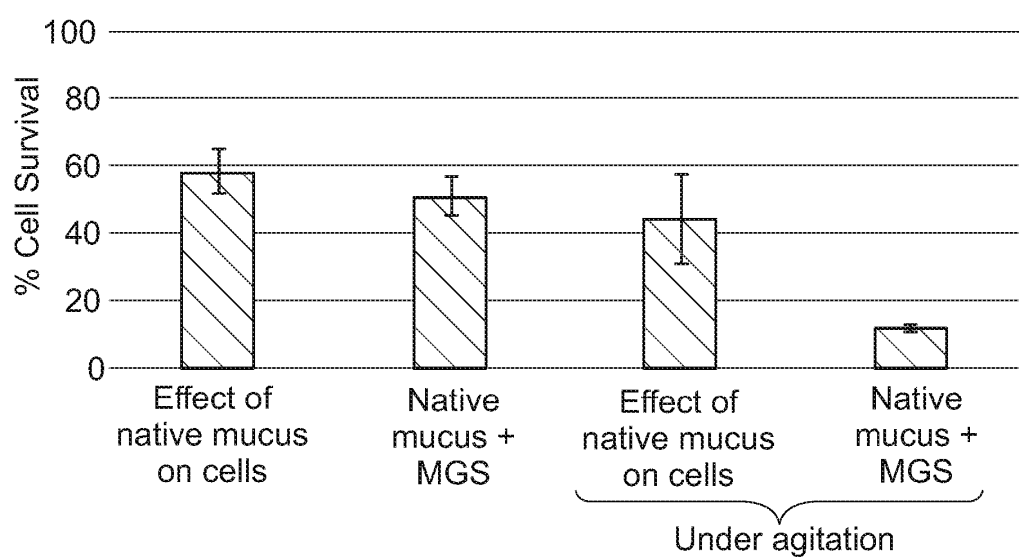


1/21



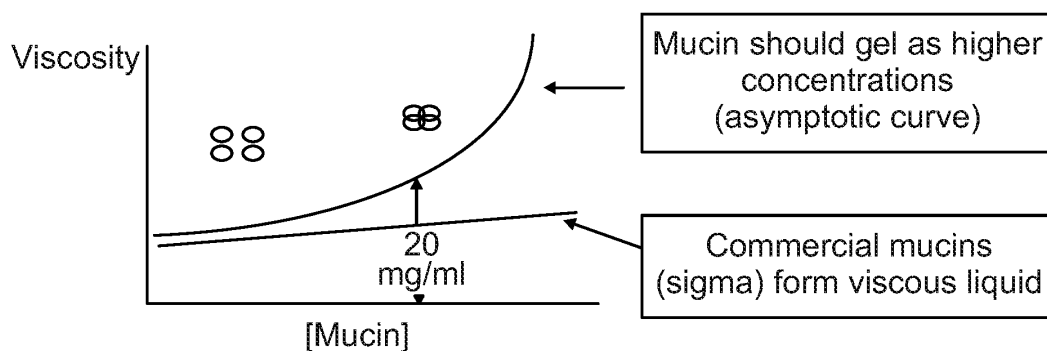
- Native mucus kills cells
 - But confers some protection of the remaining live cells by GI fluids
- Under agitation the ability of native mucus to protect cells is lost

Fig. 1

2/21

Problems modelling mucus

- Human mucus difficult to obtain
- Native mucus kills cells
- Isolation process can alter mucins
 - Process must not include boiling step, or exposure to proteolytic/glycolytic enzymes
- Commercial mucins
 - Ability to form mucin:mucin interactions is lost



In vivo mucin concentration = 30 - 50mg/ml

Fig. 2

3/21

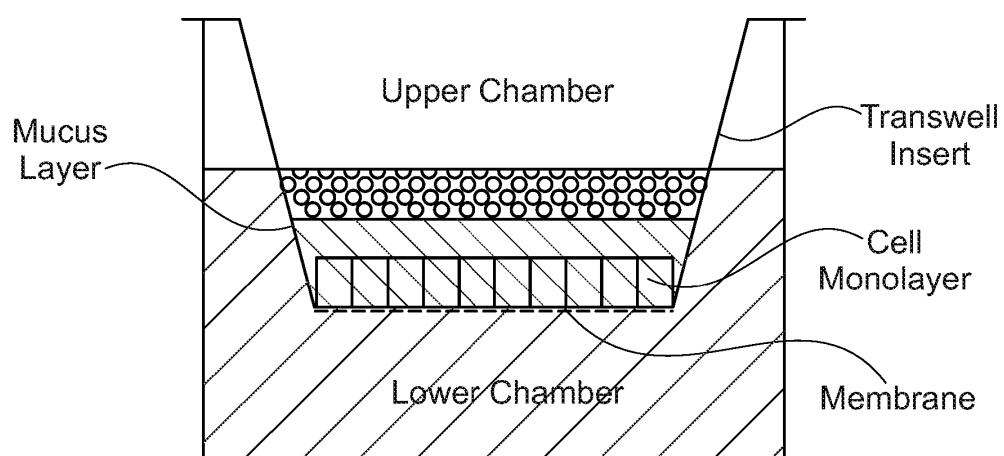


Fig. 3

4/21

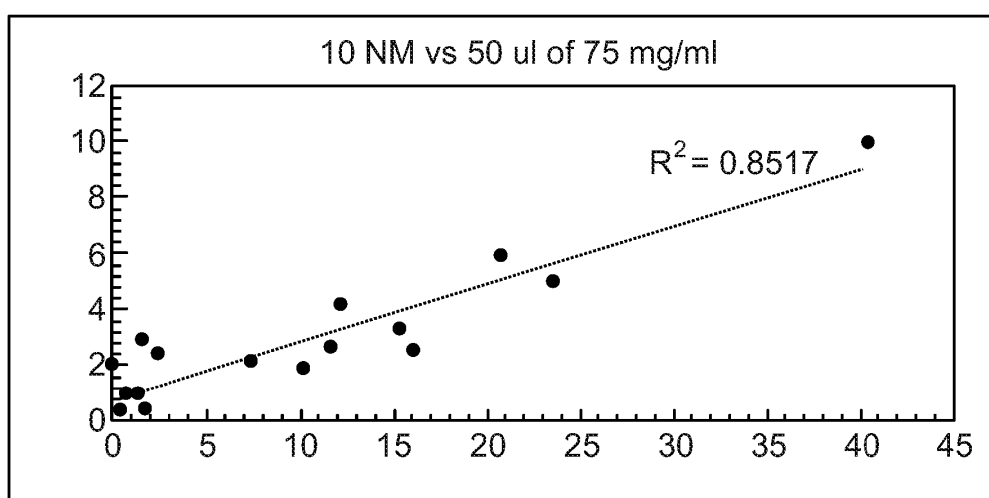


Fig. 4

5/21

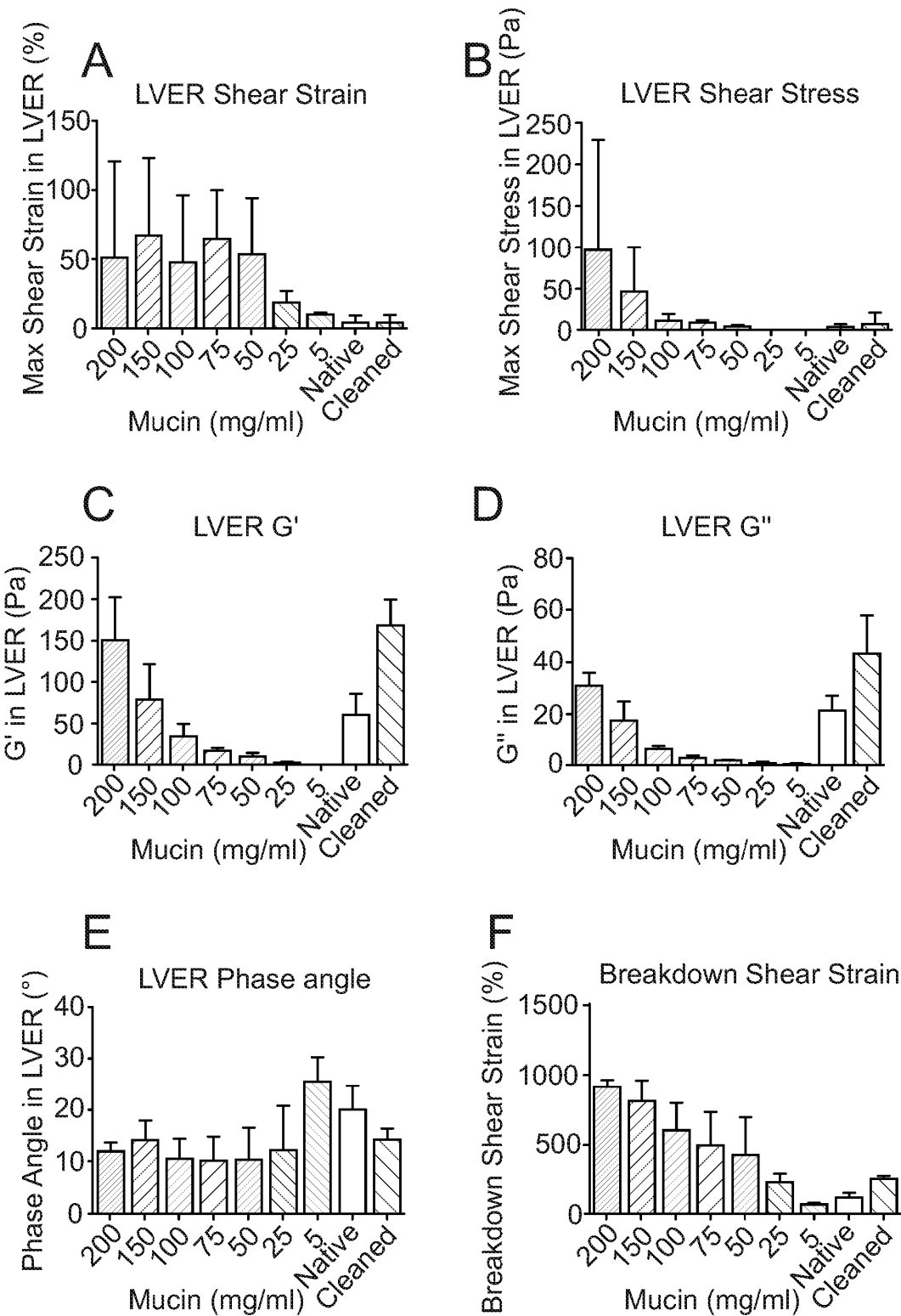


Fig. 5

6/21

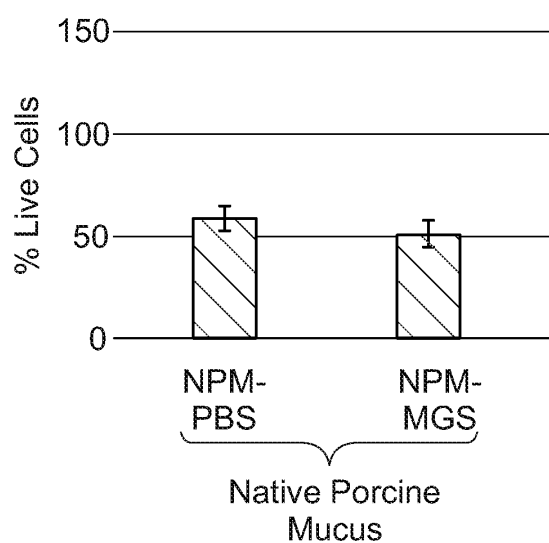


