

Supplementary materials

Table S1: Haralick features extracted from confocal microscopic images of single cell or cell cluster-laden alginate films: angular second moment (ASM), contrast, and correlation.

| Cell microstructures | ASM | Contrast | Correlation |
|-----------------------------|------------------------|-------------------------------|------------------------|
| Native | 0.31±0.03 ^a | 24402.92±1775.47 ^a | 0.19±0.03 ^a |
| P/D cluster | 0.37±0.01 ^a | 17761.47±780.76 ^b | 0.37±0.02 ^b |
| P+P/A cluster | 0.53±0.06 ^b | 11511.34±1877.12 ^c | 0.47±0.03 ^c |

* Data are shown as mean±SD of n=5 images. One-way ANOVA model results showed significant main effect of cell microstructures for all three features. Different superscript lowercase letters indicate significant difference among films with different cell microstructures (p<0.05).

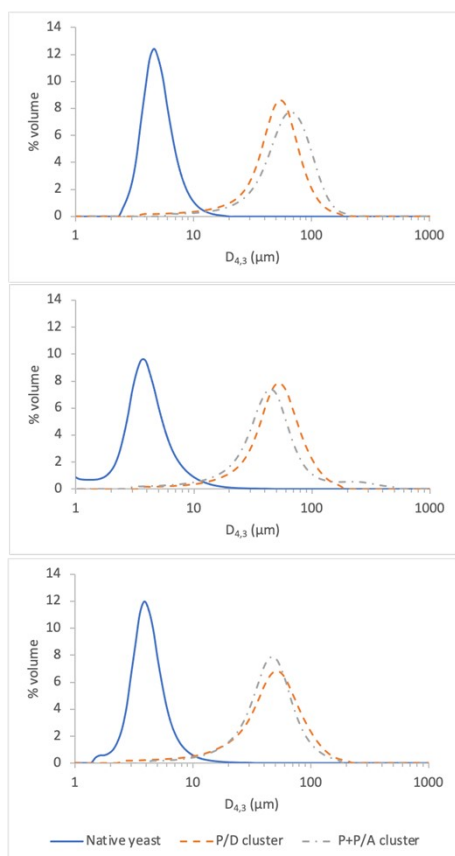
Table S2: Estimated parameters of the empirical swelling kinetics models for single cell or cell cluster-laden alginate films in enzyme-free, bile salt-free SGF and SIF.

| Condition | Cell microstructures | Peppas's model | | | Peleg's model | | | Exponential association equation model | |
|----------------------------|----------------------|----------------|------|----------------|----------------|----------------|------|--|------|
| | | k | n | R ² | k ₁ | k ₂ | RMSE | k _{R1} | RMSE |
| Enzyme-free SGF | Native | 0.38 | 0.15 | 0.81 | 5.00 | 0.36 | 0.21 | 0.05 | 0.43 |
| | P/D cluster | 0.41 | 0.15 | 0.77 | 4.35 | 0.33 | 0.26 | 0.04 | 0.41 |
| | P+P/A cluster | 0.40 | 0.15 | 0.78 | 4.35 | 0.30 | 0.24 | 0.04 | 0.47 |
| Enzyme, bile salt-free SIF | Native | 0.22 | 0.23 | 0.91 | 6.31 | 0.20 | 0.57 | 0.02 | 1.31 |
| | P/D cluster | 0.30 | 0.19 | 0.84 | 4.40 | 0.21 | 0.44 | 0.02 | 0.97 |
| | P+P/A cluster | 0.34 | 0.17 | 0.78 | 3.80 | 0.22 | 0.45 | 0.03 | 0.82 |

Table S3: Statistical summary of the two-way ANOVA model for the fraction retention of curcumin association with cell clustering and ECM for each time point during *in vitro* gastric and intestinal digestion. *

| Sources of variance | p-value for curcumin retention fraction in: | | | | | | | | | |
|---------------------|---|-----------|--------------------|-----------|-----------|-----------|-------------------|-----------|-----------|-----------|
| | SGF | | High bile salt SIF | | | | Low bile salt SIF | | | |
| | 1 hour | 2 hours | 0 hour | 1 hour | 2 hours | 3 hours | 0 hour | 1 hour | 2 hours | 3 hours |
| Cell clustering | 1.71 e-02 | 1.88 e-01 | 1.05 e-02 | 2.30 e-02 | 6.41 e-04 | 1.04 e-02 | 5.31 e-03 | 2.95 e-02 | 5.05 e-02 | 4.60 e-01 |
| ECM | 1.21 e-02 | 8.65 e-03 | 5.59 e-10 | 2.90 e-08 | 3.96 e-07 | 2.70 e-07 | 3.34 e-05 | 3.24 e-04 | 3.16 e-07 | 5.77 e-03 |
| Cell clustering*ECM | 1.29 e-01 | 2.04 e-02 | 2.29 e-02 | 3.36 e-02 | 1.64 e-03 | 3.11 e-02 | 1.07 e-02 | 3.15 e-02 | 9.42 e-02 | 5.96 e-01 |

* SGF = simulated gastric fluid, SIF = simulated intestinal fluid. The sources of variance in this model are effects from cell clustering and ECM, as well as their interaction effect. Shaded table cells are significant values ($p < 0.05$).



| | Native | P+P/A cluster | P/D cluster |
|-------------------|---------------------------------------|----------------------|--------------------|
| Percentile | Before digestion | | |
| 10 | 3.32 | 28.54 | 23.04 |
| 50 | 4.64 | 60.14 | 49.40 |
| 90 | 7.13 | 102.2 | 82.37 |
| Percentile | After low bile salt digestion | | |
| 10 | 2.14 | 18.03 | 21.47 |
| 50 | 3.66 | 41.53 | 48.09 |
| 90 | 6.59 | 90.18 | 85.38 |
| Percentile | After high bile salt digestion | | |
| 10 | 19.64 | 17.73 | 17.25 |
| 50 | 43.18 | 40.47 | 46.20 |
| 90 | 77.00 | 71.26 | 88.03 |

Fig. S1: Particle size distribution of native yeast, P/D cluster, and P+P/A cluster before digestion (a), after low bile salt digestion (b), and after high bile salt digestion (c). The 10th, 50th, and 90th percentile particle diameter for each plotted distribution is summarized in the table.

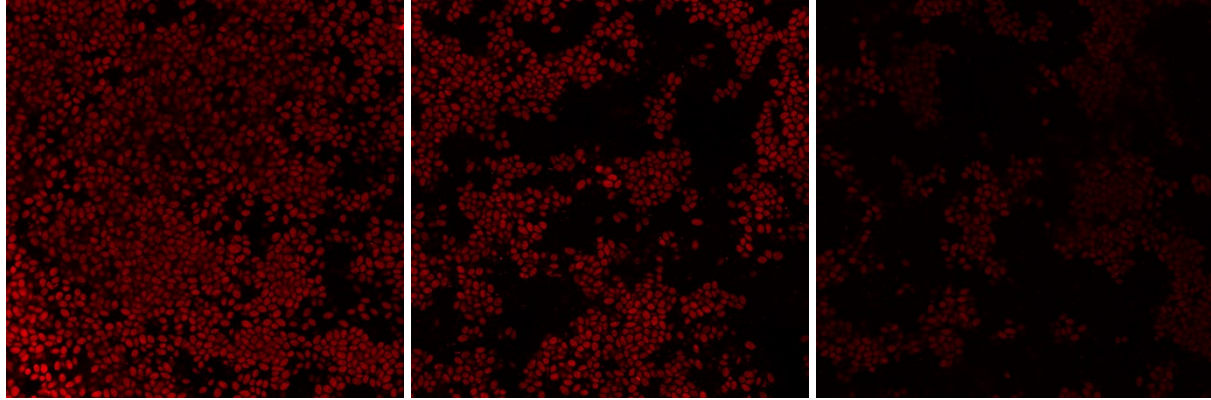


Fig. S2. Individual slice in the z stack confocal microscope images of native cell (left), P/D cluster (middle), and P+P/A cluster (right) in alginate film. Figure 6 showed the 3D projection of the same z stack for each cell microstructure. A pulsed laser tuned to 488 nm was used for excitation and emission signals were detected in the range of 498-591 nm. The images were taken using a 20X objective.

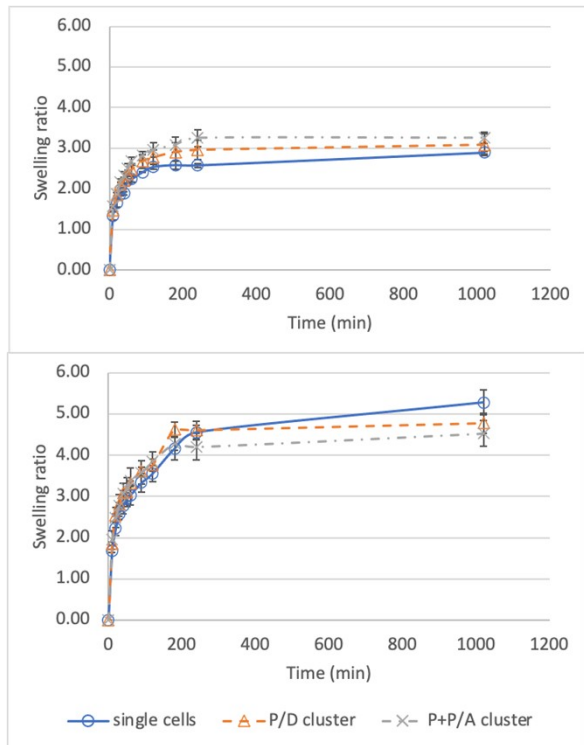


Fig. S3: Swelling kinetics of single cell or cell cluster-laden alginate films in enzyme-free SGF (a) and enzyme-free, bile salt-free SIF (b).