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The Bio-inspired Changeable Production System – A Stem Cell Approach

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Abstract

Volatility can be addressed through changeability. A new bio-inspired approach based on the stem cell differentiation process is presented to meet the needs of a changeable production system. Stem cells possess the property of a raw product that can be processed into various final products. These products are manufactured based on their demand in the same production system with the same production resources. This paper aims to translate the production system from biology to the real world. It does so by translating molecules and their biological mechanisms into production resources, information, and transportation pathways. The paper describes eleven different change scenarios based on Nyhuis' three-axis changeability model, which correspond to change pathways in the stem cell system and the production system. This model has high potential for use in industry to achieve a changeable production.

Keywords: bio-inspiration; stem cell; changeability; production system

1. Introduction

In recent years, the occurrence of unpredictable events such as the COVID-19 pandemic and wars has accelerated the rate at which needs and markets change. This has resulted in fluctuations in raw material prices, energy and transport costs, trade prices, and production volumes. To remain profitable, production systems (PS) across industries must be able to quickly adapt to these new market realities. On the other hand, society is moving towards a demand-driven economy where personalised goods are produced in the required quantity. Speed and changeability are the keys to dealing with volatility. Changeability is defined as a forward-thinking solution that enables a quick response when necessary. To implement changeability, it is necessary to rethink the design of the future PS.

When discussing the topic of changeability in nature, it is important to note that the changeability of plants and animals is the result of mutations that have developed over hundreds of years through evolution. This changeability did not occur overnight, but rather through a gradual process of mutation and adaptation. Therefore, it is not appropriate to attribute rapid changes solely to random mutations. However, it can be deduced that changeability is essential for survival. This discovery can be directly applied to a business objective. Unlike random mutation processes, stem cells (SC) undergo biological processes that facilitate rapid changes at the cellular level. These processes rely on messenger substances that signal changes and initiate new processes within cells. SCs are fundamental cells that can develop (differentiate) into any specific cell, such as blood cells, skin cells, or bone cells, depending on the signals they receive. The process of transferring biological systems or principles to technical systems is known as bio-inspiration or bionics. The challenge is to comprehend the biological system, abstract it, and then translate it into a technical system. The aim of this publication is to describe a PS as a SC model capable of rapid transformation.

Section 2 presents the relevant state-of-the-art literature, Section 3 describes the approach, and Section 4 presents and discusses the results before providing a summary and outlook in Section 5.

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2. State of the Art

Changeability models for PS: The changeability of PS refers to the degree of freedom that allows for quick reactions to external changes in a turbulent environment, creating pressure to change. Various definitions of this concept can be found in the literature [1]. Turbulence or disruption can affect a PS due to a combination of external and internal factors. External factors may include changes in technology, such as a shift in product life cycle, or changes in the environment, such as resource scarcity, politics, such as deregulation, society, such as individualized customer preferences, or the market, such as a shift in demand. The levels of a PS that are affected by various factors include network, plant/factory, area/line, work station, machine/module, and submodule [2]. A machine is considered changeable if it can be modified by functional units in the event of an unexpected development. A factory is considered changeable if it can accommodate a highly dynamic product policy in response to sudden market changes. Modularity is an important cornerstone, enabling new combinations of areas, their expansion, or their demolition [1]. It belongs to the so-called change enablers, which are the levers to realize the ability to change. Nyhuis et al. defined the five change enablers as universality, mobility, scalability, modularity, and compatibility [3]. The combination of change enablers, receptors, and levels of a PS results in a three-axis model. The purpose of the three-axis model is to provide concrete solutions for combinations of the three axes and to determine the optimal degree of changeability. For example, changes to a product (receptor) at the area level (level) can be addressed by universality (change enablers) in the team structure (people as a solution option). Nyhuis uses receptors that were originally defined by Cisek in 2002, inspired by biology. According to Cisek, a receptor is sensitive to a specific stimulus and transmits a signal. The specific receptors include product and its variants (P), quantity (QN), time (T), costs (C), quality (QL), and the number of system elements. Cisek argues that all requirements arising from turbulence can be mapped with these six variables, thus creating a link between external changes and their impact on a PS [4].

Table 1. Three-axis model according to Nyhuis et al. giving an overview of different changeability pathways.