Fig. 6

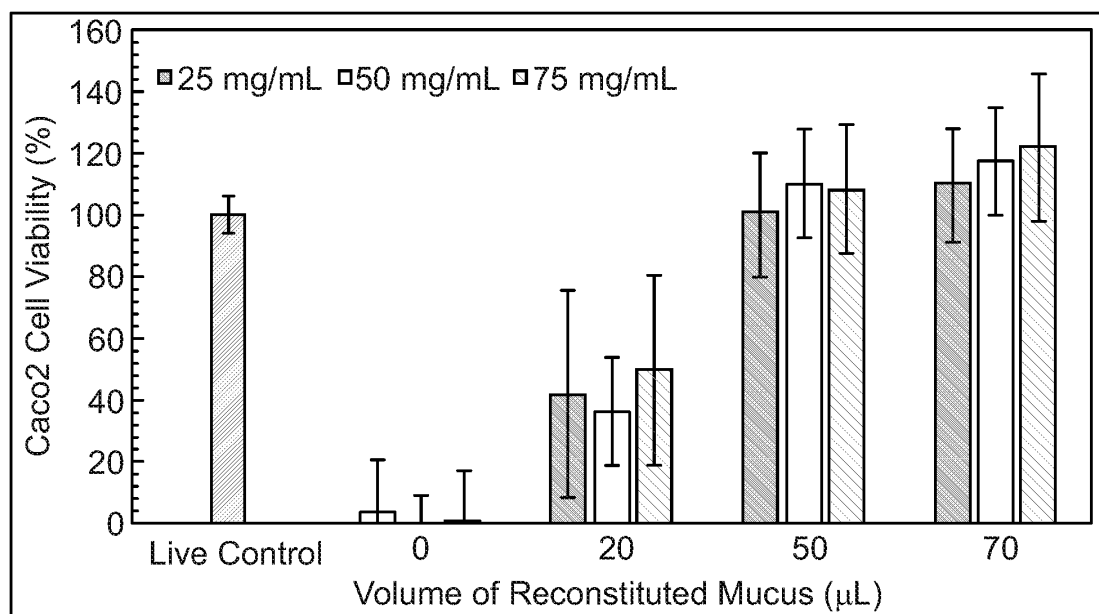


Fig. 7

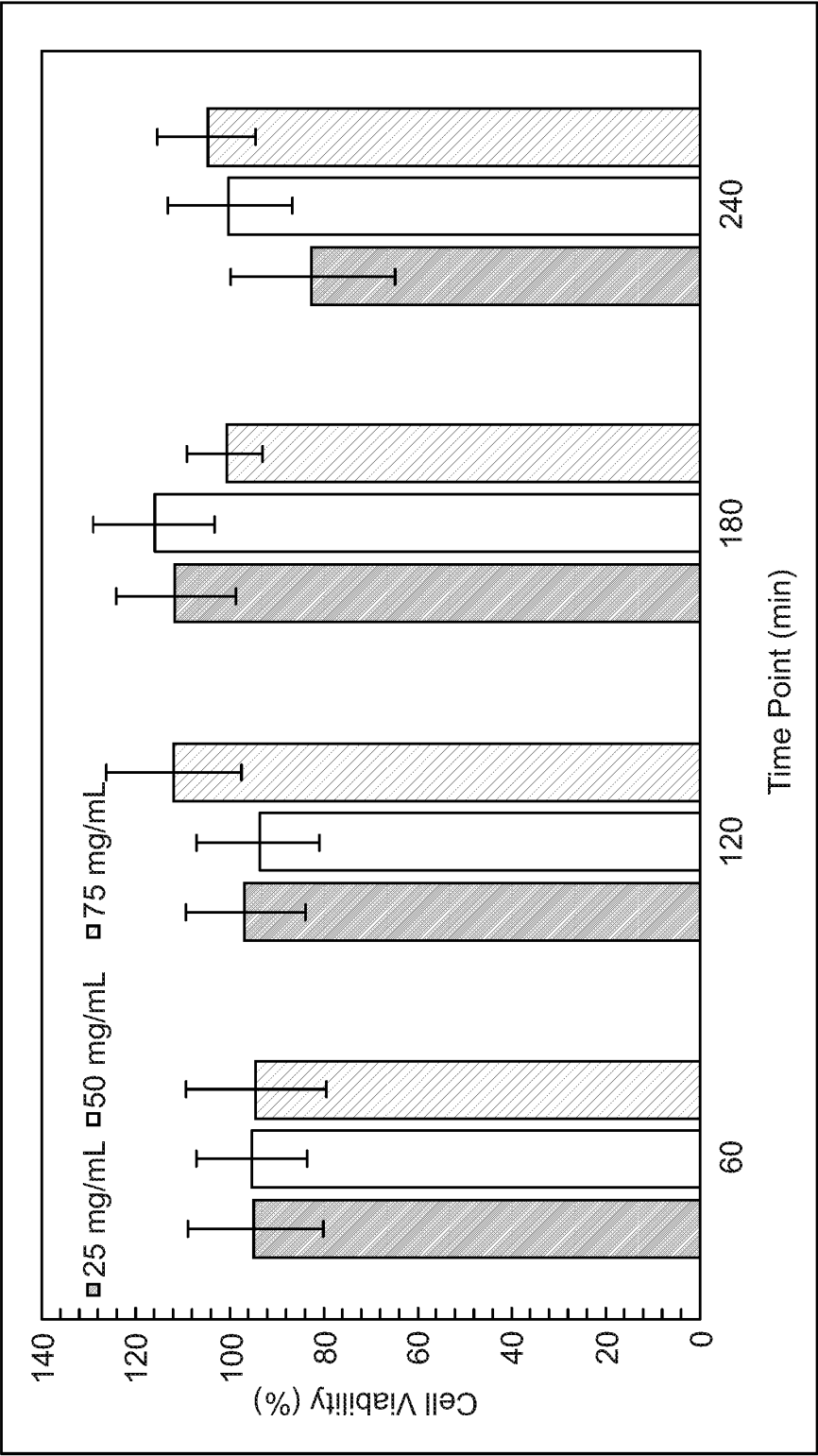


Fig. 8

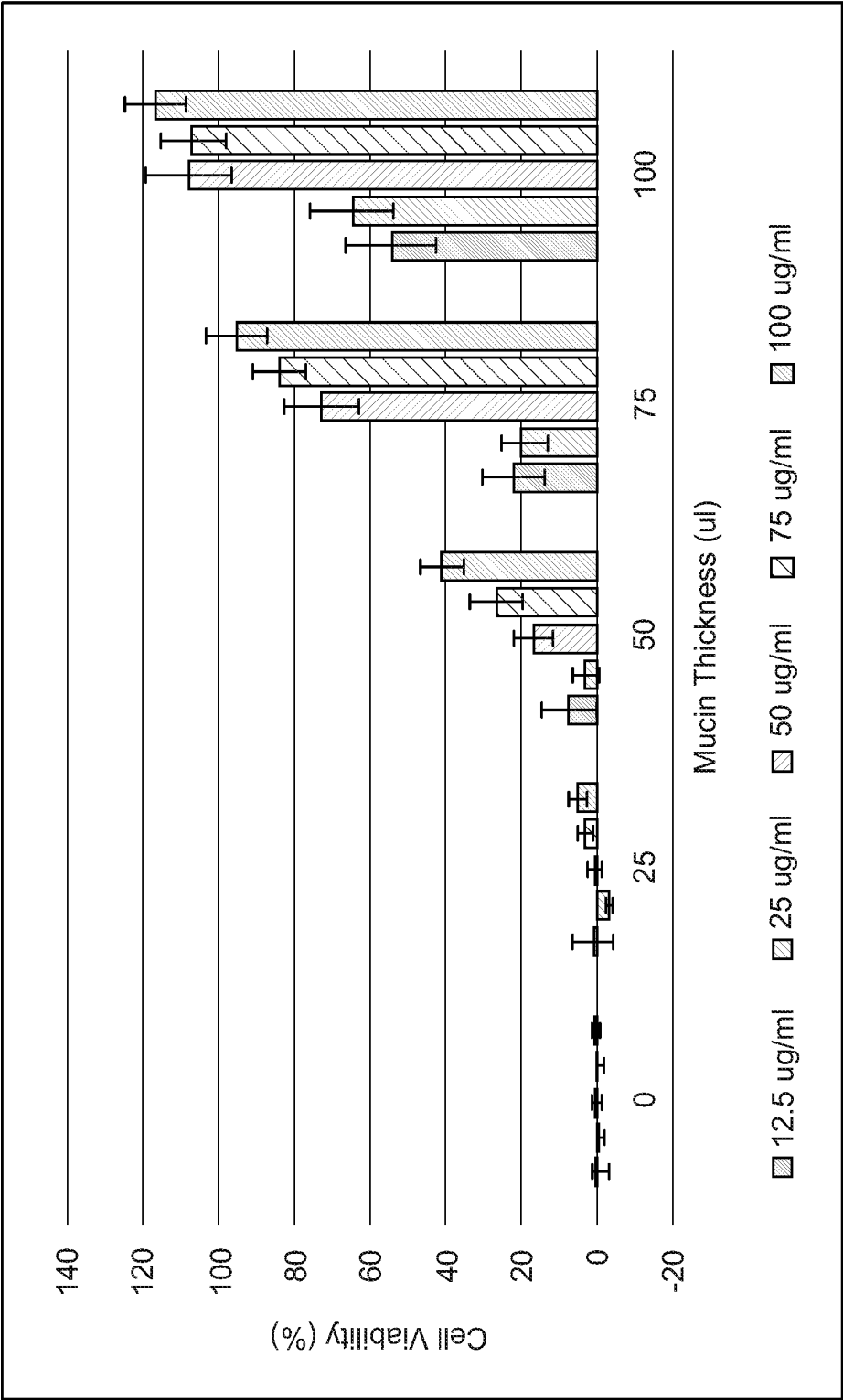


Fig. 9

9/21

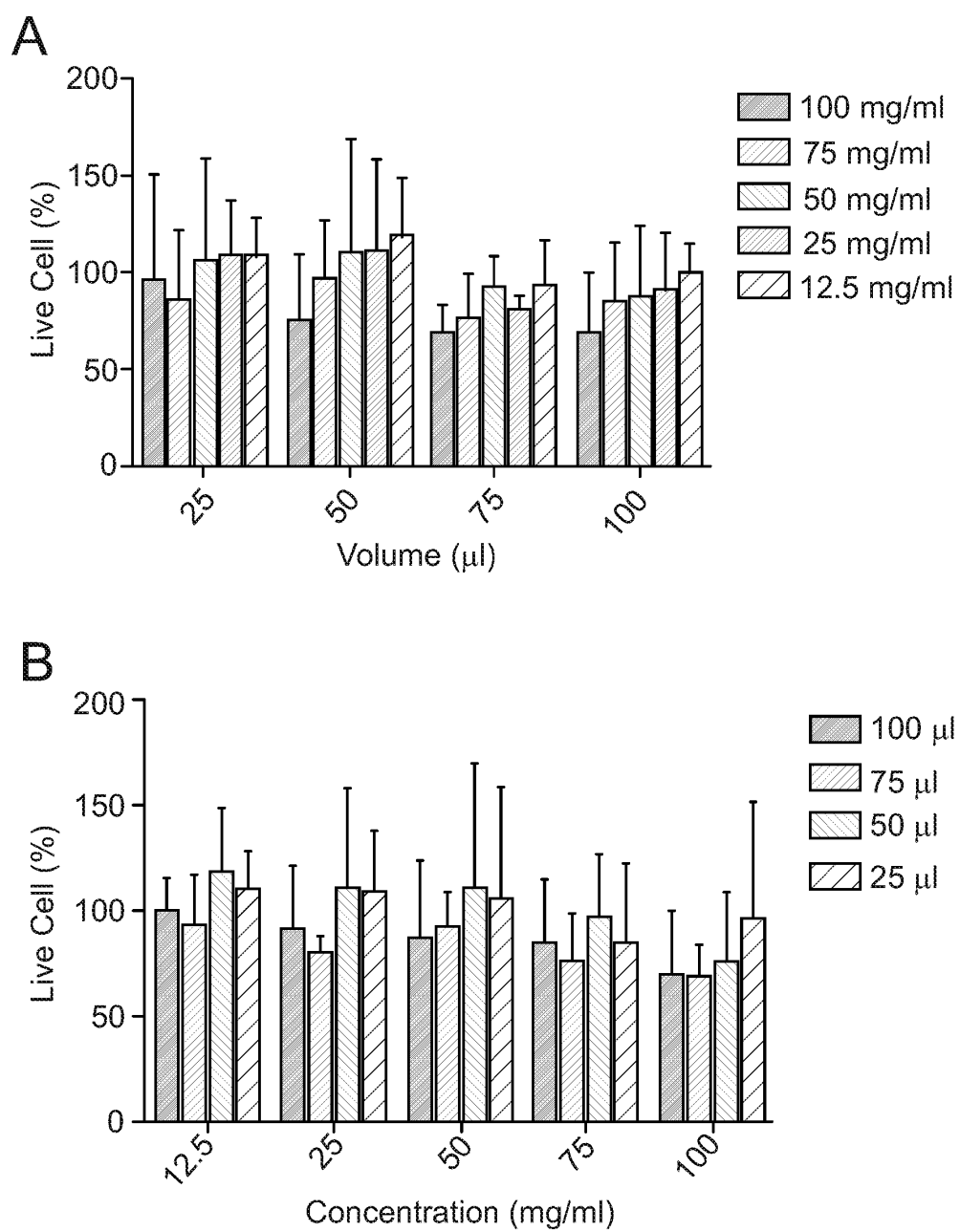
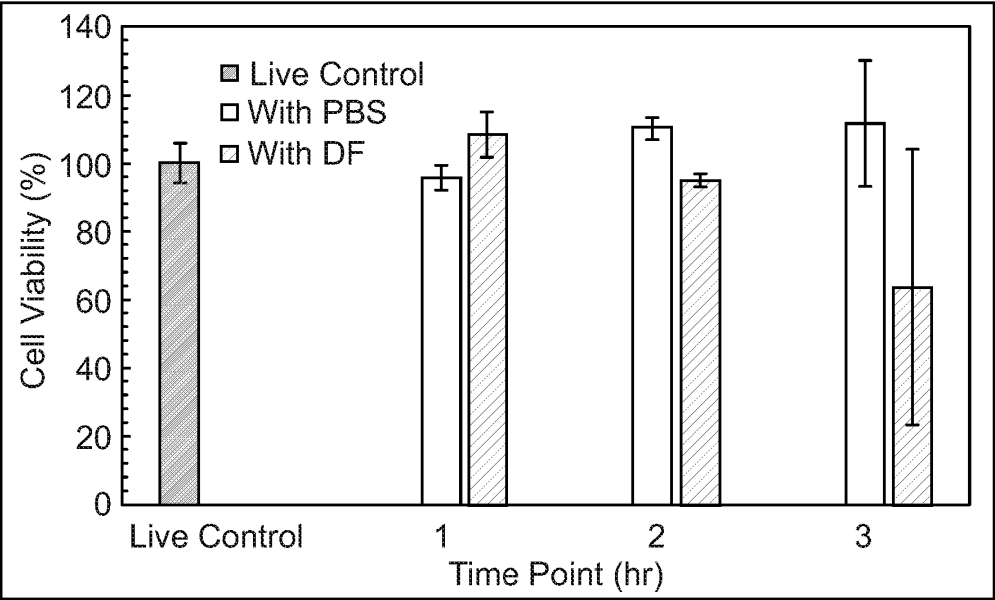


