Simulation of two-phase air–liquid flows in a closed bioreactor loop: Numerical modeling, experiments, and verification

Irina G. Nizovtseva1,2 | Ilya O. Starodumov1,3,4 | Alexander Y. Schelyaev4
Andrey A. Aksenov5 | Sergey V. Zhlukto5 | Marina L. Sazonova4
Oleg N. Kashinsky6 | Leonid S. Timkin6 | Vladimir G. Gasenko6
Roman S. Gorelik6 | Dmitri V. Chernushkin7 | Igor Y. Oshkin8

1Laboratory of Multi-Scale Mathematical Modeling, Ural Federal University, Ekaterinburg, Russia
2Otto-Schott-Institut fur Materialforschung, FSU, Jena, Germany
3Ural State Medical University, Ekaterinburg, Russia
4TESIS Ltd., Moscow, Russia
5Joint Institute for High Temperatures, RAS, Moscow, Russia
6S. S. Kutateladze Institute of Thermophysics, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia
7NPO Biosintez Ltd., Moscow, Russia
8Winogradsky Institute of Microbiology, Research Center of Biotechnology, Russian Academy of Sciences, Moscow, Russia

Correspondence
Irina G. Nizovtseva, Laboratory of Multi-Scale Mathematical Modeling, Ural Federal University, 620000 Ekaterinburg, Russia.
Email: Nizovtseva.irina@gmail.com

Communicated by: D. Alexandrov

1 INTRODUCTION

In view of the extensive use of two-phase gas–liquid flows in various technical and biotechnical devices, the problem of mathematical modeling, calculation, and optimization of this kind of flows has been addressed in a large number studies. Many theoretical and semi-empirical models of varying complexity have been published.1–4 The simulation of such flows
is complicated by the lack of qualitative experimental data, as well as by the inherent flow characteristics associated with the strong mutual influence of the carrier and dispersed phase. The interaction of the phases generates an array of physical phenomena: momentum and energy exchange between the flow phases, a particular structure of flow pulsations, phase transitions, bubble effects, and gas-phase dissolution processes which significantly change both the flow structure and all mass transfer properties of the flow.5–8 This paper has studied the properties of two-phase gas–liquid vertical flows. The structure of such flows significantly depends on the direction of the flow phases.9 There is a major difference between the upward and downward flow characteristics in vertical channels. In a bubble flow, one of the main factors determining the distribution of phases along the channel cross-section is a lateral force acting on a gas bubble floating relative to the liquid.1–8,10 Since the sign of this force is opposite for the upward and downward flows, the nature of gas-phase distribution across the channel cross-section in these modes is also different. Earlier, studies11–16 have noted significant differences in the values of channel-width-averaged bubble velocities in upward and downward flows. However, the data available in the contemporary literature are not systematic. This study employed a comprehensive approach to studying the hydrodynamics of the local characteristics of downward and upward bubble flows in a monodispersed bubble gas–liquid mixture by conducting original measurements of local values of friction on the pipe wall, phase velocities, and gas content, as well as numerical experiments. The hydrodynamic and mass-exchange characteristics were studied on the installations equipped with measuring equipment (measuring sensors, primary electronic transducers, and interfaces for communication of measuring circuits with PC), allowing obtaining full-scale data on two-phase gas–liquid flows and conducting qualitative and quantitative cross-verification of the new model of two-phase mixture downward and upward flow based on the FlowVision software package.

2 | APPROACHES AND METHODS

The most modern methods of analysis and scaling of process solutions based on achievements of practical physics, chemistry, and biotechnology are based on computational fluid dynamics (CFD) tools.4,6 The experimental information about the flow structure, its averaged, and pulsation properties is essential both for computer analysis of the two-phase gas–liquid medium motion inside a large class of process devices and for controlling the state of two-phase flows that determine the hydrodynamic environment and mass transfer processes, in particular, in bioreactors.17–25 The development of integro-differential models and using them to simulate complexly interacting carrier and dispersed phase is an urgent interdisciplinary task. The new models allow for a broader fundamental understanding and management of the hydrodynamic environment in bioreactor circuits26–30 and can provide the basis for comprehensive systematic microbiological studies of the behavior of microorganisms in local apparatus, such as fermentation devices that implement aerobic biosynthesis processes. The literature31–33 notes that the researches in this area are still conducted mainly by empirical methods. There is virtually no integrated approach to the development of a classical experimental–theoretical framework, new experimental setups, new adapted software tools, and approaches to their use for real industrial apparatus. At present, there is a particular lack of data on local velocity and gas content profiles for monodispersed mixtures, especially for the phase slip velocity in the downward flow. In conducting the simulation experiments, the authors were guided by a number of assumptions that ensure the feasibility of the claimed results and do not have a qualitative impact on the results of the work presented.10–13,34 Dissolving air in the fluid is not taken into account in the calculations. The two-phase flow is assumed to be isothermal. The generation of turbulence by bubbles is not taken into account. The simulation tasks are solved in a monodispersed formulation.

