transitional regime ($0.01 < Kn < 0.1$) CFD can still be used with specific boundary conditions imposing non-null gas velocity at the wall (i.e., partial-slip boundary condition). In the so-called molecular regime ($Kn > 1$), the flow is not dominated anymore by collisions between gas molecules, and nonequilibrium effects start being important, resulting in velocity distributions far away from the Maxwellian one (19). In these cases it is necessary to resort to alternative simulation frameworks, such as the Lattice–Boltzmann scheme.

CFD can be used to simulate pseudostationary conditions at a certain time or the entire freeze-drying cycle and the analysis can be limited to specific parts of the equipment (i.e., chamber, condenser, duct and valve, etc.), or can include the entire apparatus. As an example, in Figure 2 the computational geometry used to investigate a pilot-scale freeze-dryer (LyoBeta™ by Telstar, Terrassa, Spain) and some results are shown. In this case, the grid describes the entire equipment from the sublimating sources, i.e., the product contained inside vials positioned on the shelves or directly displayed in trays (on the shelves), to the condenser where the solvent (typically water) is sublimated and the inert gases are extracted with a vacuum pump. The possibility of working with unstructured codes (such as Fluent or openFoam) combined with the possibility of using very irregular grids (with hexahedral and tetrahedral elements) allow to resolve most of the relevant geometrical details with adequate accuracy.

From Figure 2 (upper right) it is possible to see that water vapor to flow from the chamber to the condenser has to overcome some pressure drop, and this increases with increasing the sublimation rate. This factor plays a crucial role since the local pressure values and thus the product temperatures (as highlighted in Fig. 1) change from point to point in the chamber, potentially resulting in batch heterogeneity. CFD can be profitably used to design chambers that minimize this effect and can also allow estimating the minimum pressure obtainable in the chamber, and the solvent and inert gas partial pressure, as a function of the operating conditions.

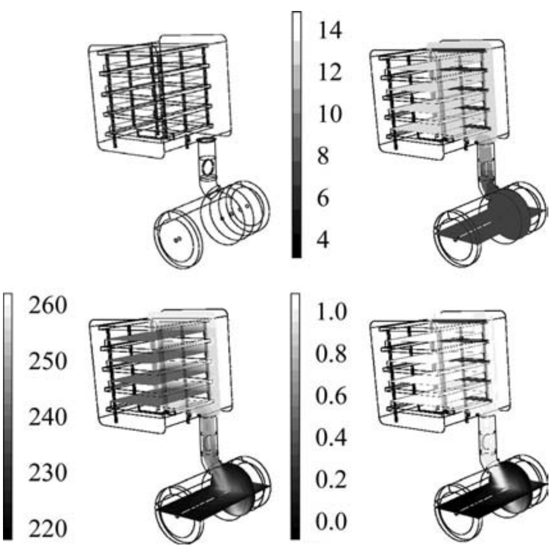

FIGURE 2 Simulation of a small pilot-scale equipment (LyoBeta™ by Telstar) using CFD; the grid was created with Gambit and consisted of about 300,000 cells, and a finite rate mechanism has been included as submodel for ice formation in the condenser. From left to right and top to bottom: Geometry of apparatus and contour plots for absolute pressure (Pa), static temperature (*K*), and water mass fraction (dimensionless) for an average sublimation rate on each single shelf equal to 0.4 kg/h m^2. By permission of Telstar, Terrassa, Spain.