Fig. 10

10/21

Dialysed mucus 50 kda mwco



Dialysed mucus 50 kda mwco and spun 90 min at 9000 rpm

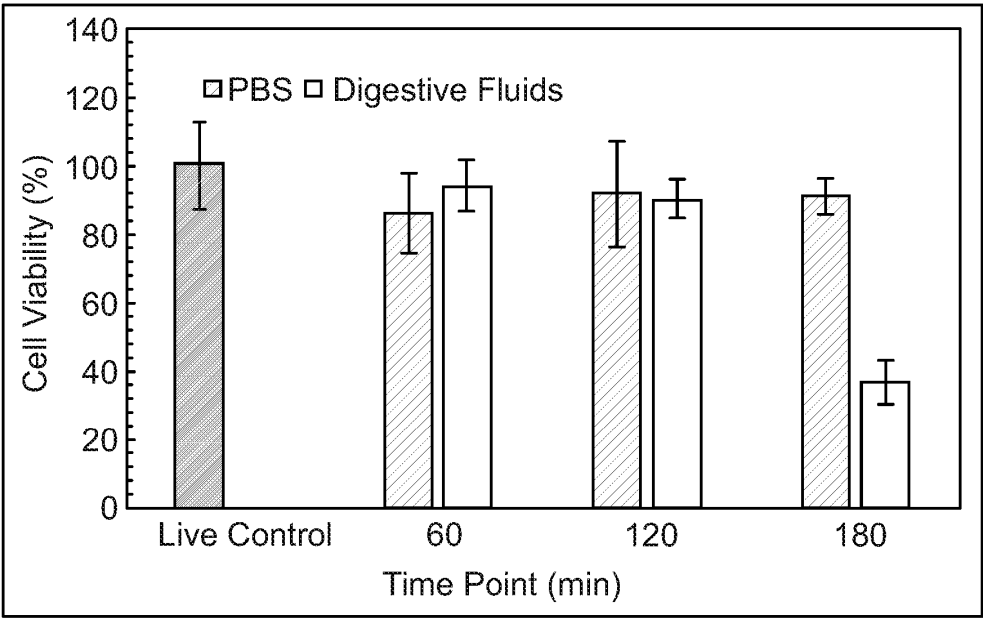


Fig. 11

11/21

These solvent cleans produce a mucin that remains compatible with cell culture:

