the generation of construction materials that support infrastructure.[25] Importantly, *microorganisms play a key role* in facilitating efficient resource and process integration, by transforming waste streams into valuable products.

Although biomanufacturing systems have been widely studied, the focus of most studies has been on their technical and operational characteristics, with limited attention on transportation cost. Specifically, few studies have addressed the techno-economic feasibility of biomanufacturing under the unique challenges posed by operation in space.[17] To effectively design and evaluate biomanufacturing in such environments, it is essential to develop conceptual design and computational modeling tools.[26,27] Computational models can offer valuable insights into key drivers of system efficiency, enabling the quantification of resources and energy, and ultimately of overall performance and cost. The use of models also facilitates the quick exploration of different designs and operating scenarios.

Deploying biomanufacturing systems in space requires of a fundamentally *different process design* approach. The traditional paradigm for process design is objective-driven, in the sense that the system is engineered to maximize or minimize specific performance goals (e.g., return on investment or cost). When designing a system in space, however, the mass/size of the system is the critical factor that takes priority due to strict limitations of transportation and resources. As such, the design of space systems is constraint-driven. Moreover, space systems are subject to different disturbances and externalities (e.g., gravity and cosmic radiation) that pose non-obvious and often unknown constraints. For instance, the survival and performance of microorganisms used in bioreactors can be affected by storage/preservation conditions, gravity, and radiation.A useful approach that facilitates the design of space manufacturing systems is the Equivalent Systems Mass (ESM) analysis. ESM is a metric that maps different physical resources such as feedstocks, power, cooling, and equipment into mass (a unifying metric).[28] The focus on mass can reveal interesting and hidden aspects of process components that inform necessary innovations in bioprocesses.

In this work, we present a computational framework to evaluate space biomanufacturing system designs for lactic acid production (a valuable platform chemicals) based on system mass. By comparing different microorganisms such as (*Escherichia coli, Saccharomyces cerevisiae*, and *Pichia pastoris*), our analysis reveals the critical components responsible for the largest mass in system design. These insights underscore the importance of in-situ biomanufacturing to minimize launch mass, reduce reliance on Earth-based resupply, and support long-term space missions.

2 Computational Framework

This work evaluates designs by using system mass as a metric to compare different options. We evaluated different microorganisms, such as *Escherichia coli, Saccharomyces cerevisiae*, and *Pichia pastoris*, as well as various culture media (including liquid and lyophilized cultures) and their fermentation capabilities for lactic acid production. Lactic acid bioproduction on Earth has been widely studied, as it is an important platform chemical with diverse applications (i.e., chemical, pharmaceutical, food, cosmetics, and plastic industries).[29] For instance, lactic acid has gained interest due to its capacity to be transformed into polylactic acid (PLA), a biodegradable polymer with applications in the production of packaging and new components via 3D printing.[30]

2.1 Equivalent System Mass

The evaluation of a manufacturing process by means of the ESM allows for the quantification of resources and components on a common basis, expressed in terms of units of mass (kilograms). This common basis facilitates comparison and trade-off of systems components. In space missions, the cost of transporting a load is proportional to its mass (proportional to fuel usage); therefore, a mass-based measure such as ESM is useful to quantify the launch cost of the system. In this regard, through

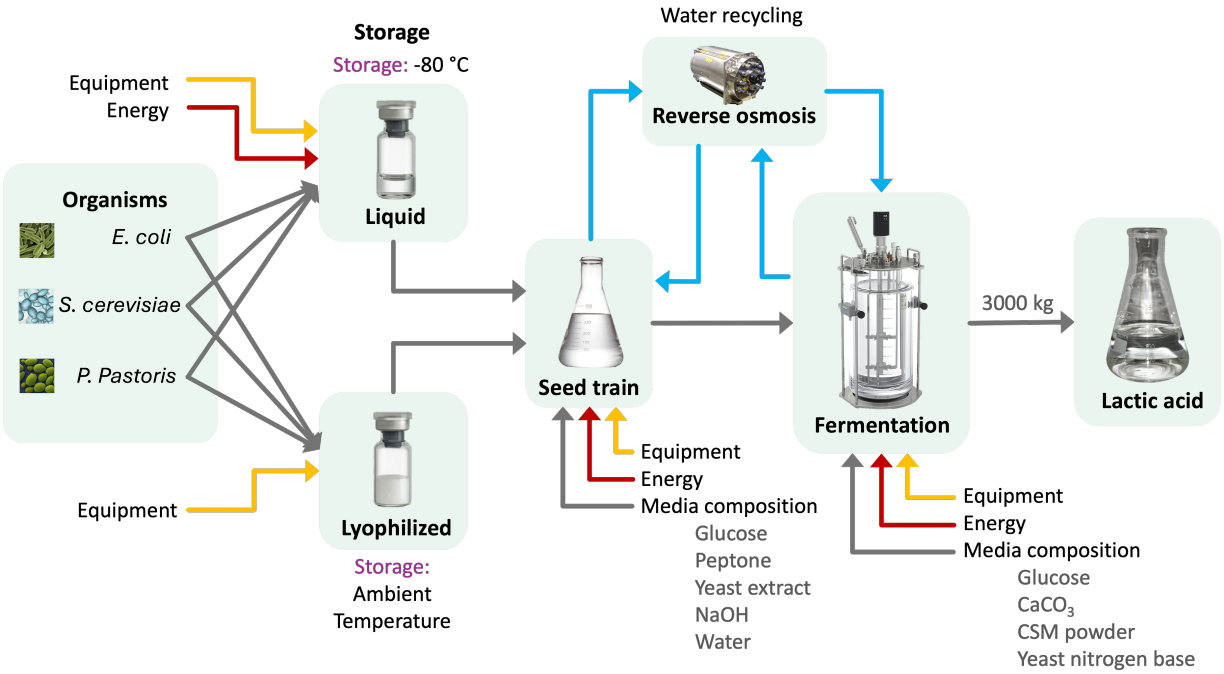

Figure 1: Conceptual design framework for the biomanufacturing system under study. Input resources across storage, seed train, and fermentation are quantified to determine the total mass of the system, utilizing different organisms preserved in various culture modalities.

ESM analysis, it is possible to identify which of the several options can meet all specified requirements and have the lowest launch cost in relation to mass, power, and cooling:

$$ESM = \sum_i M_i + P_i \delta^{power} + C_i \delta^{cooling} \tag{2.1}$$

ESM is computed using 2.1, where i is the index of a system component. The terms δ^{power} and $\delta^{cooling}$ denote the electrical power and cooling conversion factors (typically set to 87 kg/kW and 146 kg/kW, respectively); these factors capture the mass of equipment and resources needed for power and cooling supply and are reported in the NASA Life Support Baseline and Assumptions Document (BVAD).[31] The term M_i refers to the mass of components that constitute the system (e.g., chemicals, glass, stainless steel, polyethylene), P_i represents the power consumption (i.e., electrical power demand) and C_i is the thermal demand rejected from the system.

3 Techno-Economic Analysis

The biomanufacturing system under study was evaluated considering the following key components: storage, seed train, and fermentation (Figure 1). To determine the total system mass, the batch time was first determined by taking into account the duration of the seed train τ^{st} (which we obtained from the experimental data), the fermentation time for lactic acid production τ^{ferm} (obtained from the literature[32–34]), and by accounting for 24 hours of cleaning time (τ^{clean}). Based on these time

parameters, the total number of batches that can be processed in one year (n^{batch}) was determined, as shown in (3.2).

We then computed the fermentation equipment volume (ν^{fer}) that is required to achieve a target lactic acid production of 3,000 kg (Φ^{target}), according to the initial glucose concentration in the fermentation media ($C_0^{glucose}$) and the yield from glucose to lactic acid ($\eta^{product}$), as shown in (3.3).

$$n^{batch} = \frac{\tau^{year}}{\tau^{st} + \tau^{ferm} + \tau^{clean}} \tag{3.2}$$

$$\nu^{fer} = \frac{\Phi^{target}}{n^{batch}\eta^{product}C_0^{glucose}} \tag{3.3}$$

The total system mass (M^{Total}) is obtained by combining the mass for all process stages, as shown in (3.4). The mass of each stage involves the mass associated with the equipment, the chemicals utilized, and the energy requirements (e.g., power for the seed train and fermentation, cooling for storage). This breakdown is described in (3.5)- (3.10).

$$M^{Total} = M^{sto} + M^{st} + M^{fer} \tag{3.4}$$

The mass associated with storage (M^{sto}) accounts for the equipment mass ($M^{eqpt-sto}$), the mass of the chemicals used ($M_i^{chem-sto}$), and the cooling requirements (C^{sto}), as shown in (3.5).

$$M^{sto} = M^{eqpt-sto} + M_i^{chem-sto} + C^{sto} \tag{3.5}$$

The mass for the seed train (M^{st}) is determined by adding the mass of the equipment used in the seed train ($M^{eqpt-st}$), the mass of the chemicals employed ($M_i^{chem-st}$), and the power requirements for this stage (P^{st}) (Equation (3.6)).

$$M^{st} = M^{eqpt-st} + M_i^{chem-st} + P^{st} \tag{3.6}$$

The mass associated with the fermentation stage (M^{fer}) is determined by using the mass of the fermenter ($M^{eqpt-fer}$), the mass of the chemicals required for the fermentation process ($M_i^{chem-fer}$), and the power consumption for fermentation (P^{fer}), as shown in Equation (3.10).

$$M^{fer} = M^{eqpt-fer} + M_i^{chem-fer} + P^{fer} \tag{3.7}$$

The breakdown of these stages is represented in Figure 1, which illustrates the mass perspective framework for designing biomanufacturing systems for space applications.

3.1 Storage

We evaluated a couple of storage/preservation modalities for the microorganisms: liquid and lyophilized cultures.

Liquid cultures are cell cultures suspended in a bulk fluid and cryopreserved at temperatures near -80°C. During the freezing process, the cells are gradually dehydrated to prevent the formation of ice crystals from intracellular water, thus protecting the cells; therefore, as long as samples remain frozen, cells are maintained viable. However, this method requires constant maintenance to keep the valuable materials intact.

Lyophilization has become a viable alternative to avoid the limitations of liquid cultures. This preservation method, also known as freeze-drying, is a dehydration method where samples are quickly cooled down and subjected to low surrounding pressure. This allows the frozen water to sublimate directly from the solid phase to the gas phase, resulting in a dry end product that preserves cells and maintains their functionality over extended periods and under various conditions.[35] In addition, lyophilization reduces the weight and volume of the cell product, making it more practical for transportation and storage, especially in space-limited environments. Given these benefits, we evaluated and compared the liquid and lyophilized cultivation modalities using the ESM.

For the liquid cultures, we considered using a cryogenic freezer that weighs 42.5 kg and has the capacity to store 360 vials of 2 ml each, allowing for a total storage volume of 720 ml of liquid culture. The energy required to store cells at -80°C was determined assuming that the freezer consumes 7 kW. For the lyophilized cultures, we considered using a desiccator that weighs about 10 kg, along with 200 grams of desiccant. The energy required to store cells in this preservation modality was assumed to be zero, since lyophilized cultures can be stored at room temperature.