Receptor	Level of PS	Change enabler
Product (P)	Plant/Factory	Universality
Quantity (QN)	Line/Area	Mobility
Time (T)	Workstation	Scalability
Costs (C)	Module	Modularity
Quality (QL)		Compatibility

One approach is Product-Production-Co-Design (PPCD), which links products and production systems throughout their lifecycle over generation [5].

Bio-inspired models for changeable PS: Many processes and designs in production resemble those in biology. A digital "Manufacturing Genome" is being developed to enable rapid changes in product design and the underlying production adaptations [6]. Production research draws inspiration from the nervous and immune systems due to their ability to store knowledge and exhibit learning behaviour used for task and resource planning [7,8]. In the project 'heterogeneous, workload-optimized robot teams and production architectures', AI is used to decompose upcoming tasks based on knowledge about the resources and their capabilities. The PS can then be automatically calibrated according to the process line's configuration. Additionally, the manufacturing equipment coordinates itself autonomously via internal communication channels and knowledge about the future production sequence [9]. Cellular adaptive structures are employed to implement capabilities of self-growth and automatic distribution [10]. Another approach is based on swarm-intelligence and uses mobile machines on AGVs, which can be easily repositioned. This creates an autonomous PS, which enables individual mass production of products and largely controls and coordinates itself through cyber-physical systems [11].

Bio-inspired factory layouts: Bio-inspired approaches for factory layouts exist to mimic the spatial arrangements and structures found in nature. The production layout can be based on spider webs or nautilus shells to minimize transport routes between production units [12]. Another approach involves designing an adaptable and flexible production layout based on the spatial arrangement of a cell. The factory's non-movable resources are arranged in the center, forming a cell core. Flexible production resources, such as resource input, energy supply, assembly cells, and dispatch stations, are arranged around this core. This allows for efficient rearrangement of non-fixed resources when the production program is realigned [13].

In conclusion, a changeable factory requires components at all levels designed based on the five change enablers. This includes flexible and modular machines and workstations that can be easily adapted, as well as flexible media and power supply. Digitization is a key enabler, encompassing digital twins of production resources and products, as well as self-controlling, learning, and automatically calibrating equipment to adapt even faster to new situations. In addition, the layout is essential for quick changes. While there are many approaches, none of them focuses on SCs as a model.

3. Approach

The aim of this publication is to demonstrate how SC differentiation functionality can be translated into a PS, providing a pathway to make the PS changeable. To achieve this, it is necessary to consider where the ability to change lies and then to translate the SC system in the language of a PS. The following steps are taken:

1. Identify properties that make the SC system changeable.
2. Analyse the SC's functioning and mechanisms behind the change-related properties.
3. Abstract and translate the biologic components into factory components. Present a multi-modal system that includes various transformation pathways.
4. Identify systemic solution options and propose actions in response to specific changes.

4. Results

4.1. Identification of change-related properties

The first step is to examine the properties of a SC system that are related to change. These properties should also be present in a changeable PS environment. Table 2 displays the pertinent properties of SCs that are desirable in a changeable production environment.

Table 2. Properties of SCs described in literature that are desirable in a changeable production environment.

Property / Lit.	[14]	[15]	[16]	[17]	[18]
Changeable		x			x
Adaptable	x	x	x		
Self-configurable		x		x	x
Self-renewing	x	x	x	x	
Self-recyclable	x	x			
Spatially organized	x		x	x	
Communicating	x			x	
Autarkic				x	x
Potent / Robust	x	x	x		x
Resistant	x				

4.2. Analysis of the SC system's mechanisms

The second step is to understand the basic mechanisms of SC systems that underlie their properties related to change. SCs are the fundamental cells that give rise to all other cells with specialized functions in the body through a process called 'differentiation'. This process occurs under specific conditions and results in the formation of specialized cells such as blood cells, brain cells, muscle cells, and so on. It is important to note that SCs are the only cells with the ability to form new cell types. The specific conditions can arise from various sources, either external (outside the system) or internal (inside the system). Differentiation is the process of change triggered by a specific stimulus with a particular aim.

A similar phenomenon can be observed in the 'cellular stress response', which can also be considered a process of change triggered by a specific stimulus. It refers to the molecular changes that cells undergo in response to environmental stressors, such as mechanical injury, exposure to toxins, viral infections, or nutrient deprivation. This response can range from activating pathways that promote cell survival to eliciting programmed cell death to eliminate damaged cells. The initial response of a cell to a stressful stimulus is aimed at defending against and recovering from the insult. The examination of stress response will not be pursued further due to its potential to result in programmed cell death.

The goal is to develop a system with the ability to change as a characteristic property, allowing for repeated activation of different pathways. SCs have the ability to divide asymmetrically, resulting in either self-renewal (where the daughter cell retains SC characteristics) or differentiation into a specific cell type (where the daughter cell has developed). The differentiation potential is determined by the cell's potentiality. There are three types of SCs: totipotent SCs (embryonic SCs) which can form an entire organism, pluripotent SCs (adult SCs) which can form multiple cell types, and unipotent SCs which can only form one cell type. Pluripotent SCs are considered in this approach.

To comprehend the activation of distinct pathways for differentiation, it is necessary to examine the entire 'SC niche', which is a specific environment for the functions of SCs. The niche has three fundamental properties: The SC is anchored to other cells and maintains its character through signals from the niche. It has two levels of regulation: the inner level includes all processes and signaling pathways within the SC, while the external level includes all processes and signaling pathways outside the SC, such as in the SC niche. The SC niche can be compared to a PS, with different stations and defined tasks surrounded by transportation and information flow paths.

Figure 1 shows the differentiation process of a blood cell (erythrocyte), which is used in the following as an exemplary. The SC undergoes several stages until it develops into the mature blood cell. Throughout this process, SC-typical structures are lost and only metabolic pathways relevant to the blood cell are supported. The cell nucleus and mitochondria, along with other cell organelles that are not required for the final blood cell, are degraded and excreted. Ribosomes and mRNA synthesize hemoglobin, which is the main component of a blood cell.

In the context of a PS, the SC is the fundamental material from which any product is processed through several stages until it becomes the final product. The erythrocyte is the end product, and the pathway or chain of differentiation is the specific sequence of processes and processing steps, i.e. the value creation process of a particular product. Some processes remove, edit or convert the material, while others add or combine components or functions to the product. The various stages of the cell represent the different stages of the semi finished product.

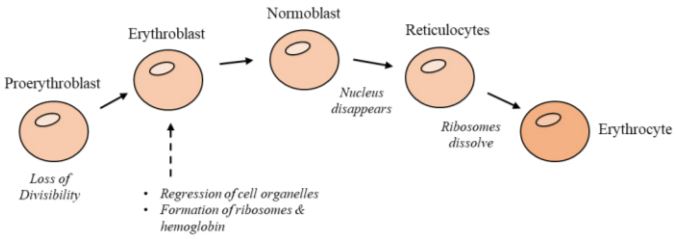

Fig. 1. Differentiation of a SC into a blood cell (erythrocyte).

4.3. Translation of the biological system into a PS and demonstrating the pathways of change

The following section provides an exemplary use case of the biological system's changeability mechanism and translates it to a PS. The functioning of SC system is described in a step-by-step manner, with the participating objects (molecules) being translated into objects of a classical PS (lines, stations, machinery, raw material, products, transportation and information flows).

To demonstrate the system's changeability, an external disturbance will be introduced. In this particular scenario, the external disturbance in the biologic system is a lack of oxygen. This lack increases the demand for erythrocytes. Erythrocytes hold the hemoglobin which is responsible for oxygen delivery.

The presented change is thus a change in the production volume of the product erythrocytes. The factory needs to adapt its production, in order to increase the output of this product. The factory is represented by the SC niche plus the kidney as a relevant organ. The analogous terms used in a biological system and a PS are summarised in the following Table 3.