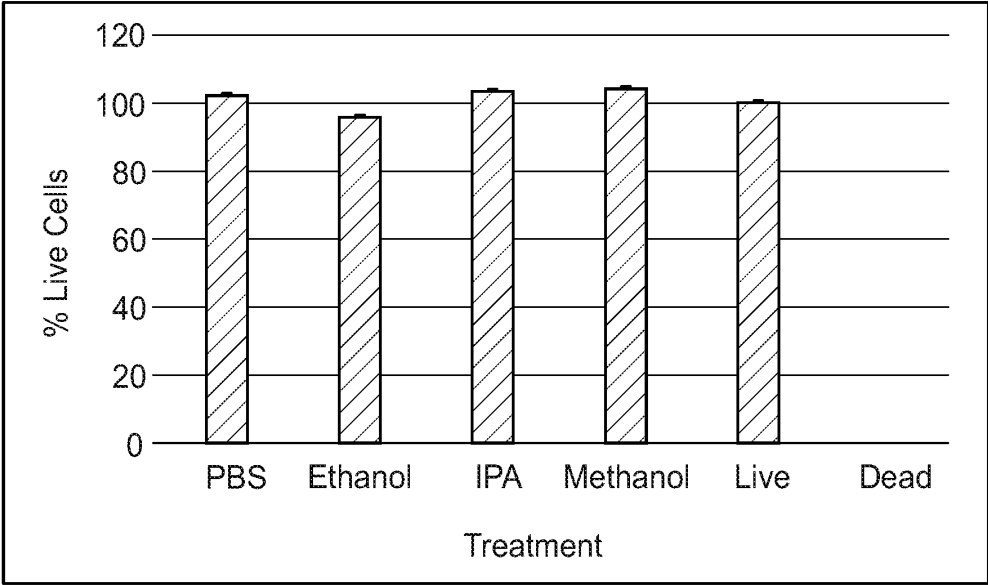


Fig. 12

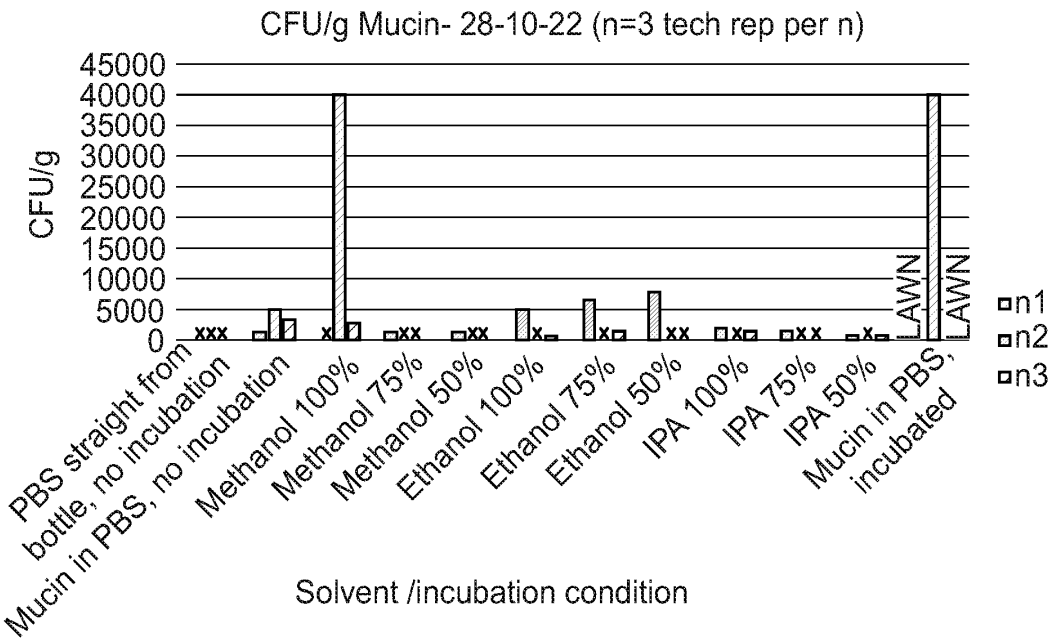
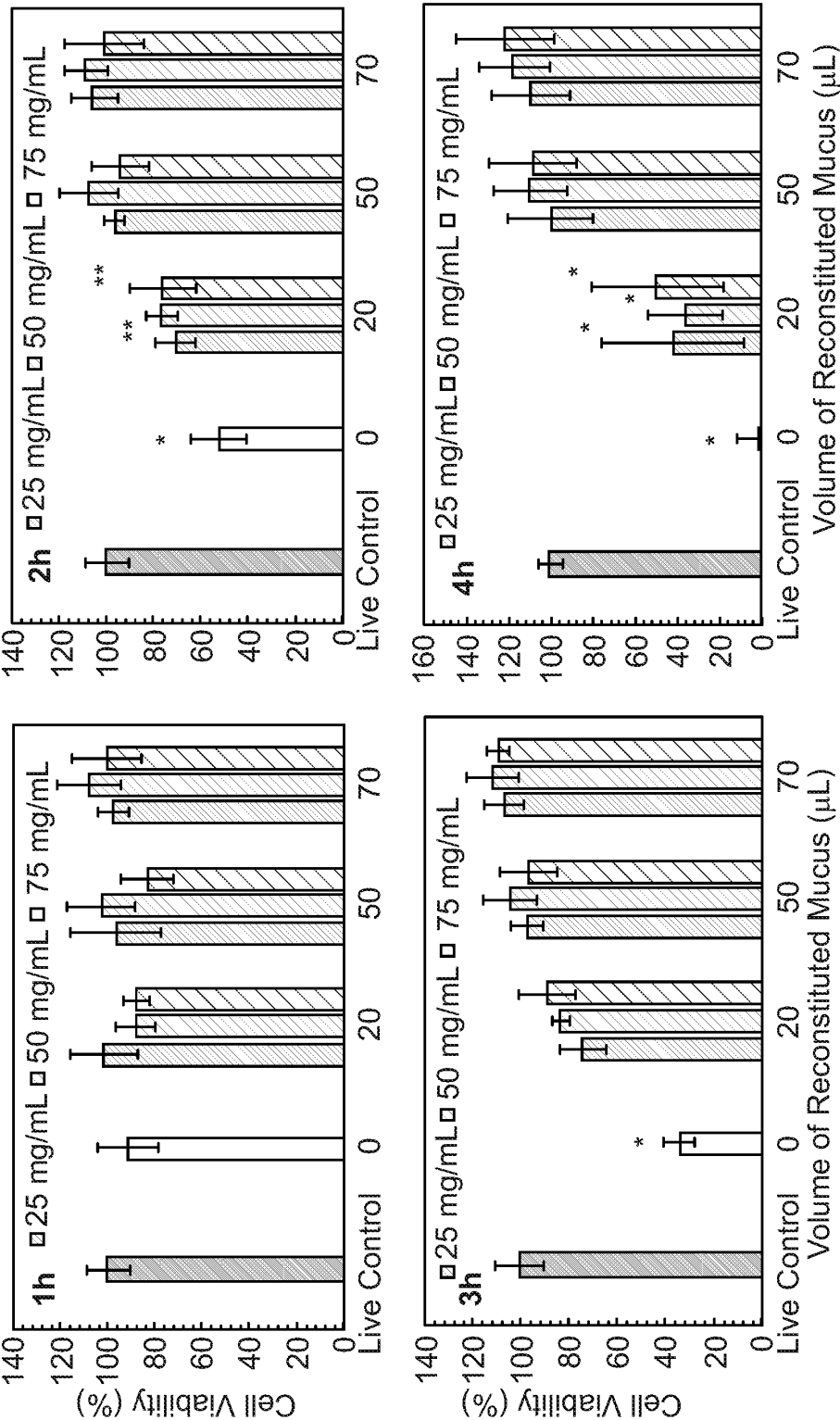