3.2 Seed train

To evaluate the mass associated with the seed train, we have considered that the strains were grown in a medium that contains 10 g/L of yeast extract, 20 g/L of peptone, 20 g/L of glucose, and 0.002 g/L of NaOH. The seed train was initiated in a 250 ml flask containing 200 ml of medium, where the content of one vial of the cryopreserved strain was added as the inoculum. After cells were grown to $1x10^7$ cells/ml, 200 ml of the solution were added to a 2 L flask to grow the cells at $1x10^8$ cells/ml, and finally, 10% of the solution was transferred to a small bioreactor with a volume equal to 10% the volume of the principal bioreactor to grow the cells to $1x10^9$ cells/ml. The culture was grown at 37 °C in the seed train. The mass of the necessary chemicals (i.e., water, glucose, yeast extract, peptone), equipment, and energy supplied to heat the cultivation media was quantified.

3.3 Fermentation

Fermentation was performed in a stainless steel bioreactor supplemented with 200 g/L of glucose, 0.79 g/L of CSM Powder, and 0.67 g/L of yeast nitrogen base. The cultivation conditions were 37 °C at a pH of 7, which was controlled using $CaCO_3$. The lactic acid production yields using different organisms are presented in Table 1.

The total mass of glucose used in fermentation was estimated by multiplying the glucose concentration ($M^{glucose}$ = 200 g/L) by the fermentation volume (ν^{fer}), see Equation (3.8).

$$M_{glucose}^{chem-fer} = M^{glucose}\nu^{fer} \tag{3.8}$$

The mass of $CaCO_3$ required for pH control was estimated using Equation (3.9), where $M_{LA}^{chem-fer}$ represents the mass of lactic acid produced, $R_{lactate}$ is the lactate ratio, and m^{LA} and m^{CaCO_3} are the molecular mass of lactic acid and $CaCO_3$:

$$M_{CaCO_3}^{chem-fer} = \frac{M_{LA}^{chem-fer} m^{CaCO_3}}{2m^{LA}} (1 - R_{lactate}) \tag{3.9}$$

The mass of other chemicals required for fermentation such as CSM Powder ($M_{CSM}^{chem-fer}$) and yeast nitrogen base ($M_{YNB}^{chem-fer}$) was estimated based on the media concentration and the fermentation volume to determine the total mass of the chemicals used in the fermentation stage ($M^{chem-fer}$):

$$M^{chem-fer} = M_{glucose}^{chem-fer} + M_{CaCO_3}^{chem-fer} + M_{CSM}^{chem-fer} + M_{YNB}^{chem-fer} + M_{H_2O}^{chem-fer} \tag{3.10}$$

The mass of the bioreactor was estimated assuming it was made of stainless steel, see(3.11); here, ρ^{fer} represents the density of stainless steel, δ^{fer} is the thickness of the bioreactor, and ν^{fer} is the volume of the bioreactor.

We also included a polyethylene layer, which is the selected shielding material that covers the bioreactor (this is needed to protect organisms from cosmic radiation). As reported by Rojdev et. al. (2009),[32] the typical values for spacecraft structures have areal density thicknesses of approximately 1 to 20 g/cm^2. We evaluated systems with 1 g/cm^2 areal density thicknesses, which means that 1 cm thickness of shielding is considered for the vessel.

$$M^{eqpt-fer} = 4\rho^{fer}\delta^{fer}\pi \left(\sqrt[3]{\frac{3\nu^{fer}}{4\pi}} \right)^2 \tag{3.11}$$

The mass associated with power use was estimated using Equation (3.12), where Cp^{water} is the heat capacity, T^{fer} is the fermentation temperature, T^{ISS} is the temperature aboard the ISS, τ^{fer} is the fermentation duration, and δ^{power} is the mass equivalency factor used to convert kW to kg.

$$P^{fer} = \nu^{fer} Cp^{water} (T^{fer} - T^{ISS}) \tau^{fer} \delta^{power} \tag{3.12}$$

We considered that water used in the fermentation system is sent to a reverse osmosis unit of the water processor assembly (WPA) and we assumed that 90% of the water is recovered and recirculated to the fermentation system. We evaluated the power needed for fermentation and the power needed to recycle water.

Table 1: L-lactic acid production of different microbial hosts using glucose as a substrate.

Organisms	Production rate, g L^{-1} h^{-1}	Yield, g g^{-1}	Reference
Escherichia coli	2.33	0.93	Dien et al.[36]
Saccharomyces cerevisiae	2.34	0.58	Lee et al.[33]
Pichia Pastoris	0.0363	0.22	Yamada et al.[34]

4 Results and Discussion

This section compares biomanufacturing systems that use *Escherichia coli*, *Saccharomyces cerevisiae*, and *Pichia pastoris* as microorganisms for the production of lactic acid in liquid and lyophilized preservation modalities. We evaluated diverse scenarios assuming that shielding is sufficient to protect the cells and does not alter the yield of the organisms, as well as scenarios where the yield is reduced under radiation exposure (10 Gy) by 9 - 28%, based on experimental data.

4.1 Equivalent System Mass

We set a target production of 3,000 kg of lactic acid in one year. Given that each organism has a different fermentation time, we first evaluated the total time required to perform a batch. The time of a batch was estimated considering the seed train time, the fermentation time and 24 hours of clean up time to start another batch. After estimating the batch time, we determined the number of batches that can be performed in one year. Using this data, together with the glucose to lactic acid yield, we were able to determine the volume of the main bioreactor to produce 3,000 kg of lactic acid in one year at the end of the fermentation process (without evaluating the separation process).

The volume of the fermenter for the seed train stage was determined to be 10% of the volume of the main bioreactor. Once the capacity of the fermenters was determined, the mass of the equipment was estimated assuming that the fermenters are made of stainless steel. In addition, the mass associated with the shielding material was estimated, as well as the mass of the input materials according to the composition of the media in the different stages of the biomanufacturing system.

The total system mass was calculated considering the mass of the storage, seed train and fermentation for the scenarios where we assumed radiation does not affect yield (Table 2).

Our analysis shows that lyophilization systems require significantly lower mass. Specifically, results of storage analysis show that the use of lyophilized cultures lead to a 99% mass reduction compared with liquid cultures. This is mainly due to the cooling requirements to preserve cells in liquid cultures. The mass components of the storage stage are the cells, equipment, and energy. For liquid cultures, the total mass associated with energy consumption is 1,022 kg. This includes 42.5 kg for the cryogenic freezer and 0.72 kg for the cell culture itself. On the other hand, for lyophilized cultures, the total mass includes 10.4 kg for the desiccator and 0.2 kg for the cell culture. Thus, the

total mass required for storing liquid cultures is 1,065 kg, while for lyophilized cultures is 10.6 kg. These results highlight that lyophilized preservation modalities are excellent alternatives for storing cells, as they provide significant advantages in terms of system mass.

Table 2: System mass (kg) across various stages for different biomanufacturing designs.

Organisms	**Preservation Modality**	**Storage**	**Seed train**	**Fermentation**	**Total Mass**
Escherichia coli	Liquid	1,065	578.7	6,557.6	8,201.4
Escherichia coli	Lyophilized	10	502.3	6,656.4	7,169.1
Saccharomyces cerevisiae	Liquid	1,065	631.7	9,827.0	11,523.8
Saccharomyces cerevisiae	Lyophilized	10	627.7	9,848.0	10,486.0
Pichia Pastoris	Liquid	1,065	1,322.9	25,276.4	27,664.3
Pichia Pastoris	Lyophilized	10	1,323.4	25,312.2	26,646.0

The mass analysis for the seed train for the different organisms is presented in Table 2. We found that using *Escherichia coli* leads to the lowest mass footprint (502 kg). In contrast, *Saccharomyces cerevisiae* and *Pichia pastoris* require 627 kg and 1,323 kg, respectively. It is worth noticing that the total mass of the system for *Escherichia coli* is 30% lower than that of *Saccharomyces cerevisiae*. The lower mass footprint observed for *Escherichia coli* is largely due to its higher lactic acid production yield, which directly influence equipment sizing and resources used (ultimately captured in the total system mass).

For the three systems, we found that approximately 70% of the total mass of the seed train is associated with water supply. As such, the mass footprint of water use and recycle is a dominant aspect of the biomanufacturing system (even if 90% of the water is recycled). Followed by water, the rich media is the element that requires the greatest mass in the system, with 7% glucose and 7% peptone. On the other hand, the mass associated with the principal fermentation represents approximately 80% of the total mass of the system for liquid cultures and 90% of the total mass for lyophilized cultures. For both preservation modalities, glucose is the primary consumable and represents 48% of the mass in the fermentation stage, followed by $CaCO_3$ and water, which represents 25% and 21% of the fermentation mass.

To evaluate the production efficiency of lactic acid in each of the systems, we used a lactic acid to total mass ratio. A higher value of this metric indicates greater efficiency (with less system mass). Results show that there are no significant changes with respect to the metric used among the preservation modalities (Figure 3). However, in all cases, lyophilized systems present better performance. The best system uses *Escherichia coli* in lyophilized cultures.

The results indicate that *Escherichia coli* in lyophilized cultures would require the lowest mass to produce the desired lactic acid (7,169.1 kg) (see Figure 2). On the other hand, *Pichia pastoris* requires

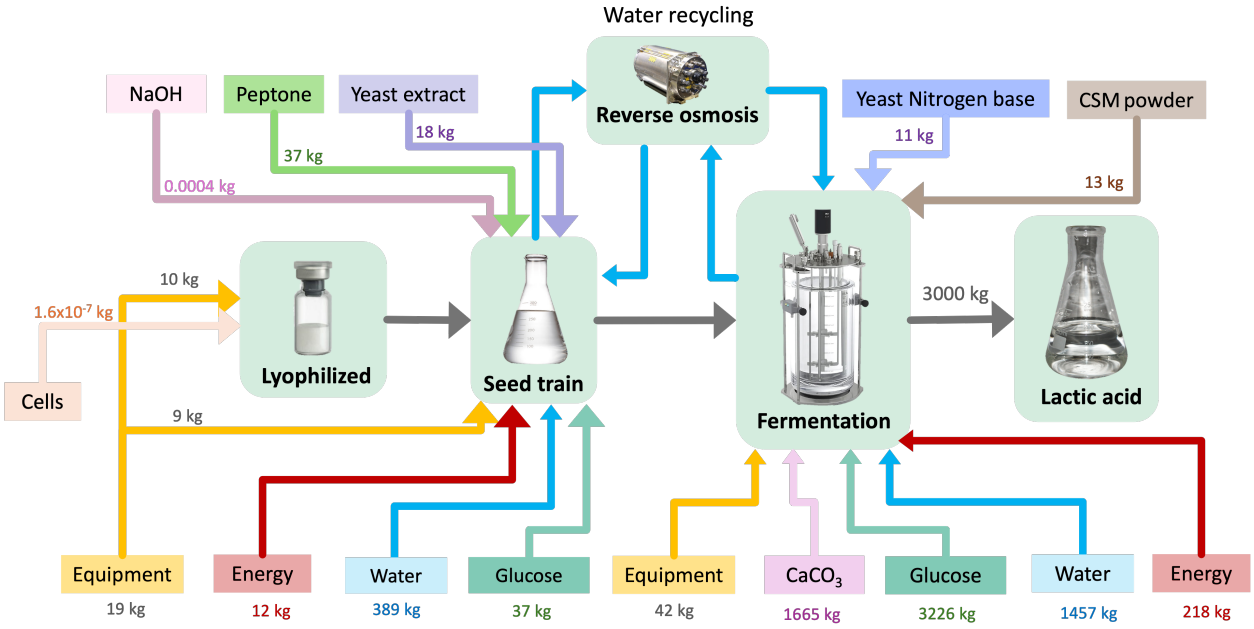

Figure 2: System mass analysis for the production of lactic acid using *Escherichia coli* in lyophilized cultures.

