A Peristaltic Oxygenating Mixer for Miniature Integrated Bioreactors

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We have developed a mixer and corresponding fabrication process to address problems involved in the development of a miniaturized parallel integrated bioreactor array system, whose functional objectives include: (1) the ability to support cell growth of aerobic micro-organisms without oxygen limitation, (2) scalability to a large number of reactors, (3) online sensing of culture parameters, and (4) individual control over pH. In order to achieve these design objectives, we have developed a flat form factor, all PDMS (silicone elastomer), peristaltic oxygenating mixer (Figure 1), using a fabrication process that allows integrating multiple scale (100µm-1cm) and multiple depth (100µm-2mm) structures in a simple molding process. The flat form factor ensures a high surface area to volume ratio for high oxygen transfer rates, and the peristaltic action achieves in-plane homogeneous mixing within 5-20 seconds, depending on the depth of the well and actuation parameters, which is three orders of magnitude faster than lateral mixing from diffusion alone. The peristaltic action also contributes to mixing in the vertical direction, which further improves the oxygen transfer rate. The volumetric oxygen transfer coefficient (k,a) was measured by a gassing-in method [1], using an integrated platinum-octaethylporphyrine based dissolved oxygen sensor [2]. Calibrated measurements of the oxygen transfer coefficient (Figure 2) in devices of various well depths agree with theoretically expected oxygen transfer coefficients for unmixed devices. For devices mixed with various actuation frequencies, the measured oxygen transfer coefficient falls short of the theoretical values due to non-instantaneous vertical mixing. Even with non-optimized devices, preliminary results from eight simultaneous bacteria growth experiments, using four different medium compositions with online measured optical density and dissolved oxygen concentration, indicate that the oxygen transport is sufficient to maintain a greater than 55% dissolved oxygen concentration for the duration of the bioreaction.

REFERENCES: