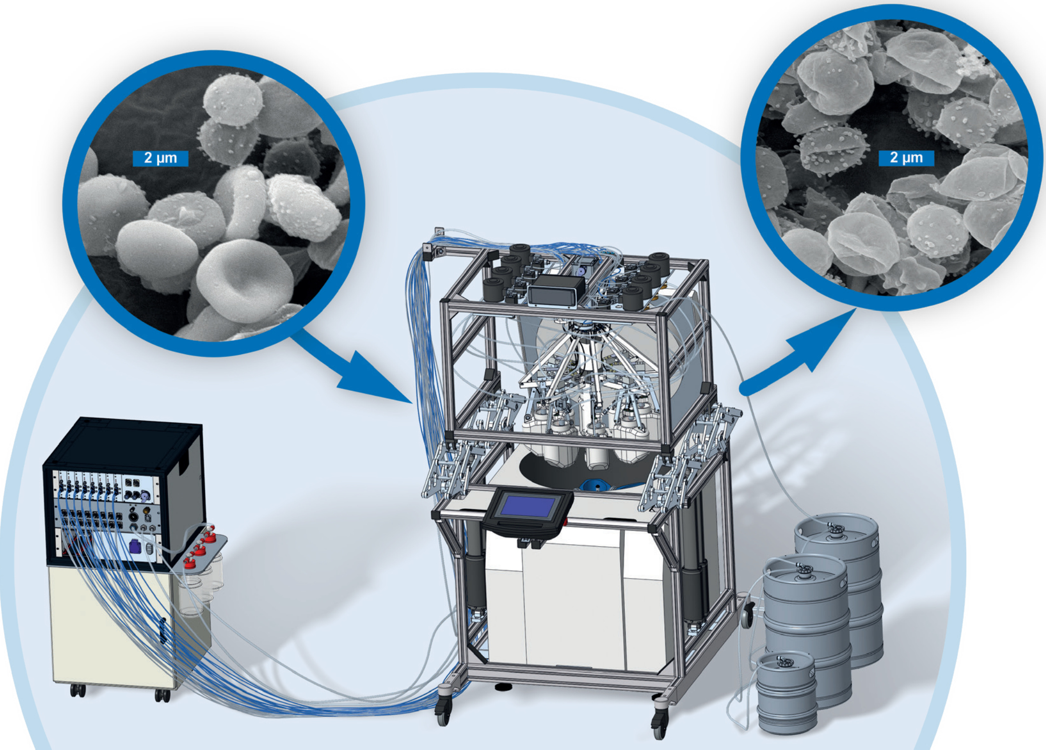
Band 69

Malte Schöps

Design, Verification and Validation of a Novel Large-Volume Production of Ghost Cells



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Herausgeber:

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Design, Verification and Validation of a Novel Large-Volume Production of Ghost Cells

Konstruktion, Verifizierung und Validierung einer neuartigen Großmengenproduktion von Ghost Cells

Von der Fakultät für Maschinenwesen der
Rheinisch-Westfälischen Technischen Hochschule Aachen
zur Erlangung des akademischen Grades eines
Doktors der Ingenieurwissenschaften genehmigte Dissertation

vorgelegt von
Malte Schöps

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Univ.-Prof. Dr.-Ing. Andreas Jupke

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Abstract

Mechanical circulatory support is mainly based on moving actuators in the organism blood, such as the blades of centrifugal blood pumps. Using these devices in the treatment of patients exposes blood to unusual stress, causing hemolysis. Hemolysis is still one of the major challenges in the development of mechanical circulatory support devices, apart from thrombocyte activation. Close to the surface between rotor and blood, high shear stress acts on red blood cells. As soon as shear stress exceeds a threshold value, it leads to hemolysis, destroying red blood cells by rupturing their membranes.

The fluorescent hemolysis detection method (FHDM) developed by Jansen et al. [1] investigates hemolysis in more detail. With this method, a spatial resolution of hemolysis hotspots is realized based on ghost cells. Ghost cells are red blood cells with reduced intracellular hemoglobin. The FHDM is limited by the small amounts of ghost cells produced. Larger volumes would allow to perform this method even according to international standards and on real size models of mechanical circulatory support systems. The aim of this study was to develop a process engineering system using semi-automatic mechatronic technology to increase ghost cell production volume.

Until now, production volume was limited to 10.3 mL of ghost cells with a hematocrit of 30 % due to predominantly manual process steps. By implementation of a novel semi-automated large-volume batch production system (LVBPS) in the existing method, productivity was increased 22-fold while multiplying process efficiency by 34 times. Time-consuming manual work such as pipetting was supported by sensor-based process engineering. In addition to increased efficiency, process monitoring was implemented in the system to ensure consistent process parameters and semi-automation of the production process. Moreover, the properties of ghost cells as blood substitute such as rheology and deformability were maintained or even enhanced compared to manual production. With the help of the LVBPS, the objective of producing large volumes of ghost cells was successfully achieved.

Zusammenfassung

Mechanische Herz-Kreislauf-Unterstützung basiert größtenteils auf bewegten Aktoren im Organismus Blut, wie beispielsweise die Rotoren von Zentrifugalblutpumpen. Sobald diese Systeme bei der Therapie von Patienten zum Einsatz kommen, wird das Blut außerordentlichen Belastungen ausgesetzt. Die Hämolyse ist, neben der Thrombozytenaktivierung, nach wie vor eine der größten Herausforderungen bei der Entwicklung von mechanischen Herz-Kreislauf-Unterstützungssystemen. Sobald die Schubspannungen einen Schwellwert überschreiten, reißt die Membran der roten Blutkörperchen und führt zu deren Zerstörung — der Hämolyse.

Um dieses Phänomen genauer zu untersuchen, entwickelten Jansen et al. [1] die sogenannte Fluorescent Haemolysis Detection Method (FHDM). Mit dieser Methode wird zusätzlich zu der bisher bewährten zeitlichen und quantitativen Hämolyse-Evaluierung auch eine räumliche Auflösung auf Basis von Ghost Cells realisiert. Ghost cells bezeichnen rote Blutkörperchen mit reduzierter intrazellulärer Hämoglobinkonzentration. Limitiert ist die FHDM jedoch durch das geringe Volumen an Ghost Cells, das bisher produziert werden konnte. Größere Volumina würden es erlauben, diese Methode auch an mechanischen Herz-Kreislauf-Unterstützungssystemen realer Größe und gemäß internationaler Normen durchzuführen.

Durch die Implementierung einer Halbautomatisierung in das etablierte manuelle Verfahren mittels eines neuartigen Großvolumen-Batch-Produktionssystems (LVBPS) konnte die Produktivität um das 22-fache und die Effizienz um das 34-fache erhöht werden. Zeitaufwändige manuelle Arbeiten wie z. B. das Pipettieren, werden nun durch sensorgesteuerte Verfahrenstechnik automatisiert. Neben der gesteigerten Effizienz sorgt die Prozessüberwachung für konstante Prozessparameter und für eine Teilautomatisierung der Produktion. Darüber hinaus konnten die Eigenschaften des Blutersatzfluids wie Rheologie und Verformbarkeit im Vergleich zur manuellen Produktion beibehalten oder sogar verbessert werden. Mit Hilfe des LVBPS wurde das Ziel, große Mengen an Ghost Cells herstellen zu können, erfolgreich umgesetzt.

Content