2.1 | Experimental methods

In order to analyze the characteristics of upward and downward flows of multiphase flows in vertical channels and to obtain verification data for the mathematical model, an experimental setup was used employing techniques to measure local fluid velocity profiles and fluid velocity pulsations by local electrodiffusion sensors.35 The inclusion of these sensors via the conductivity method also made it possible to measure local gas content profiles. The simultaneous use of a specially adapted laser Doppler anemometer (LDA) with a short measuring volume (about 0.1 mm) allowed local measurements of gas bubble velocity and bubble diameters, taking into account the position of bubble centers in the flow.36 To study gas–liquid flow, an experimental setup was used, which was a vertical stainless steel tube of 6.5-m height and 14.8-mm inner diameter. The unit is equipped with a liquid flow meter series, a storage tank, a centrifugal pump, a gas flow meter, a gas–liquid mixing chamber with a bubble generator, and a thermal stabilization system (Figure 2).13 The experimental setup involves feeding the liquid into the pipe through a 90-mm inner diameter mixing chamber made
of plexiglass and installed at the top of the pipe (for downward flow) and at the bottom of the pipe (for upward flow). Different gas injectors (M and P injectors) can be installed in the interior of the chamber to generate bubble mixtures with different average bubble sizes and different volumetric gas contents of the two-phase flow. To measure the velocity and gas content profiles, a measuring section is installed 2.3 m below the mixing chamber. To visualize the flow, an immersion unit with optical windows filled with immersion fluid was installed in the section. A glass tube with an internal diameter of 14.8 mm is fitted inside the unit to take LDA measurements and photographic images of the flow using a Canon XL1 camcorder at shutter speeds up to 1/16,000 s and a resolution of 768 × 576 pixels. To measure the local fluid velocity and local gas content, the standard electrodiffusional probes developed in Institute of Thermophysics were used. The 60-μm diameter probe sensor tip was positioned at 10 mm below the LDA measuring volume to eliminate the physical influence of the sensor on the bubble velocity measurement. The LDA measuring volume and the electrodiffusion sensor were positioned in radial direction with an accuracy of ±0.05 mm. The standard electrochemical solution consisting of 0.01-N potassium ferricyanide and ferrocyanide and 0.25-M sodium hydrocarbonate water solutions was used as the working liquid. To control the viscosity of the solution, glycerin was added, allowing laminar flow experiments to be conducted at an increased average fluid velocity. The parameters of the working solution are given in Table 1.

The system is equipped with a standalone fluid thermal stabilization system with a heat exchanger and agitator, a data acquisition system for measuring flow velocity profiles, and multichannel friction stress on the pipe wall. Other system characteristics are as follows:

- Maximum fluid velocity: 1.0 m s\(^{-1}\), flow rate: 170 cm\(^3\) s\(^{-1}\),
- Minimum fluid velocity: 0.01 m s\(^{-1}\), flow rate: 1.7 cm\(^3\) s\(^{-1}\),
- Air supply and flow measurement system up to 15 cm\(^3\) s\(^{-1}\).

### 2.2 Numerical and CFD methods

The simulation procedure was performed entirely with the FlowVision software package, which is based on a finite-volume approach to approximate the equations of motion for fluid and gas. It employs automatic building of the computational grid, which is based on the subgrid geometry resolution method, which is a better analog of the cut-cell method. A new splitting method is used to solve the system of Navier–Stokes equations. The peculiarity of this method applied to the combined computational grid (velocity and pressure are determined in the centers of the cells) is that velocities satisfying the mass conservation law on the cell faces (transfer velocities) are determined before all equations are calculated, and then, all other equations, including Navier–Stokes equations, are solved using these transfer velocities.