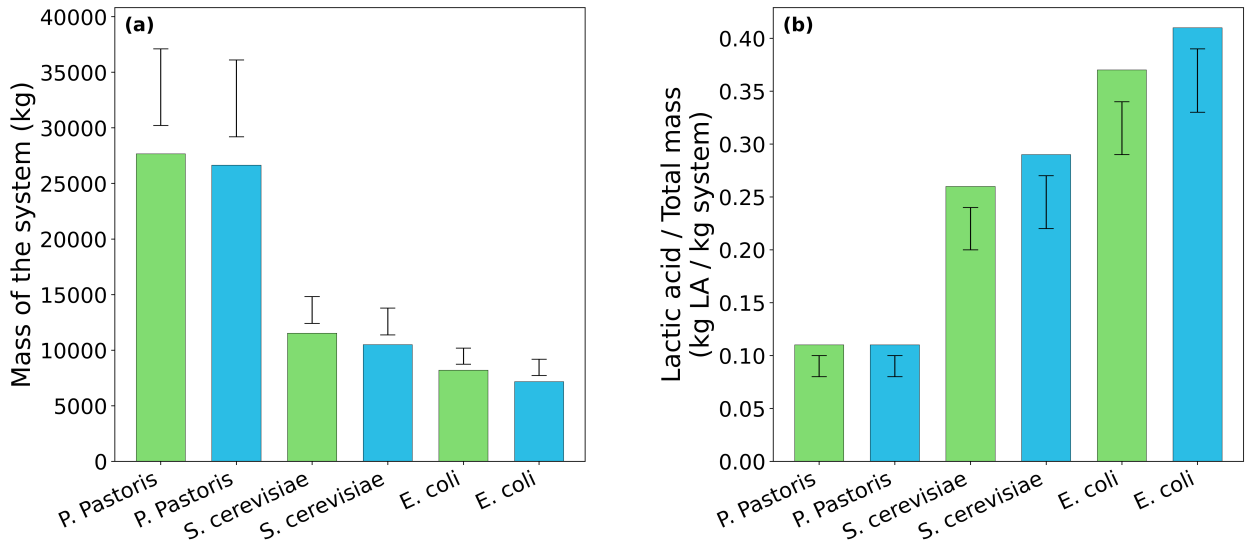

Figure 3: Results of the Equivalent System Mass (ESM) analysis for different biomanufacturing designs: a) Total mass of the system for different organisms preserved in liquid (green) and lyophilized (blue) cultures. b) Lactic acid to total mass ratio for different organisms and preservation modalities.

a large amount of mass to achieve the desired lactic acid production (26,646 kg). This is mainly attributed to the batch time and the low yield of lactic acid to produce lactic acid from glucose.

We explored the impact of cosmic radiation on microbial performance. We considered a potential reduction in yield of 9 - 28%, as suggested by experimental observations. The resulting uncertainty ranges, shown as error bars in Figure 3, illustrate the possible variation in system mass and the lactic acid to mass ratios. These bounds demonstrate that even with shifts in absolute values, *Escherichia coli* in lyophilized cultures continues to outperform other systems. The mass increase is more evident in the case of *Pichia pastoris*, where the total system mass could increase from about 27,664 to almost 37,111 kg when radiation effects on yield are considered. In comparison, the impact on *Escherichia coli* is much smaller, with an increase in system mass of around 2,000 kg (from 7,169 to 9,190 kg). These results show that changes in yield associated to radiation can directly influence the mass footprint of the system and the time required to reach the target lactic acid production.

4.2 Sensitivity Analysis

Given that some parameters, such as yield and batch time, can be influenced via genetic modifications of the organisms, we conducted a sensitivity analysis to explore the effect of these parameters.

We first studied base case scenarios where we assume that radiation does not alter the yield of the organisms (Figure 4a). We have included parameters associated with the efficiency of the organisms and some operating conditions for the biomanufacturing process, such as the ISS temperature, water recycling percentage, pH, fermentation time, and the yield from glucose to lactic acid. To understand how these parameters influence the total mass of the system, we performed a sensitivity analysis by varying each parameter by ±10%.

Figure 4 summarizes results of the sensitivity analysis. The efficiency and the amount of water that can be recycled are the most influential factors in the total mass of the system. Regarding the percentage of recycled water, it is clear that increasing the amount of water recycled enhances the circularity of the system and reduces the need for water to be supplied from the Earth. A 10% increase in the amount of recycled water would reduce the mass of the system by 18%. Likewise, the yield plays a very important role in the production of lactic acid, this suggests that the genetic modification of *Escherichia coli* should be improved to enhance the efficiency of glucose conversion to lactic acid. In this analysis, an increase in the yield could decrease the mass of the system by 2%. Furthermore, if the organism can ferment faster, the mass of the system would also be reduced because the scale of the system would decrease. This means that if the goal is to produce a certain amount of lactic acid in a year, fewer fermentation batches would be needed, allowing for a smaller fermenter and a reduction in the amount of feedstocks required.