Table 3. Analogous terms used in biological systems and PS:

General term in biological system	Exemplary use case: blood cell production	Analogon in PS
Factory levels		
SC niche & other organs	SC niche & Kidney	Factory
SC niche		Main production line (line 1) incl. information & transportation flows
Other organs	Kidney cells	Supporting production lines (line 2)
Differentiation process of cells	Differentiation process of erythrocytes	Value creation process for main product, (station 1)
Cells that produce cytokines	Stroma cells, T-cells	Machinery for precursor production (station 2, 3)
Mitochondria in cells	Mitochondria in stroma & Kidney cells	Machine-individual power plants
Information & Transportation flows		
Antigen	Antigen for T-cell	Information signal
Cytokines	IL3, SCF, EPO	Information signal and precursors
Blood vessels		Fixed transportation path
Diffusion/Osmosis		Free transportation path
Material & Products		
Pluripotent SC	Hematopoietic SC	Raw product, starting material for many products
Partly differentiated SC, stage 1	Myeloid SC	Semi-finished product
Partly differentiated SC, stage 2	Reticulocyte	Final product without finishing process
Differentiated cell	Erythrocyte = red blood cell	Final product
Amino acids, carbohydrates, lipids		Ubiquitous and modular components / raw materials
Material from other organs or the intestine		Externally supplied material: raw product & material / components

Figure 2 assigns visually the components and mechanisms from the SC system to the PS. The starting point is the external turbulence. A signaling cascade follows until the production of the desired product in the desired amount begins.

A signaling molecule (antigen) enters the T-cells, which release another signaling molecule (cytokine IL3). Cytokines play a crucial role in the biological system. In a PS, antigens and cytokines can be likened to employees or information flows that initiate a production process only through the influence of external turbulence. The employees are responsible for scheduling and planning activities based on the information. Cytokines serve as precursors to another process. Based on the number of cytokines present in a certain species, the SC niche can control which and how many products are produced. According to Figure 2, cytokine IL3 is produced in station 3 (T-cells) and reaches station 1 (value creating process). Another cytokine SCF is produced at station 2 (stroma cells) and also reaches station 1. Together they build the main production line 1. Transport takes place via free transport pathways. In general, transport follows either free routes (diffusion/osmosis) or fixed routes (blood vessels). These routes allow mobility in production. The use of a free transport pathway makes the process highly variable. This ensures that the necessary precursors always reach the station where they are most needed. Both cytokines together then initiate the production of the required product in station 1.

At the same time, the external turbulence directly triggers the production of a third cytokine: EPO. It is produced in a separate production line 2 (kidney cells) and then transported via a fixed route to the SC niche. The use of a fixed transport route ensures the safe delivery of the EPO component to its destination. This cannot be guaranteed with diffuse or autonomous transport over long distances between two production lines. The external production of EPO contributes to the stability of the PS. It ensures that the additional production of EPO does not interfere with the steps controlled by stations 1, 2 and 3, which are important for the overall process.

The different cell types like T-cells, stroma cells and kidney cells stand for the machinery, as they produce the precursors. They have their own power plant for the provision of energy. Hereby, the SC niche achieves compatibility as well as a certain stability and independence of individual stations from each other. In a PS, this could be realized by providing movable sockets that ensure that working modules can be used anywhere and independently of the local energy supply.

At station 1, the supply process begins with the delivery of the universal raw product: the hematopoietic SCs. The raw product is processed to a semi finished product, which is the myeloid SC, and then further processed to the final product, which is the erythrocyte. The pathway from SC to final product is called differentiation process in biological systems and can be translated to the value creating process from raw product to a final product in a PS. The raw and the semi finished product are also used for generating many other final products besides erythrocytes, which makes the line very flexible in terms of product variants. The raw product which is constantly needed in production, is delivered via fixed routes. Mass flow can be adjusted to control scaling and transformability.

Ubiquitous components/ raw materials are used and added to the raw product to create the final product. These are amino acids, carbohydrates and lipids in the biological system. These ubiquitous components/ raw materials are used in all lines and stations, ensuring the modularity of the system. The different components/ raw materials can be disassembled and reassembled through cell recycling, if unused. The components/ raw materials are externally sourced, i.e. they are delivered from suppliers, quality checked and transported to the factory via a fixed and secure transport system. In the target production line, diffusion transport is used to ensure even distribution within the line and stations. To guarantee the system's transformability and stability, it is essential to secure the supply of components/ raw materials.

The production of the erythrocyte is not fully completed at line 1, as inaccurately shown in Figure 2. Instead, a product that does not hold hemoglobin yet (reticulocyte) exits the SC niche.