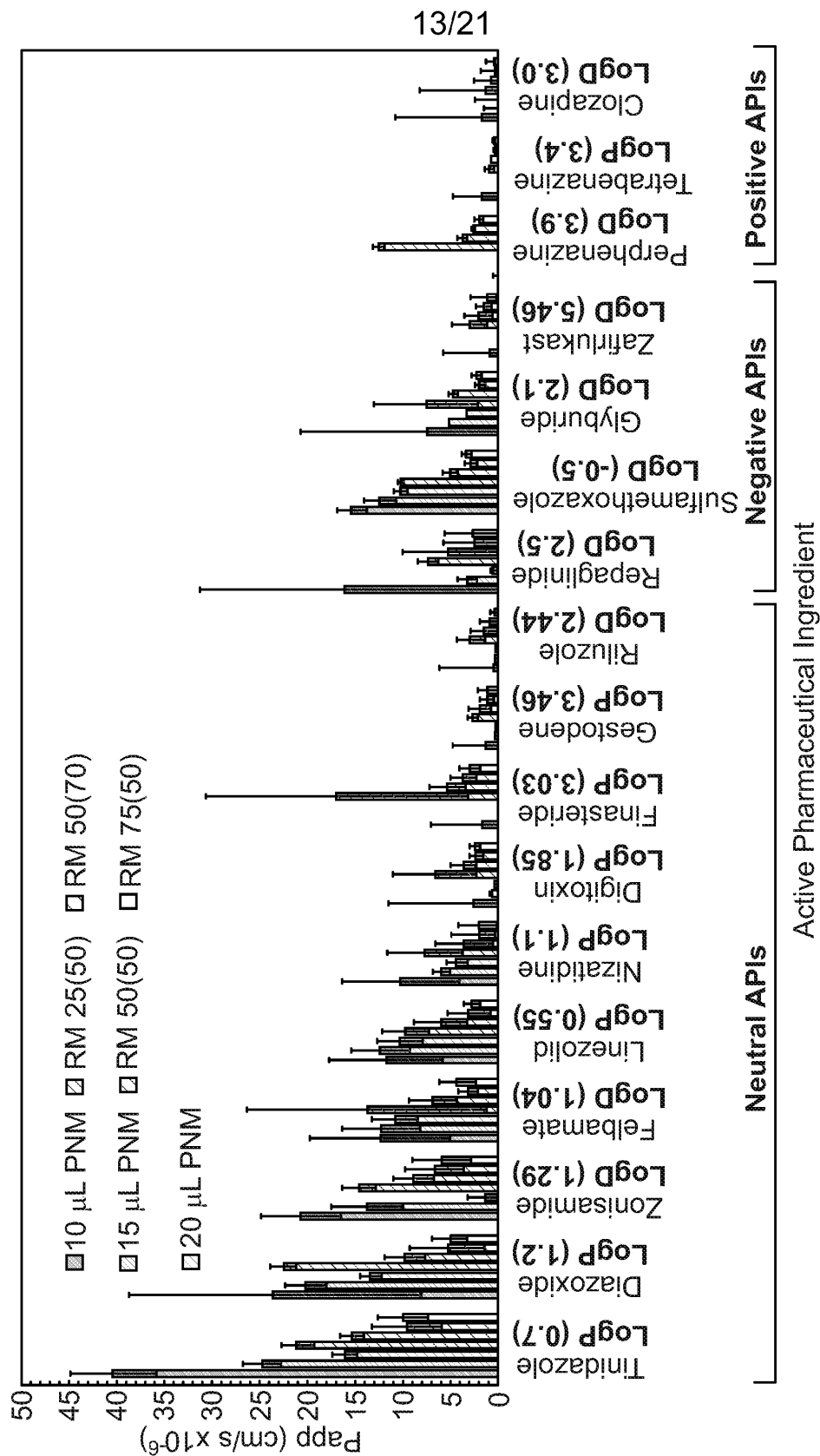
Fig. 13

12/21



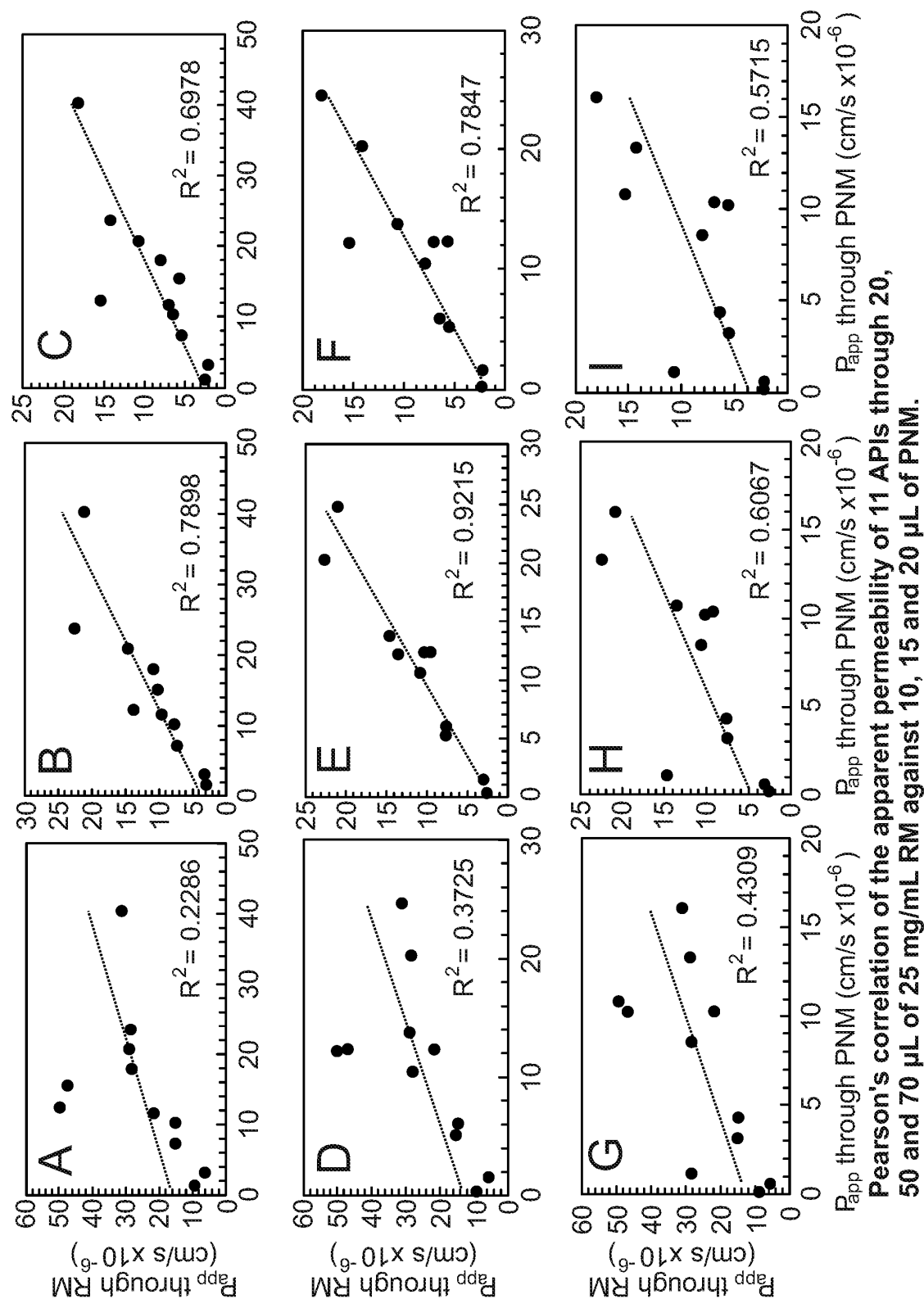
Caco-2 cell viability of cells incubated with a layer of RM at various concentrations and volumes, with EPDF applied to the surface of the mucus layer (n=3).

Fig. 14



Graph depicting all apparent permeability values for all APIs for all mucus concentrations and volumes

Fig. 15



Pearson's correlation of the apparent permeability of 11 APIs through 20, 50 and 70 μ L of 25 mg/mL RM against 10, 15 and 20 μ L of PNM.

Fig. 16

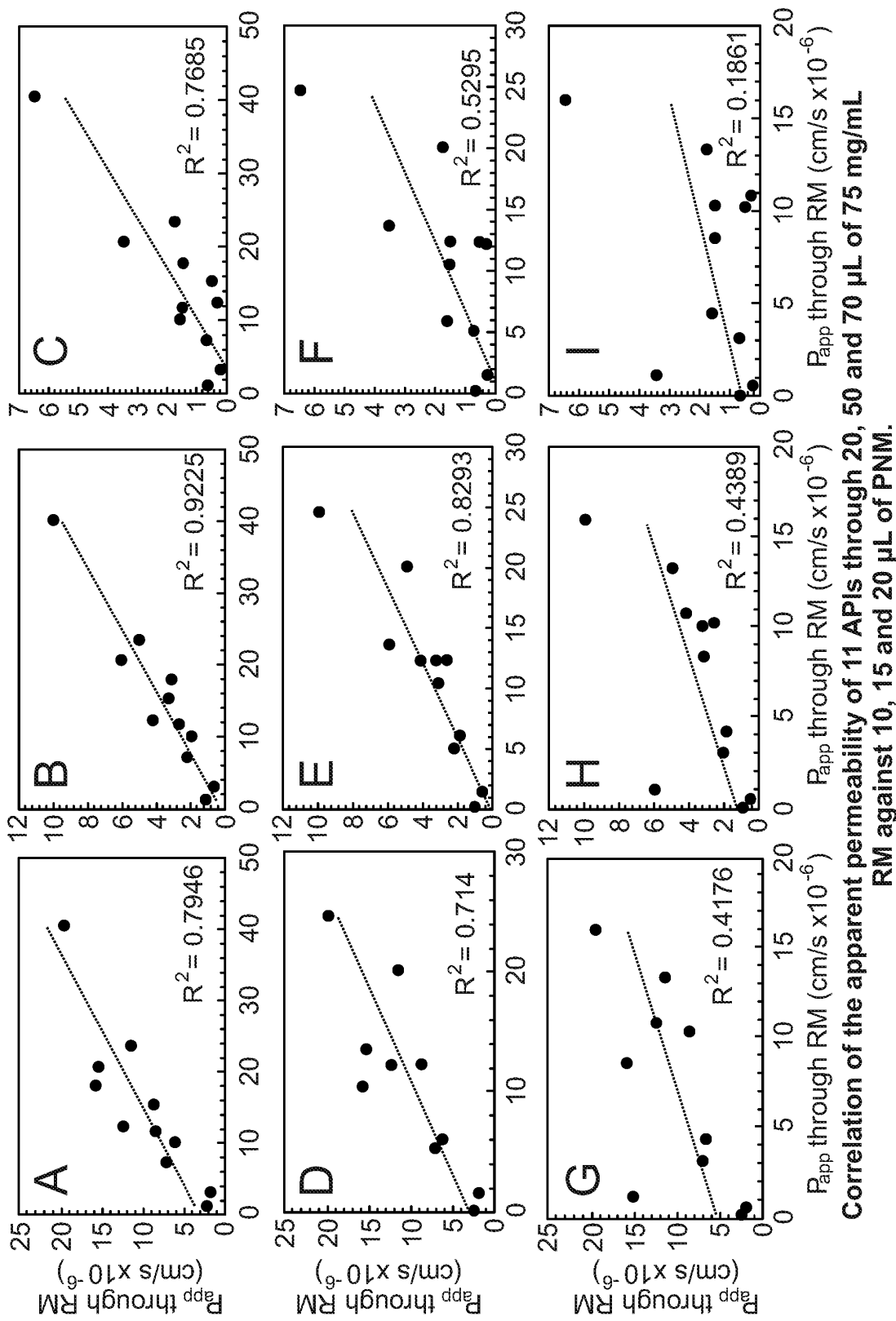
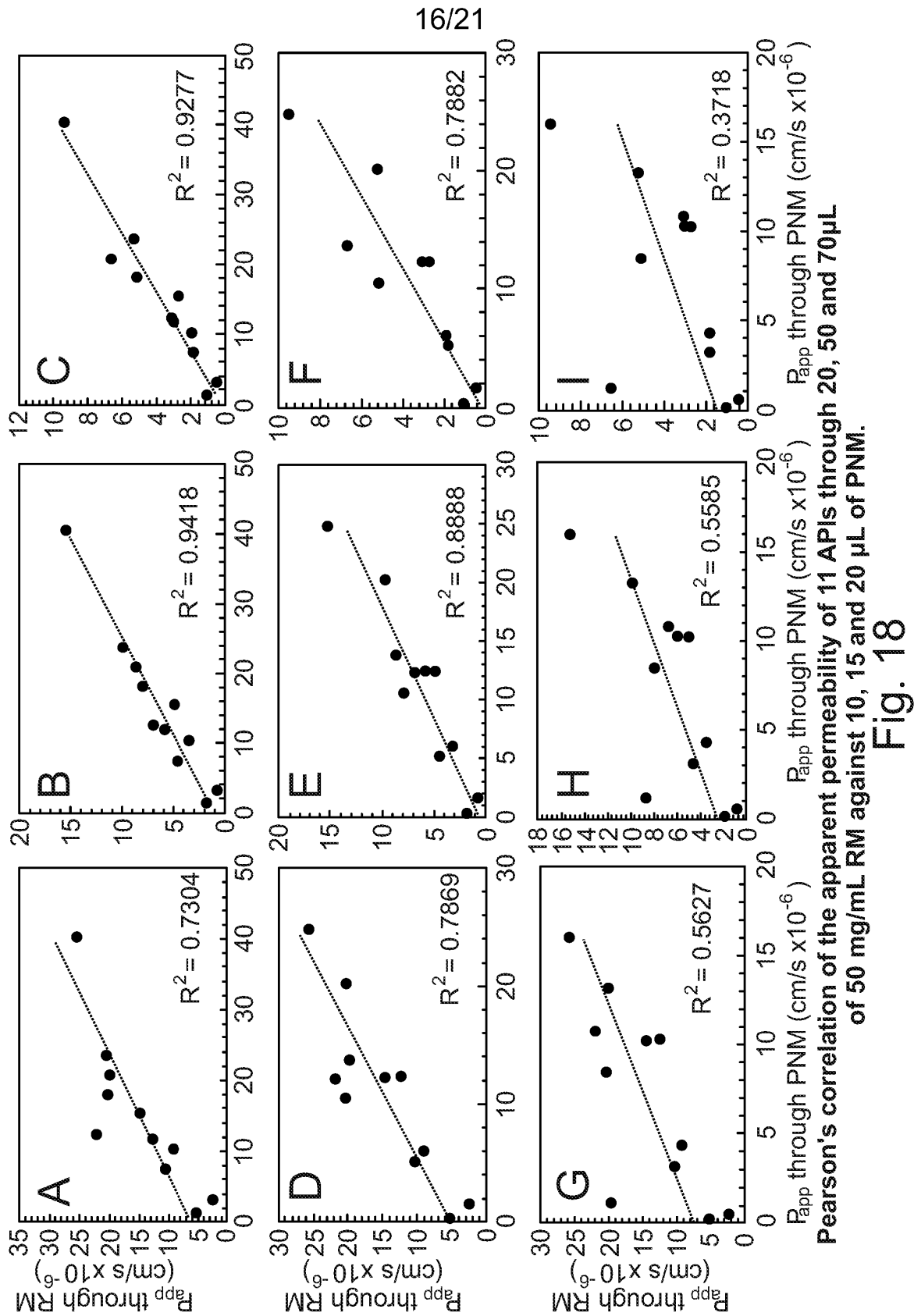