We can also see that the operating conditions such as the ISS temperature and the pH do not impact significantly the mass of the system. In the case of the ISS temperature, the energy in terms of mass is quite small compared with the total mass of the consumables to produce lactic acid. There-

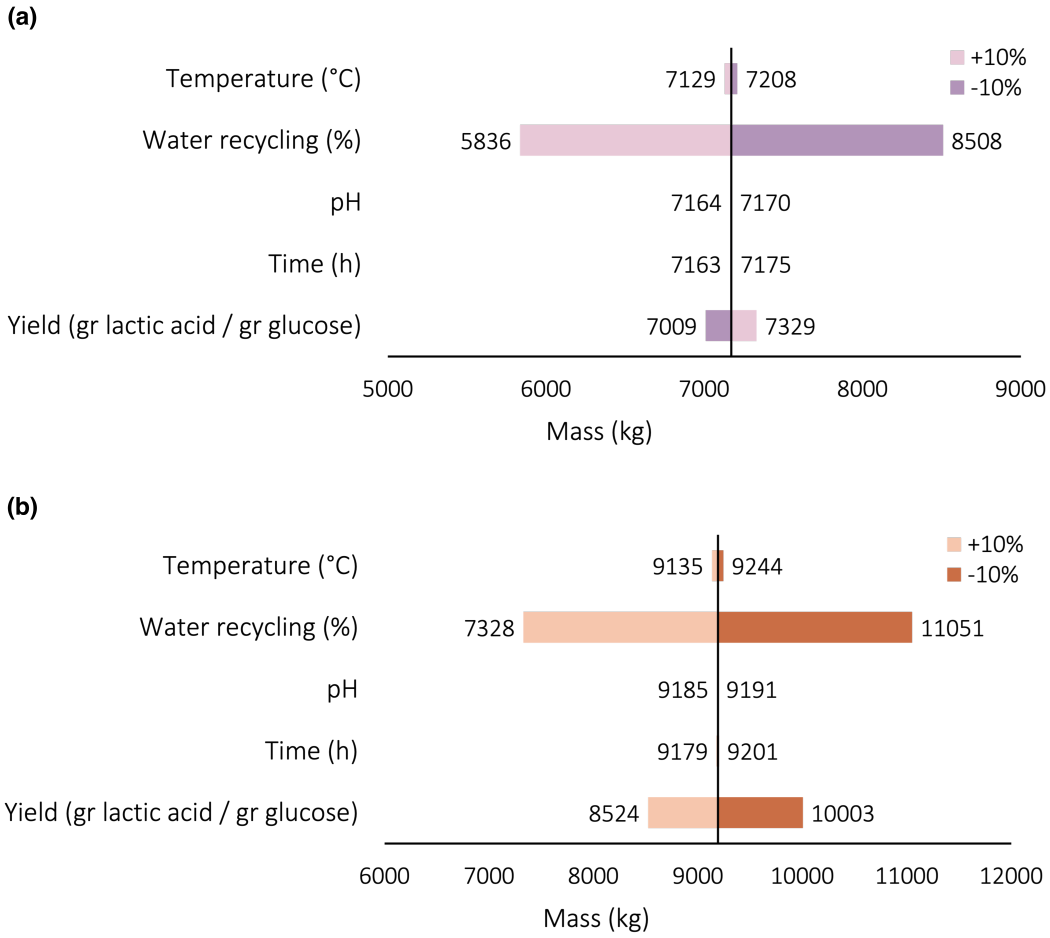

Figure 4: Impact of key parameters on the total mass of the *Escherichia coli* in lyophilized cultures system. a) Scenario assuming that radiation does not affect microbial yield. b) Scenario considering a 72.4% reduction in yield due to radiation exposure (worst-case scenario).

fore, there is no significant change in the total mass of the system. In the case of pH, although the neutralizing agent used to control pH is a primary consumable in the fermentation process, changes in pH do not affect the total mass of the system. However, pH remains a crucial parameter and must be carefully selected based on the survival conditions of the organisms used.

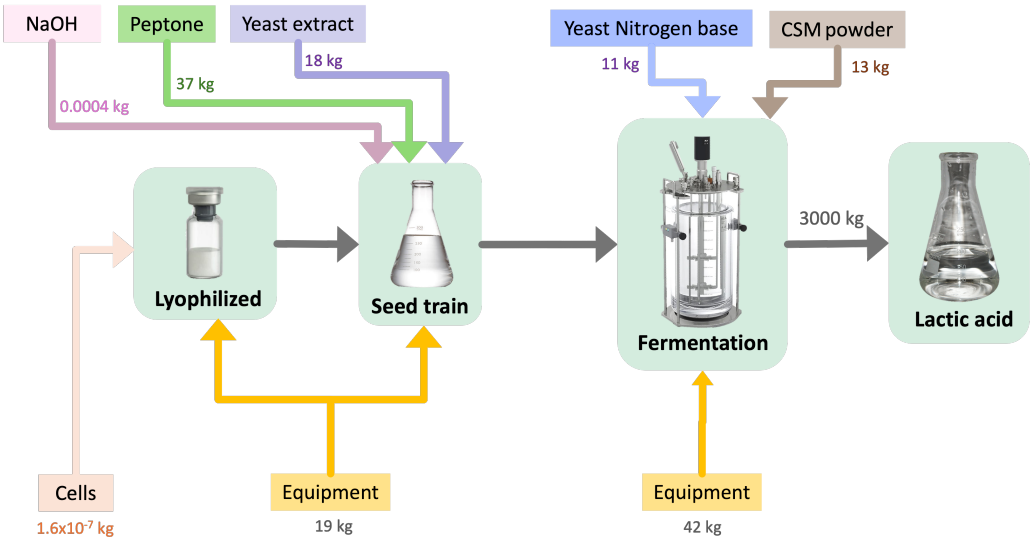

Figure 5: System mass analysis for the hypothetical case of coupling additional biomanufacturing systems that supply water, glucose, and neutralizing agents to the system.

We also evaluated a radiation exposure scenario in which the yield of *Escherichia coli* is reduced (Figure 4b). In the worst case, we considered the 28% decrease in yield, which was taken as the radiation baseline. Under this assumption the resulting system mass is 9,190 kg. Figure 4b compares ±10% variations around this radiation baseline. A further decrease in 10% yield raises the mass to 10,003 kg, whereas an increase in 10% yield lowers the system mass to 8,524 kg. Changes in temperature and pH have a minor effect (less than 1%). By contrast, increasing water recycling by 10% reduces the mass by 20%. These results confirm that, under radiation exposure, the design is most sensitive to yield and water recycling. Therefore, improving glucose to lactic acid conversion through genetic modification and maximizing water recovery provide the largest mass savings.

4.3 Circular Biomanufacturing System

We used our framework for analyzing a system for PLA production. To conduct this analysis, we used *Escherichia coli* in lyophilized culture.

Figure 2 shows the mass inputs for the biomanufacturing system to produce lactic acid; note here that CaO, glucose, and water are the main consumables in the fermentation process. However, these materials can be sourced from alternative systems in space (e.g., CaO is present in lunar regolith, and glucose and water can be obtained from wastewater treatment processes and the water recycling system aboard the International Space Station). This reduces the mass of materials that need to be

shipped to space. Therefore, if we address a hypothetical case study where CaO, glucose, and water can be obtained from in situ resources, the mass of the system required to produce 3,000 kg of lactic acid in one year would be about 154 kg, which includes 42 kg for the fermenter, 13 kg for shielding material, and 79 kg for consumables (primarily the nutrients for the media) (see Figure 5).

Lactic acid must be first converted to lactide (with a 73% conversion yield), and lactide must be converted to PLA (with a 74% conversion yield).[37] Therefore, for a system that produces 3,000 kg of lactic acid, 1,620 kg of PLA would be produced. However, to quantify the mass of PLA required to create a lunar habitat, we selected the Mars Dune Alpha[38] as a case study to compare the cost of shipping the required PLA to create the habitat versus the cost of producing PLA in space. The dimensions of the selected habitat are 28 x 60 feet, and the mass of the habitat is approximately 85 tons, considering the floor, walls, and ceiling.

To estimate the costs of the system, we used the Parametric Take or Make model.[39] Based on this, to estimate the cost of transporting PLA for habitat in space, we considered the mass required to create the habitat (85 tons) and multiplied its mass by the transportation cost ($10,000/kg). This indicates that the cost to take PLA and ship it into Space is about 850 MMUSD. However, if we consider the hypothetical scenario of producing lactic acid in space using the proposed biomanufacturing system (assuming we can obtain $CaCO_3$, water, and glucose from in-situ resources), we would need to produce 157 tons of lactic acid to generate 85 tons of polylactic acid (PLA), taking into account the conversion factors from lactic acid to lactide and from lactide to PLA. Consequently, 52 systems would be required to produce 157 tons of lactic acid in one year, which translates to transporting 8 tons of equipment and consumables to implement the biomanufacturing system. This, in turn, represents a cost of 80 MMUSD, an order of magnitude lower than the direct-delivery case.

Assuming the system would be installed within a Mars Dune Alpha lunar habitat, the maximum fermenter volume would be limited to 11.5 m^3. To assess feasibility within this constraint, we evaluated the cost of systems across a range of production capacities. Figure 6 summarizes these results, presenting the delivered cost as a function of annual lactic acid production (blue, left axis) together with the corresponding fermenter volume (green, right axis). The cost curve decreases at low production capacities because the fixed mass of equipment and consumables dominates the system. As production capacity increases, the cost per ton of lactic acid becomes more favorable, and the total cost converges to about 50 MMUSD for systems producing more than 100 tons per year. This trend highlights that most of the economic benefit from scaling is realized once the system reaches mid-scale operation, while further increases in capacity do not decrease the cost significantly.

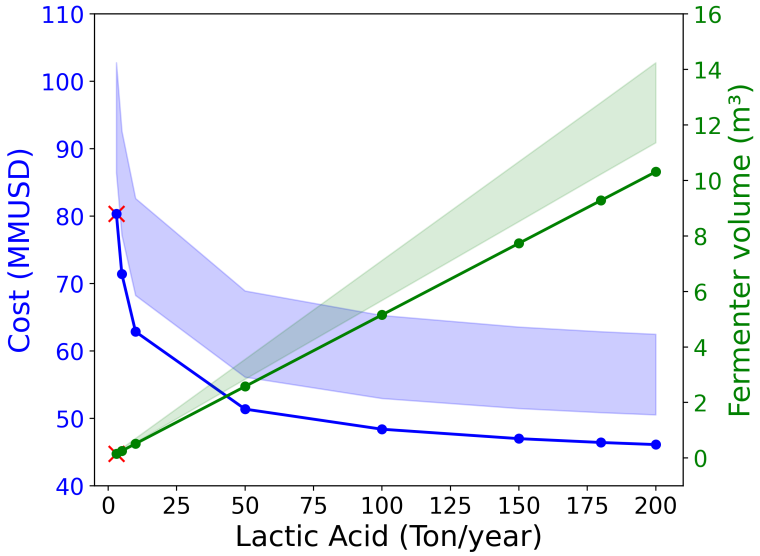

Figure 6: Equivalent system mass cost (blue, left axis) and fermenter volume (green, right axis) for lactic acid production at different system capacities. The solid lines represent the scenario assuming no yield reduction due to radiation. The shaded areas indicate the uncertainty range under scenarios where radiation reduces organism's yield. The red marker denotes the reference case of a system producing 3,000 tons of lactic acid per year.

5 Conclusions and Future work

This study presented a computational framework to guide the design of biomanufacturing systems in space using a mass perspective to provide an estimate of the launch cost of the system. The framework, therefore, aims to identify the best organisms and preservation modality to minimize the mass of resources that would need to be sent from Earth. We conducted the technoeconomic analysis based on the ESM metric, which enables mapping all of the design components (e.g., energy, resources) into a common basis in terms of mass. In this way, ESM makes it easier to compare transportation costs for space missions by correlating launch costs with payload mass.