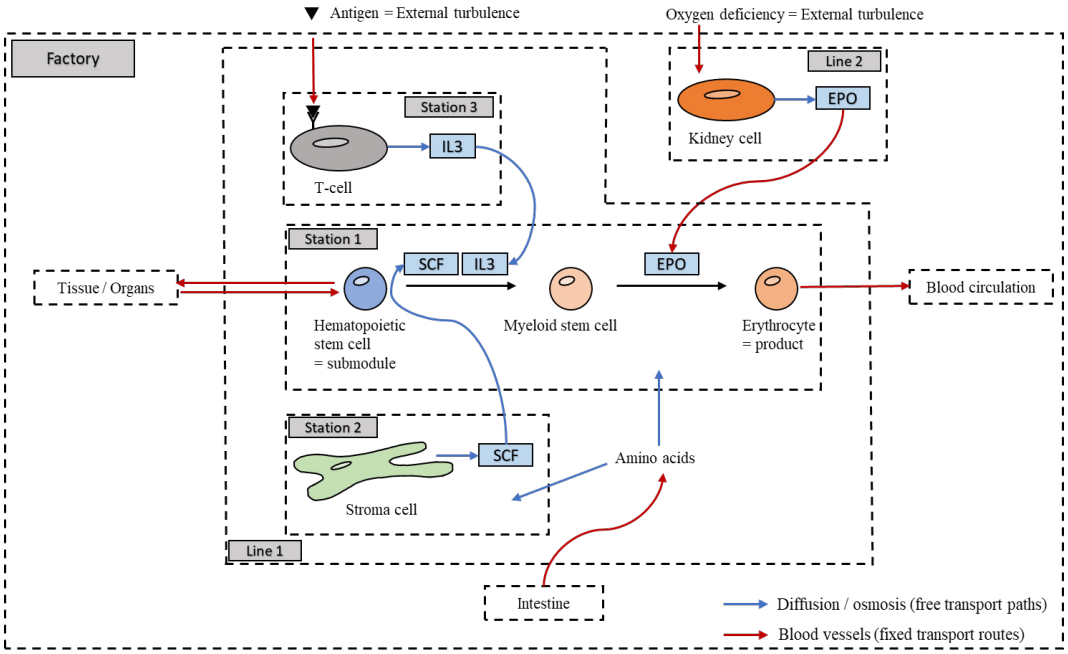

Fig. 2. The SC model translated into components of a PS including information and material flows.

Table 4. Different scenarios of change and corresponding change pathways in a SC system and translation to a PS.

Scenario	Recep-tor	Change enablers SC system	Change enablers PS
1) Customer wants modified X	P, QL	Information flow from outside enters SC niche in which differentiation to modified cell takes place/ signalling cascade is changed	Factory: Can react to changes in the product (Universality) Line: Must change in composition of sub-modules (Modularity) Station: Underutilised sub-module is added to line X (Mobility, Compatibility)
2) Higher quantity of X is required	QN, T	SC niche scales production upwards through increased distribution of neurotransmitter	Factory: Capacity of the entire plant is increased (Scalability) Line: Line for X is populated with additional modules (Modularity, Mobility) Station: more workers need to operate the modules (Universality)
3) New product is implemented in factory	P, QL	If new product information is stored in DNA, it can be built from the same ubiquitous resources.	Factory: Can implement new product (Universality, Scalability) Line: Line X can produce Y in parallel with X (Scalability) Station: Stations are added (Scalability, Mobility)
4) Quality requirements for product change	P, QL	Control modules of SC niche need to be replaced/ inhibited and others activated	Line: Line for product is changed, new modules to meet requirement (Mobility, Modularity) Station: Additional station is moved to location (Mobility)
5) X is needed less, Y more	P, QN	Neurotransmitter for product X are downregulated and reach the SC niche less. Simultaneously, signalling cascades for product Y are triggered	Line: One area is scaled up and the other is scaled down (Scalability)
6) X does not pass final inspection due to defective assembly	QL	SC niche would detect defect before final inspection and would disassemble / recycle the wrong product	Line/ Station: Includes several quality checks and poka yoke principles (Universality Modularity) Product Design: Design for Disassembly is integrated (Modularity)
7) Time for manufacturing a product must be shortened	T	Production time in SC niche can be adjusted by scaling up neurotransmitters and production. Production takt per individual protein cannot be accelerated, as it is already optimized	Line: Numbering up stations for speed up (Scalability) Station: Converting other station to produce the more required product. (Compatibility)
8) Central energy supply collapses	T, QN	SC can, e.g. for a short time, generate energy via an anaerobic pathway (lower energy yield)	Station: Switches to self-sufficient supply based on batteries for example
9) Limited raw materials are available	QN, C, QL	SC niche switches metabolism down to the most necessary mechanisms	Factory: Focuses on production of highest priority products and goes into ‘saving mode’ Line: Obtains intermediate product from another line (as it is available in abundance there) and processes this further
10) Entire production line X fails	QN, QL	Countless production lines exist for each product (protein), so that just one failure does not cause a failure	Line: Line for Y is extended by modules to be able to produce X as well (compatibility, scalability, modularity)
11) Incorrect transfer (data center to PS) information/ building instructions	QL	SC would recognise error and eliminate affected memory (=DNA) through apoptosis	Line: Anomaly detection compares current state and desired state and informs worker to act

The synthesis of hemoglobin is then completed during its journey to the site of action (to the customer). This allows for faster and more mobile delivery of the product, while also unburdening the PS of the SC niche to ensure that essential processes are not disrupted. This concept could be applied to a PS by outsourcing finishing processes or by shifting finishing processes to the transport process.

The production lines can produce multiple products and maintain constant capacity utilization. Additionally, there are non-exhausted production lines (e.g. line 2). This is essential as, it must be available for emergency activation (e.g. by increasing the EPO concentration). Thus, the PS becomes scalable. Compatibility is achieved through all levels. A precursor from line 2 can be integrated into line 1.

The model of this bio-inspired factory was applied in a real greenfield production planning for a metal manufacturer that sells a wide range of metal hoses, bellows, pipes, offering both standardised and customised products. The rough and fine layout was arranged according to the SC model, which enabled a unification of the structuring principles: equipment and product orientation on the same level. Machines with universal capabilities were arranged at the intersection of product areas, allowing the use of synergies. A number of changeability measures were incorporated, including modular design and expansion areas. This enabled the main criteria of the manufacturer, namely clear material flow, synergy potential, and changeability, to be fulfilled with the SC model.

4.4. Identification of systemic solution options and proposals for action in the case of concretely named changes

In the following, different changeability scenarios are depicted. They each assume an external turbulence acting on a receptor. Starting from the receptor, different levels of the PS are addressed and these levels in turn are equipped with change enablers according to the three-axis model of Nyhuis, see Table 1. This is followed by the analogous behaviour of a SC system. Specific transformation pathways can be identified.

If a scenario is considered in which the customer demands a modified product X, the receptors product and quality are addressed. In the case of the SC, a flow of information from outside enters the SC niche where differentiation into a modified cell occurs or the signalling cascade is altered. For this case, the analogous effects on the PS can be divided into three levels: Factory, Line, and Station. The factory can respond to changes in the product (Universality). In Line, the line must change in the composition of submodules (Modularity). Finally, at the station level, underutilized submodules are included in the line for product X (Mobility, Compatibility). Another scenario is the limited availability of raw materials. The receptors addressed are quantity, cost, quality, and elements. This causes the change enablers in the SC to downshift metabolism to the most necessary mechanisms. In parallel, the focus is on the high priority products in the Factory of a PS. The PS goes into "saving mode". If intermediates from another line are abundant, the Line obtains them and processes them further.

Overall, eleven different scenarios are summarized in Table 4. For each scenario, it is listed which receptors are addressed, how this affects the change enablers of the SC, and what the analogous change enablers of the PS are. These scenarios are intended to validate the transferability of SC change enablers to factory design. The receptors are abbreviated as listed in Table 1, whereas X and Y refer to product X and Y.

5. Conclusion

A changeable PS was developed based on an SC model approach and presented as an example of stem cell differentiation into blood cells. The components, mechanisms, material, and information flows were successfully translated from the biological to the production system. Different change scenarios, based on Nyhuis' three-axis model, were executed with the SC model and also translated to the PS, demonstrating that the SC model is an excellent example for a changeable PS. The model was applied to a metal manufacturer. The next step is using KPIs to measure the positive effects in different change scenarios. However, the presence of flexible and modular components and products throughout the factory maximises the realisation of such a model in any case.

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