Fig. 17



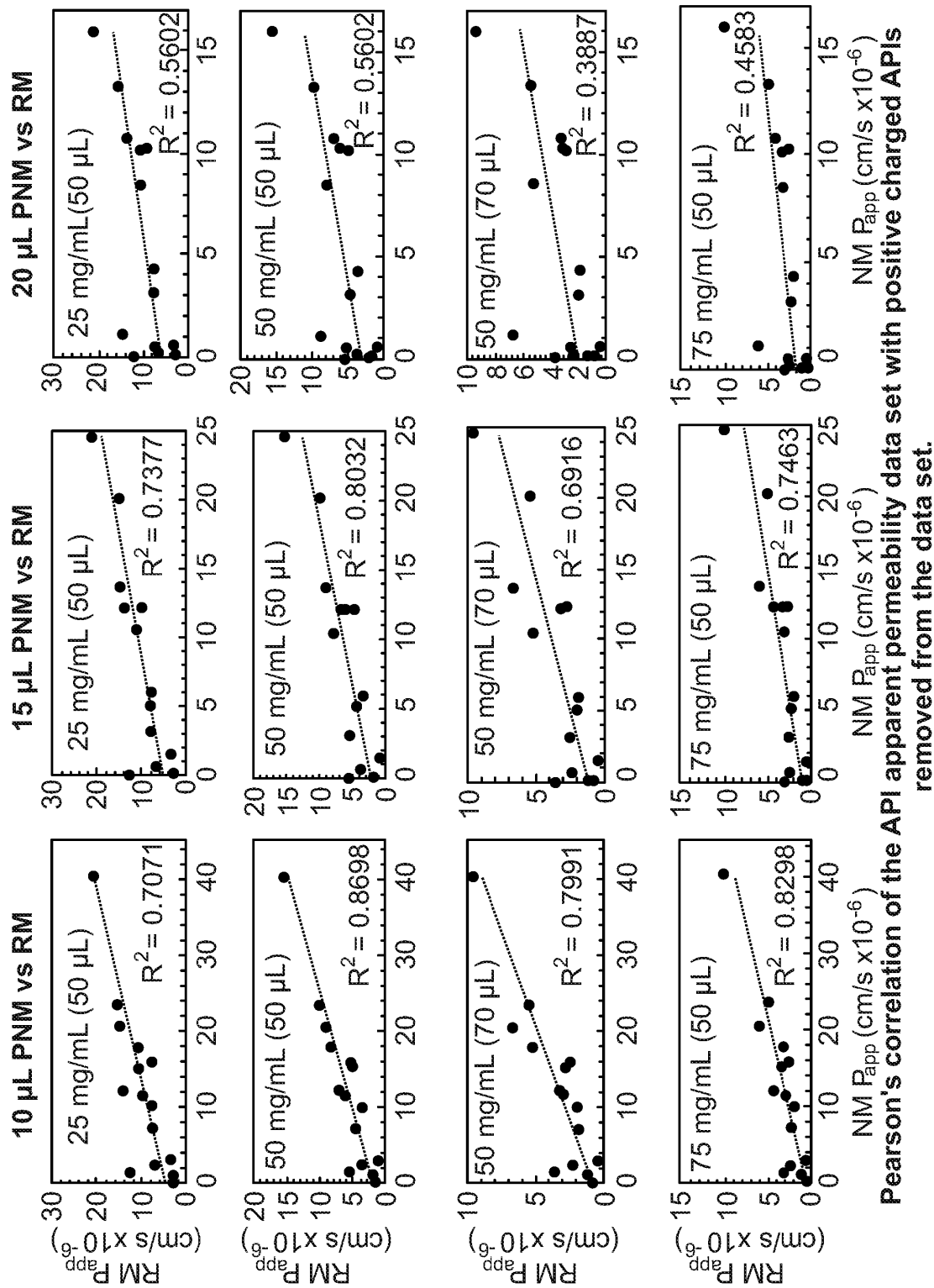
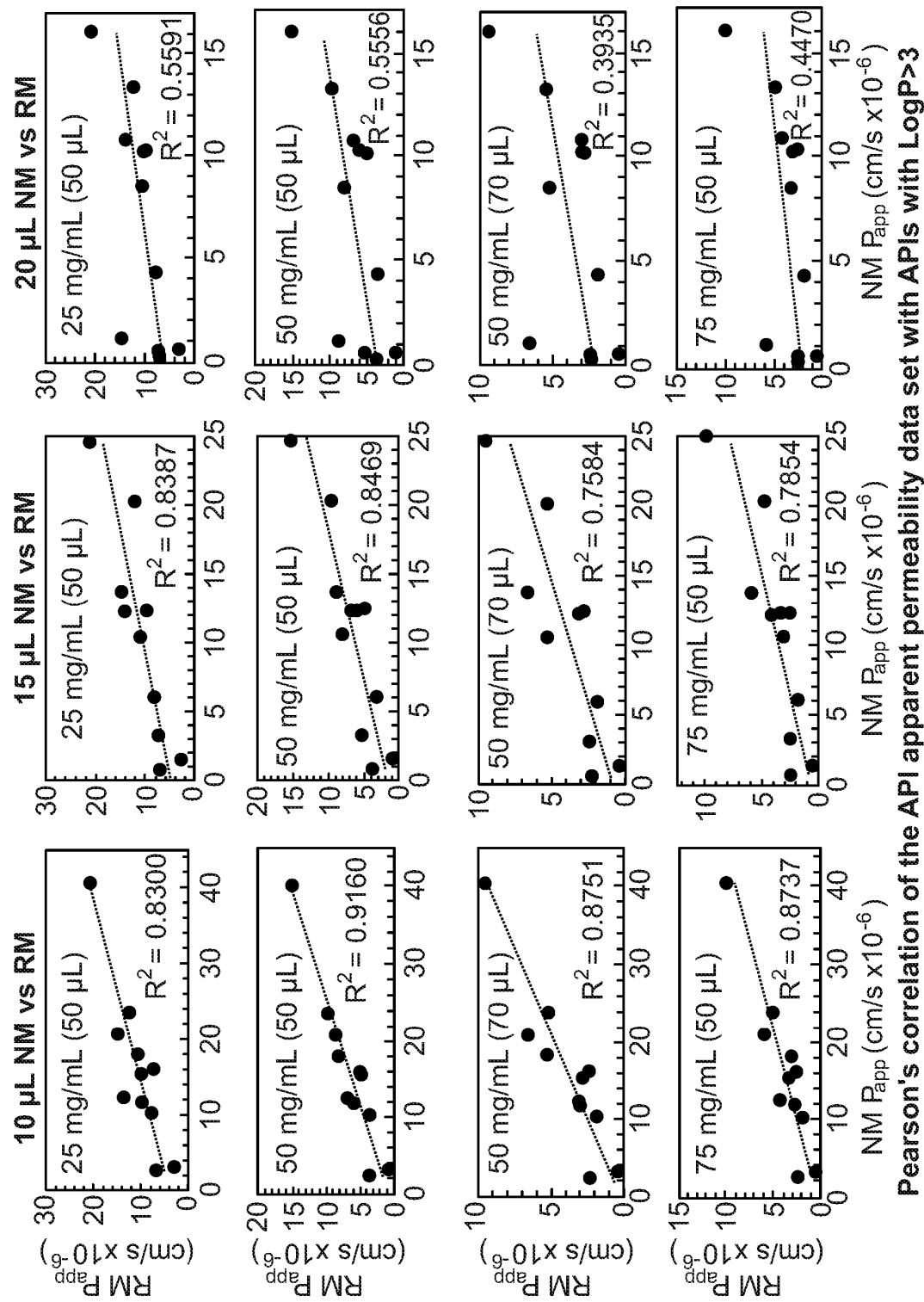