### 3 RESULTS AND DISCUSSION

Below is the complete system of equations of the mathematical model in accordance with Rosa et al. The mass transfer coefficient for bubble flow is the ratio of the specific mass flow of air at the phase interface to the difference in air concentrations at the phase interface and away from it:

\[
K = \frac{J_d}{Y_{air,s} - Y_{air,b}}, \quad K = \frac{J}{\rho_{Liq} (Y_s - Y_b)} = \frac{J_d}{(Y_s - Y_b)}. \tag{1}
\]

\(J_d\) (m s\(^{-1}\)) is the diffusion flux of air from the bubbles into the liquid and \(Y_{air}\) is the mass fraction of gas in the liquid (concentration). The local mass transfer coefficient is determined using the Sherwood criterion:

\[
K = \frac{Sh_d \nu_c}{Sc_c d_b}, \tag{2}
\]

where \(Sh_d\) is the Sherwood number, defined in terms of the size \(d\) of the gas dispersed phase; \(Sc_c\) is the Schmidt number for the continuous (liquid) phase; and \(\nu_c\) is the kinematic coefficient of molecular viscosity of the continuous (liquid)
phase \((m^2 \text{s}^{-1})\). If we have a monodispersed (of the same diameter) bubble medium, then \(d_b\) is the diameter of bubbles (m) and the expression for the Sherwood number:

\[
Sh_d = 2 + 0.46 \text{Re}_d^{0.55} \text{Sc}_c^{0.33},
\]

\[
\text{Re}_d = \frac{d|V_c - V_d|}{V_d},
\]

\[
\text{Sc}_c = \frac{V_c}{D}.
\]

Based on the above ratios, the determining parameter for the mass transfer coefficient is the bubble slip velocity. The value of the slip velocity depends on the gas content, the size of the bubbles and the speed of the carrier phase. The above flow characteristics for determining the mass transfer coefficient are calculated by solving a system of mathematical model equations, which are given below. Sherwood number includes a very important parameter, which is the local bubble slip velocity relative to the fluid. Only in the simplest case, that is, the one-dimensional motion with constant slip velocity of a monodisperse sufficiently dilute cloud of bubbles, can these simple formulae be used to calculate the integral (total) mass transfer in the apparatus. In real systems the motion is considered to be multidimensional and nonhomogenous and the slip velocities and, consequently, the local mass transfer coefficients are varying at different points of the apparatus. This is because the slip velocity depends on the local gas content, the local bubble size, and the local velocity of the carrier phase. Consequently, the total mass yield (a very important parameter in practice) can only be determined from detailed mathematical simulations of hydrodynamics and mass transfer using numerical methods.

### 3.1 Equations describing the processes in the dispersed phase

#### 3.1.1 Motion

The equation of motion for the dispersed phase can be written as

\[
\frac{\partial n_d}{\partial t} + \nabla \cdot (V_d n_d) = 0.
\]

Here, \(n_d (m^{-3})\) is the concentration of particles, and \(V_d (m \text{s}^{-1})\) is the velocity of the dispersed phase (particles). The momentum transfer of the dispersed phase (particles) is described by the nonhomogeneous convection–diffusion equations for the conservative variables \(V_d, M_d, n_d\):

\[
\frac{\partial (V_d M_d n_d)}{\partial t} + \nabla \cdot (V_d M_d n_d) = -n_d \frac{\pi d_3}{6} v p + n_d \frac{\pi d_3}{6} (\rho_d - \rho_c) g + F_{D,i} + F_{L,i} + F_{W,i},
\]

\[
F_D = n_d \rho_c C_D \frac{\pi d_3^2}{8} |V_c - V_d| (V_c - V_d),
\]

\[
F_L = n_d \rho_c C_L \frac{\pi d_3^3}{8} (V_c - V_d) \times \omega_c,
\]

\[
\omega_c = \nabla \times V_c,
\]

\[
F_W = n_d \rho_c C_W \frac{\pi d_3^3}{6} \max \left\{0, \left(1 - \frac{1}{D_w}\right)\right\} (V_c - V_d)^2 n.
\]

