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Taming morphogenesis: employing the biophysical basis of tissue self-assembly to build living structures of prescribed geometry

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We exploit the fundamental morphogenetic capacity of cells and tissues to build three- dimensional organ-like modules of prescribed shape. Morphogenesis is under strict genetic control, but genes do not create form and shape: physical mechanisms do. As an example we discuss one such mechanism based on tissue liquidity. Specifically, we demonstrate that the in vitro fusion of embryonic heart cushion tissue explants matches the in vivo behavior of this tissue during the establishment of cardiac chambers, and proceeds both qualitatively and quantitatively in analogy with the coalescence of liquid drops. Based on this and similar findings we designed experiments and built models to show that homotypic or heterotypic multicellular aggregates behave as self-assembling single color or multicolor "bio-ink" particles. We illustrate this by the layer-by-layer printing of these bioink particles (either manually or using specifically designed bioprinters) into hydrogel-biopaper, according to pre-designed three-dimensional pattern, namely tubes. By appropriate tuning of the embedding gel's physical properties, the cellular bio-ink particles, due to their liquid-like properties, fuse into toroidal and lumen-containing vessel-like organ modules.