In this work, the bioproduction of lactic acid using *Escherichia coli*, *Saccharomyces cerevisiae* and *Pichia pastoris* was evaluated by considering different fermenter materials and volumes to identify the bottlenecks in the design configurations in terms of mass and yield. Our analysis reveals that the preservation mode is a key factor, as significant differences in the mass associated with the preservation of the organisms were observed. When comparing liquid and lyophilized media, we found that the mass of the lyophilized system is reduced by up to 99% (approximately 1,055 kg) compared to the liquid medium. This significant difference is attributed to the energy consumption required to maintain liquid media cells at a temperature of -80°C. The results indicate that the design scenario using *Escherichia coli* in lyophilized culture has the highest lactic acid to total mass ratio (0.42).This suggests that, under these conditions, more lactic acid (3,000 kg) can be produced with a lower system mass (7,169 kg), mainly due to the high yield of *Escherichia coli* lactic acid production.

In addition, we identified that the highest mass-consuming resources in the system are water, glucose, and $CaCO_3$. Reducing the mass of these resources could significantly lower the overall mass of the system. Implementing such strategies could reduce the need for resupply missions, making biomanufacturing systems a more economically viable option for producing other critical items, such as habitats, for space exploration. This highlights the importance of coupling biomanufacturing systems with the appropriate organisms that can integrate waste resources into valuable products in remote environments, where resources are limited. Thus, designing more circular systems that address specific challenges and optimize resource use is a key step towards sustainable biomanufacturing in space.

We also evaluated system designs exposed to 10 Gy of radiation. In these scenarios, we considered the reduction in yield (grams of lactic acid produced per grams of glucose) caused by radiation to estimate the mass requirements of the system under these conditions. For *Escherichia coli* in lyophilized cultures, the system mass increased by approximately 28% compared to the base case (from 7,169 to 9,190 kg). These results emphasize that yield is a critical parameter, as reductions in efficiency directly affect system scale and, consequently, production cost. These findings reinforce that yield stability under radiation exposure is the critical design factor. Protecting the yield of the organisms, whether through strain engineering or shielding, will be essential to enable reliable, low-mass biomanufacturing systems for future space habitats.

Addressing the design of systems under space conditions requires different perspectives and considerations that are difficult to evaluate and reproduce in terrestrial conditions. ESM is a potential tool to evaluate new systems. As a cost metric, ESM may not be capable of capturing how performance is impacted by different radiation levels. Because of this, additional analyses are required to identify the trade-offs between engineering hosts to have better performance in high radiation environments compared to the addition of more radiation shielding material. In addition, other mechanisms to reduce shielding requirements and protect organisms against radiation (for example, different preservation modalities) should be evaluated in the design of the space bioprocess. In this regard, immobilized cell methods such as lyophilization and hydrogel systems, wherein microbes are encapsulated are good alternatives to suspend cell cultures and are characterized by their long-term and sustained metabolic. Therefore, for future work, the modeling framework needs to be complemented with biomanufacturing design alternatives that could reduce the impact of radiation. Such a study could help to assess trade-offs between strain resistance, preservation modalities, and overall process economics.

6 Nomenclature

Symbol	Description
n^{batch}	Number of batches per year
τ^{year}	Total time in a year (h)
τ^{st}	Seed train duration (h)
τ^{ferm}	Fermentation time (h)
τ^{clean}	Cleaning time (h)
ν^{fer}	Fermenter volume (L)
Φ^{target}	Target lactic acid production (g/year)
$\eta^{product}$	Product yield (g lactic acid / g glucose)
$C_0^{glucose}$	Initial glucose concentration (g/L)
ESM	Equivalent System Mass (kg)
M_i	Mass of component i (kg)
P_i	Power requirement of component i (kWh)
δ^{power}	Mass equivalency factor for power (kg/kWh)
C_i	Cooling requirement of component i (kWh)
$\delta^{cooling}$	Mass equivalency factor for cooling (kg/kWh)
M^{Total}	Total system mass (kg)
M^{sto}	Mass associated with storage stage (kg)
M^{st}	Mass associated with seed train stage (kg)
M^{fer}	Mass associated with fermentation stage (kg)
$M^{eqpt-sto}$	Mass of storage equipment (kg)
$M_i^{chem-sto}$	Mass of chemicals used in storage (kg)
C^{sto}	Cooling requirement in storage (kWh)
$M^{eqpt-st}$	Mass of seed train equipment (kg)
$M_i^{chem-st}$	Mass of chemicals used in seed train (kg)
P^{st}	Power used in seed train (kWh)
$M^{eqpt-fer}$	Mass of fermentation equipment (kg)
$M_i^{chem-fer}$	Mass of chemicals used in fermentation (kg)
P^{fer}	Power used in fermentation (kWh)
$M_{CaCO_3}^{chem-fer}$	Mass of calcium carbonate used in fermentation (kg)
$M_{LA}^{chem-fer}$	Mass of lactic acid produced in fermentation (kg)
$R_{lactate}$	Molar fraction of lactate in fermentation
m^{LA}	Molar mass of lactic acid (g/mol)
$M^{chem-fer}$	Total mass of chemicals in fermentation (kg)
$M_{glucose}^{chem-fer}$	Glucose mass used in fermentation (kg)
$M_{CSM}^{chem-fer}$	CSM mass used in fermentation (kg)
$M_{YNB}^{chem-fer}$	YNB mass used in fermentation (kg)
$M_{H_2O}^{chem-fer}$	Water mass used in fermentation (kg)
ρ^{fer}	Fermenter material density (kg/m^3)

Continued on next page

Symbol	Description
δ^{fer}	Fermenter wall thickness (m)
Cp^{water}	Heat capacity of water (kJ/kg·K)
T^{fer}	Fermentation temperature (°C)
T^{ISS}	ISS internal temperature (°C)

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