Here, \(M_d (kg)\) is the local mass of particles, \(d (m)\) is the particle diameter, \(p (Pa)\) is the pressure in the fluid measured relative to the hydrostatic pressure, \(\rho_d (kgm^{-3})\) is the density of the dispersed phase, \(\rho_c (kgm^{-3})\) is the density of the continuous phase, \(g (m s^{-2})\) is the acceleration of gravity, \(F_D (N m^{-3})\) is the drag, \(C_D\) is the drag coefficient, \(F_L (N m^{-3})\) is lift, \(C_L\) is the lift coefficient, \(V_d (m \text{s}^{-1})\) is the phase velocity of the dispersed phase, \(V_c (m \text{s}^{-1})\) is the phase velocity of the continuous phase, \(F_W (N m^{-3})\) is the repulsive force (the force that repels bubbles from the wall in accordance with the hydrodynamic theory of lubrication), and \(D_w (m)\) is the distance to the wall, at which the action of the repulsive force stops. \(C_W\) is the repulsive force coefficient, and \(y (m)\) is the distance from the center of the bubble to the wall. \(n\) is the normal to the wall (directed towards the fluid).
For the drag coefficient of a particle cloud, the following expressions are used:

\[ C_D = C_{D0} \frac{1}{\varphi_c^2} \]
\[ \varphi_c = 1 - \varphi_d, \]
\[ \varphi_d = n_d \frac{\pi d^3}{6}. \]  

(6)

Here, \( C_{D0} \) is the drag coefficient of a single bubble, \( \varphi_c \) is the relative volume of the continuous phase, and \( \varphi_d \) is the relative volume of the dispersed phase. For the drag coefficient of a single bubble, the following expression is used: \( C_{D0} = \frac{24}{Re_d} \left( 1 + 0.15Re_d^{0.687} \right) \).

\[ Re_d = \frac{\rho_c |V_c - V_d| d}{\mu_c}. \]  

(7)

Here, \( Re_d \) is the Reynolds number for the dispersed phase, and \( \mu_c \) is the dynamic coefficient of the molecular viscosity of the continuous phase (kgm\(^{-1}\)s\(^{-1}\)).

The following expression is used for the lift coefficient:

\[ C_L = \min \left( 0.5, C_{L \text{ factor}} \frac{1}{d} \sqrt{\frac{\mu_c}{\rho_c \sqrt{S}}} \right) \frac{1}{\varphi_c^2}. \]  

(8)

Here, \( C_{L \text{ factor}} \) is the model constant, and \( \sqrt{S} \) is a scalar quantity characterizing the local velocity gradient of the fluid. The expression (8) is based on the Saffman model. The latter multiplier takes into account the particle cloud effect similar to model (6) for the drag coefficient. The lift action begins at a distance of \( D_L \) from the wall.

### TABLE 2
Steady-state calculations of the shear stress \( \tau_w \) on the pipe wall for different computational grids

| Computation, grids | Theory | 7×1267×1 | 15×1567×1 | 15×2534×1 | 30×1267×1 | 30×2534×1 |
|--------------------|--------|----------|-----------|-----------|-----------|-----------|
| \( \tau_w \) (N m\(^{-2}\)) | 0.9218 | 0.913 | 0.92 | 0.92 | 0.9214 | 0.9214 |
| (1\%) | (0.2\%) | (0.2\%) | (0.04\%) | (0.04\%) |

### FIGURE 1
Single-phase velocity profile [Color figure can be viewed at wileyonlinelibrary.com]
The following parameters, which determine the forces acting on the bubbles, are set during the calculations: \( C_W = 0.002 \) is the repulsive force coefficient; \( D_W = D_b \) is the distance from the wall, to which the repulsive force acts; \( C_L = 0.1 \) is the lift coefficient; and \( D_L = D_b \) is the distance from the wall, from which the lift begins to act.

3.1.2 Mass transfer

The mass transfer of the dispersed phase (particles) is described by the nonhomogeneous convection–diffusion equations for the conservative variables \( M_d, n_d \):

\[
M_d n_d \frac{\partial (M_d n_d)}{\partial t} + \nabla \cdot (M_d n_d \mathbf{V}_d) = 0.
\]  

(9)

3.2 Equations describing processes in the continuous phase

3.2.1 Motion

Continuity equation for the continuous medium can be written as

\[
\frac{\partial (\varphi_c \rho_c)}{\partial t} + \nabla \cdot (\varphi_c \rho_c \mathbf{V}_c) = 0.
\]  

(10)
Here, \( \varphi_c \) is the relative volume of the continuous phase. Momentum equation:

\[
\frac{\partial (\varphi_c \rho_c V_c)}{\partial t} + \nabla \cdot (\varphi_c \rho_c V_c \otimes V_c) = -\varphi_c \nabla p + \nabla \cdot (\varphi_c \rho_c g) - F_D - F_L,
\]

\[
V_c \otimes V_c = \left\{ \begin{array}{c}
V_{cx} V_{cy} V_{cz} V_{cx} V_{cy} V_{cz}, \\
V_{cx} V_{cy} V_{cz} V_{cx} V_{cy} V_{cz}, \\
V_{cx} V_{cy} V_{cz} V_{cx} V_{cy} V_{cz},
\end{array} \right\},
\]

\[
\tau = \mu_c \left( 2 \dot{S} - \frac{2}{3} (\nabla \cdot V_c) \mathbb{I} \right),
\]

\[
S_{ij} = \frac{1}{2} \left( \frac{\partial V_i}{\partial x_j} + \frac{\partial V_j}{\partial x_i} \right).
\]

Here, \( \tau \) (Pa) is the viscous stress tensor. \( \mu_c \) (kg m\(^{-1}\) s\(^{-1}\)) is the dynamic coefficient of molecular viscosity of the continuous phase, \( \dot{S} \) (s\(^{-1}\)) is strain rate tensor, and \( \mathbb{I} \) is the unit tensor.

FIGURE 3  Simulated velocity profiles of liquid \( (V_L) \) and bubbles \( (V_B) \) versus experimental data (downward flow, \( W_l = 0.4335 \) m s\(^{-1}\), \( Re = 1844 \)) [Color figure can be viewed at wileyonlinelibrary.com]
3.3 Calculation parameters and computational grid

During the calculation of the hydrostatic pressure in the pipe, the hydrostatic zero level is defined at the upper boundary of the computational domain. The computational grid for the study was selected based on the results of the simulation of a single-phase flow of the working fluid with the average velocity of $U_1 = 0.4335 \text{ms}^{-1}$. Table 2 shows the results of calculating the tangential (shear) stress $\tau_w$ on the pipe wall at a steady flow section. Figure 1 shows a comparison of the well-known “theoretical” velocity profile and the velocity profiles computed at different grids. Modeling was carried out in a vertical tube of the working session. Figure 2 shows the experimental setup including the tube section and a schematic representation of the computational area with boundary conditions. As a result of the comparison, a computational grid of $15 \times 1267 \times 1$ (hereinafter Grid 1) and $30 \times 1267 \times 1$ (hereinafter Grid 2) was selected for simulating the bubble flow. At the inlet of the pipe (see Figure 2, right panel), the velocity of the liquid sets taking into account the gas fraction:

$$V_l = \frac{W_l}{1 - \beta}.$$
\( \beta \) is the gas flow rate determined by the expression:

\[
\beta = \frac{Q_g}{Q_g + Q_l},
\]

where \( Q_g = W_g S \) is the gas volume flow (m\(^3\) s\(^{-1}\)); \( Q_l = W_l S \) is the fluid volume flow (m\(^3\) s\(^{-1}\)); \( W_g \) and \( W_l \) are flow rates of gas and liquid, respectively (m\(^3\) s\(^{-1}\)); and \( S \) is the cross-section area (m\(^2\)). The velocity of the gas is assumed to be equal to the velocity of the liquid. A zero relative pressure condition and permeability for the dispersed phase was set at the pipe outlet. The pipe diameter is \( D = 0.015 \text{ m} \), length \( L_{\text{total}} = 6.5 \text{ m} \).

**FIGURE 6** Simulated bubble slip velocity \((V_{\text{slip}})\) versus experimental data (downward flow, \( W_l = 0.4335 \text{ m s}^{-1} \), \( \text{Re} = 1844 \)) [Color figure can be viewed at wileyonlinelibrary.com]

**FIGURE 7** Simulated gas content \((\alpha)\) profiles versus experimental data (upward flow, \( W_l = 0.103 \text{ m s}^{-1} \)) [Color figure can be viewed at wileyonlinelibrary.com]
4 | SIMULATION RESULTS

4.1 | Laminar downward bubble flow

Figures 3 and 4 illustrate the local velocity and local gas content profiles in the test section obtained by simulating several laminar flow regimes in the tube of the test bench section. The computed gas content distribution is consistent with the experimental. The gas content profiles indicate the concentration of bubbles in the axial area and their absence near the walls. On the pipe axis, the velocity is lower than the corresponding single-phase laminar values, and it is almost constant in the flow core. There is a good correspondence between the computed and experimental data. The local velocity of the bubbles is less than the local velocity of the liquid. The velocity profiles of the bubbles are also almost flat in the flow core.

The size of bubbles at the computational area’s input was determined using the average experimental value in the control section, taking into consideration the pressure variation over the pipe height. The relevant comparison of the computed and experimental values of the diameter of bubbles in the control section for different modes of the downward

![FIGURE 8Simulated velocity profiles of liquid ($V_l$) versus experimental data (upward flow, $W_l = 0.103 \text{ m s}^{-1}, \text{Re} = 0.4335$)][Color figure can be viewed at wileyonlinelibrary.com]

![FIGURE 9Simulated velocity profiles of bubbles ($V_b$) versus experimental data (upward flow, $W_l = 0.103 \text{ m s}^{-1}, \text{Re} = 0.4335$)][Color figure can be viewed at wileyonlinelibrary.com]
flow is shown in Figure 5. The computed and experimental profiles of the bubble slip velocity for various modes of laminar downward flow are shown in Figure 6. The slip velocity is almost constant in the center of the pipe. There is a decrease in the local slip velocity with an increase in the local gas content.

The computational model describes correctly the characteristics of the bubble flow. The gas content profiles confirm the concentration of bubbles in the axial area and their absence near the walls. With an increase in the flow gas content, the fluid velocity on the pipe axis decreases from single-phase laminar values and becomes almost constant in the flow core. The shear stress on the pipe wall and the bubble slip velocity in the downward flow are consistent with the experimental data. The average deviation of the computed values and test data in the control section is 8% to 10%.

4.2 | Laminar upward bubble flow

Figure 7 shows the local gas content profile in the test section, obtained by simulating different modes of laminar upward flow in the pipe of the test bench working section. The computation results are presented in comparison with the data of measurements made on the test bench.
The computed and experimental gas content profiles are consistent with each other. The distribution of the local gas content is observed, with a maximum value near the pipe wall.

Figures 8 and 9 show the local fluid and bubble velocity profiles obtained from simulations of different upward flow regimes in comparison with experimental data. In the near-axial region, the fluid velocity is almost constant. The local bubble velocity is greater than the local fluid velocity. The computed data are consistent with the experimental data.

The size of bubbles at the computational area’s input was determined using the average experimental value in the control section, taking into consideration the pressure variation over the pipe height. The relevant comparison of the computed and experimental values of the diameter of bubbles in the control section for several modes of the upward flow is shown in Figure 10. The simulation was made in a monodispersed formulation.

The computed and experimental profiles of the dimensionless bubble slip velocity (normalized to the single bubble resurfacing velocity in a resting fluid) are shown in Figure 11 for a laminar upward flow. The dimensionless slip velocity in the flow is less than one and has its minimum at the peak of the gas content.

5 CONCLUSIONS

The results of this work include the development of a model for the downward and upward flow of a monodispersed bubble gas–liquid mixture and its validation based on experimental data obtained from qualitative and quantitative original measurements of gas–liquid bubble flows. Due to increasing demand on effective technological solutions in the field of production of microbial biomass from natural gas, the current manuscript provides actual information and applicable decisions valued not only for the general fundamental research in the field but also concerning its applications in developing energy-efficient bioreactors. In order to choose the reasonable experimental setup and analytical tools of the hydrodynamic model, the number of classical approaches as well as recent advanced methods for developing and scaling up industrial biotechnological processes were studied. Based on the validation results, we got a satisfactory match between the computed and experimental velocity profiles of the fluid flow corresponding to the beginning of the transition to turbulent flow over the flow. Evaluations of the profiles have shown that at these flow rates, so-called “pseudo-turbulence” has already developed, caused by local pulsations due to the presence of bubbles. The developed model describes correctly the characteristics of the bubble flow: the average deviation of the computed values and the test data in the control section is 8% to 10%, with a qualitative correspondence of the flow characteristics. The results of the in situ and simulation experiments also confirm the difference in bubble slip velocity in the downward and upward flows due to the local flow around single bubbles in gas–liquid flows; for upward flows, the gas content profiles confirm the concentration of bubbles in the near-axis area and their absence near the walls. The possibility of semi-empirical correction of the closing relationships during model validation in different modes confirms the possibility of using the FlowVision software and the developed model to realist the scale transfer and perform process performance predictions for large (geometrical and flow rate) scale plants up to industrial fermenters. Thus, the developed model, together with numerical solutions and the experimental data obtained, represents a research work for the mathematical simulation of the multiphase hydrodynamic conditions in the closed-circuit bioreactors realizing aerobic biosynthesis processes. The work is a groundwork for a comprehensive approach to the formation of a classical experimental and theoretical basis for apparatuses to be designed. The simulation results not only are of interest in terms of advances in CFD but also reveal a wide range of applicability in solving applied technological problems, in particular, in developing and optimizing apparatuses used in biotechnological production—to optimize the local characteristics of flows as factors in ensuring the continuity, efficiency, and safety of the production process. The project is part of comprehensive research by an interdisciplinary team to develop and scale up the technology for producing fodder protein based on methanotrophic microorganisms by fundamentally improving existing technology for producing protein biomass.

ACKNOWLEDGEMENT

Computations were performed using the Uran supercomputer hosted by UB RAS. Open access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST

The authors declare no potential conflict of interests.
REFERENCES

1. Sato Y, Sekoguchi K. Liquid velocity distribution in two-phase bubble flow. Int J Multiphase Flow. 1975;2(1):79-95.

2. Wang SK, Lee SJ, Jones Jr OC, Lahey Jr RT. 3-D turbulence structure and phase distribution measurements in bubbly two-phase flows. Int J Multiphase Flow. 1987;13(3):327-343.

3. Herringer RA, Davis MR. Flow structure and distribution effects in gas-liquid mixture flows. Int J Multiphase Flow. 1978;4(5-6):461-486.

4. Lu J, Biswas S, Tryggvason G. A DNS study of laminar bubbly flows in a vertical channel. Int J Multiphase Flow. 2006;32(6):643-660.

5. Lance M, Bataille J. Turbulence in the liquid phase of a uniform bubbly air–water flow. J Fluid Mech. 1991;222:95-118.

6. Yang G, Zhang H, Luo J, Wang T. Drag force of bubble swarms and numerical simulations of a bubble column with a CFD-PBM coupled model. Chem Eng Sci. 2018;192:714-724.

7. Souhar M. Some turbulence quantities and energy spectra in the wall region in bubble flows. Phys Fluids A: Fluid Dyn. 1989;1(9):1558-1565.

8. Gore RA, Crowe CT. Effect of particle size on modulating turbulent intensity. Int J Multiphase Flow. 1989;15(2):279-285.

9. Wallis GB. One-Dimensional Two-Phase Flow. Courier Dover Publications; 2020.

10. Vaidheeswaran A, Hibihi T. Bubble-induced turbulence modeling for vertical bubbly flows. Int J Heat Mass Transfer. 2017;115:741-752.

11. Ohba K, Yuhara T, Matsuyama H. Simultaneous measurements of bubble and liquid velocities in two-phase bubbly flow using laser doppler velocimeter. Bull JSME. 1986;29:2487-2493.

12. Sheng YY, Irons G. A combined laser doppler anemometry and electrical probe diagnostic for bubbly two-phase flow. Int J Multiphase Flow. 1991;17:585-598.

13. Timkin LS, Gorelik RS. Local bubble slip velocity in a downward laminar tube flow. Thermophys Aeromechanics. 2020;27(2):259-268.

14. Bhagwat SM, Ghajar AJ. Similarities and differences in the flow patterns and void fraction in vertical upward and downward two-phase flow. Exp Thermal Fluid Sci. 2012;39:213-227.

15. Hibihi T, Goda H, Kim S, Ishii M, Uhlle J. Experimental study on interfacial area transport of a vertical downward bubbly flow. Exp Fluids. 2003;35(1):100-111.

16. Kashinsky ON, Lohanov PD, Pakhomov MA, Randin VV, Terekhov VI. Experimental and numerical study of downward bubbly flow in a pipe. Int J Heat Mass Transfer. 2006;49(19-20):3717-3727.

17. Heijnen JJ, Van’t Riet K. Mass transfer, mixing and heat transfer phenomena in low viscosity bubble column reactors. Chem Eng J. 1984;28(2):B21-B42.

18. Stanbury PF, Whitaker A, Hall SJ. Principles of Fermentation Technology. Elsevier; 2013.

19. Scargiali F, Busciglio A, Grisafi F, Brucato A. kLa measurement in bioreactors. Process Biochem. 2018;53:20170207.

20. Nizovtseva IG, Starodumov IO. Analysis of stationary directional solidification of a binary melt solidification model in the presence of a quasi-equilibrium mushy region for the case of the non-linear phase diagram. J Phys Condens Matter. 2020;32(30):304003.

21. Mersmann A, Schneider G, Voit H, Wenzig E. Selection and design of aerobic bioreactors. Chem Eng Technol. 1990;13(1):357-370.

22. Benalcázar EA, Noorman H, Maciel Filho R, Posada JA. Modeling ethanol production through gas fermentation: a biothermodynamics and mass transfer-based hybrid model for microbial growth in a large-scale bubble column bioreactor. Biotechnol Biofuels. 2020;13(1):1-19.

23. Mahdini A, Cekmecelioglu D, Demirci A. Bioreactor Scale-Up. Springer; 2019;213-236.
34. Sun X, Paranjape S, Kim S, Ozar B, Ishii M. Liquid velocity in upward and downward air-water flows. *Ann Nucl Energy*. 2004;31:357-373.
35. Nakoryakov VE, Burdakov AP, Kashinsky ON, Geshev PI. *Electrodiffusional Method for Studying Local Structure of Turbulent Flows*; 1986. Institute of Thermophysics.
36. Kashinsky ON, Timkin LS. Slip velocity measurements in an upward bubbly flow by combined LDA and electrodiffusional techniques. *Exp Fluids*. 1999;26(4):305-314.
37. https://flowvisioncfd.com.
38. Rosa LM, Maurina GZ, Beal LL, Baldasso C, Torres AP, Sousa MP. Influence of interfacial forces on the mixture prediction of an anaerobic sequencing batch reactor (ASBR). *Braz J Chem Eng*. 2015;32:531-542.
39. Saffman PGT. The lift on a small sphere in a slow shear flow. *J Fluid Mech*. 1965;22(2):385-400.
40. Ritala A, Häkkinen ST, Toivari M, Wiebe MG. Single cell protein—state-of-the-art, industrial landscape and patents 2001–2016. *Front Microbiol*. 2017;8:2009.
41. Li X, Griffin D, Li X, Henson MA. Incorporating hydrodynamics into spatiotemporal metabolic models of bubble column gas fermentation. *Biotech Bioeng*. 2019;116(1):28-40.
42. Olsen D, Jørgensen J, Villadsen J, Sin G, Jørgensen S. Modeling, simulation and optimization of single-cell protein production in a U-loop reactor. In: Proceedings of the 11th International Symposium on Computer Applications in Biotechnology; 2009:502-507.
43. Yazdian F, Shojaosadati SA, Nosrati M, Haji Abbas MP, Vasheghani-Farahani E. Mixing studies in loop bioreactors for production of biomass from natural gas. *Iran J Chem Chem Eng*. 2012;31:91-101.
44. Bomgardner M. Calysta raises money for fish food. *Chem Eng News*. 2017;95(19):10-10.
45. Petersen L, Villadsen JAH, Jørgensen SB, Gernaey KV. Mixing and mass transfer in a pilot scale U-loop bioreactor. *Biotech Bioeng*. 2017;114(2):344-354.
46. Tikhomirova TS, But SY. Laboratory scale bioreactor designs in the processes of methane bioconversion: mini-review. *Biotechnol Adv*. 2021;47:10709.
47. Oshkin IY, Belova SE, Khokhlachev NS, et al. Molecular analysis of the microbial community developing in continuous culture of Methylococcus sp. Concept-8 on natural gas. *Microbiology*. 2020;89(5):551-559.
48. Strong PJ, Kalyuzhnaya M, Silverman J, Clarke WP. A methanotroph-based biorefinery: potential scenarios for generating multiple products from a single fermentation. *Bioreour Technol*. 2016;215:314-323.
49. Wu M, Huusom JK, Gernaey KV, Krühne U. Modelling and simulation of a U-loop reactor for single cell protein production. *Comput Aided Chem Eng*. 2016;38:1287-1292.
50. Krychowska A, Kordas M, Konopacki M, et al. Mathematical modeling of hydrodynamics in bioreactor by means of CFD-based compartment model. *Processes*. 2020;8:1301.
51. Yazdian F, Pesaran Hajiabbas M, Shojaosadati SA, Nosrati M, Vasheghani-Farahani E, Mehrnia MR. Study of hydrodynamics, mass transfer, energy consumption, and biomass production from natural gas in a forced-liquid vertical tubular loop bioreactor. *Biochem Eng J*. 2010;49:192-200.

**How to cite this article:** Nizovtseva IG, Starodumov IO, Shchelyaev AY, et al. Simulation of two-phase air–liquid flows in a closed bioreactor loop: Numerical modeling, experiments, and verification. *Math Meth Appl Sci*. 2022;45(13):8216-8229. doi:10.1002/mma.8132