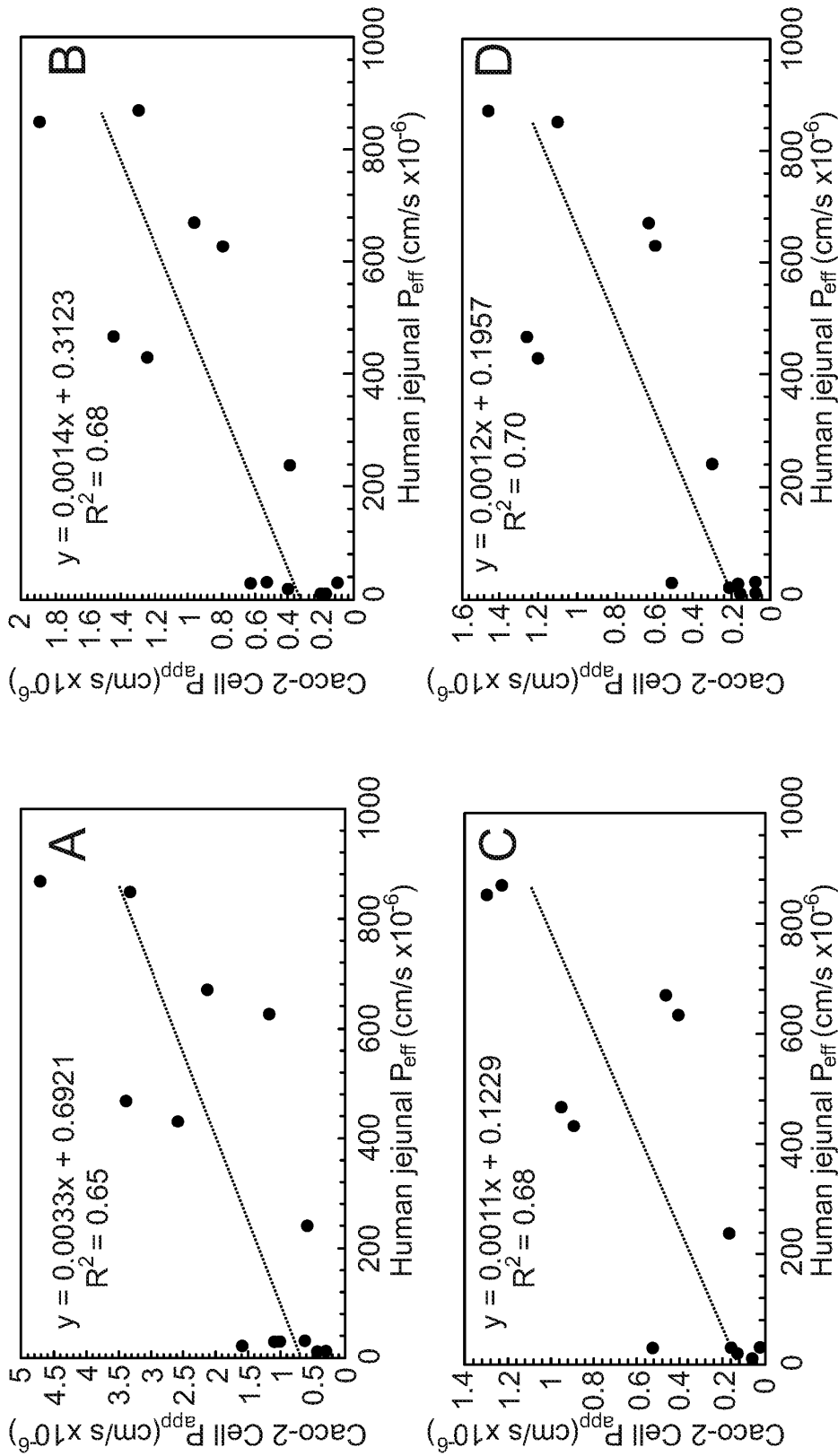
Fig. 19

Pearson's correlation of the API apparent permeability data set with positive charged APIs removed from the data set.



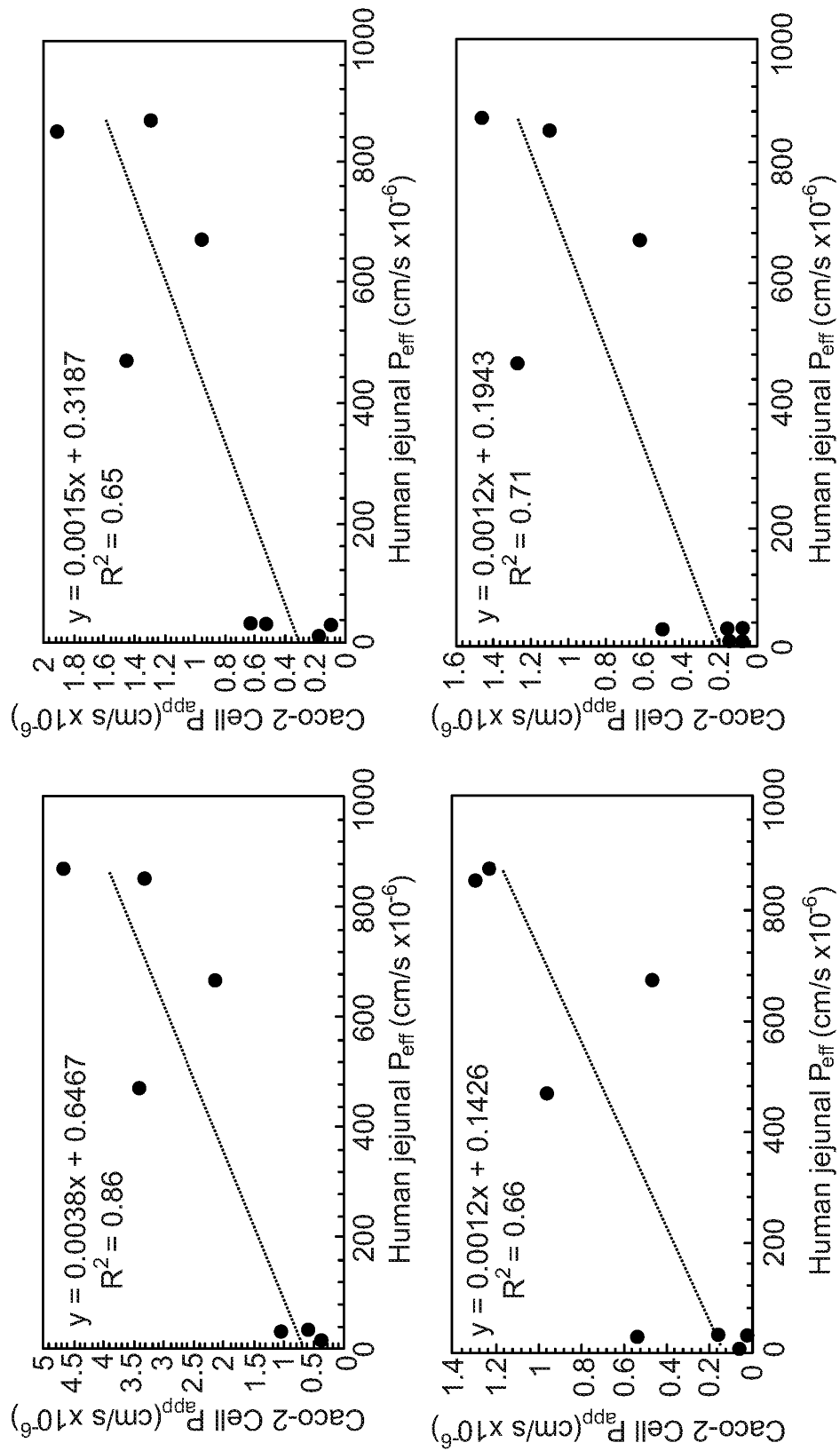
Pearson's correlation of the API apparent permeability data set with APIs with LogP>3 removed from the data set.

Fig. 20



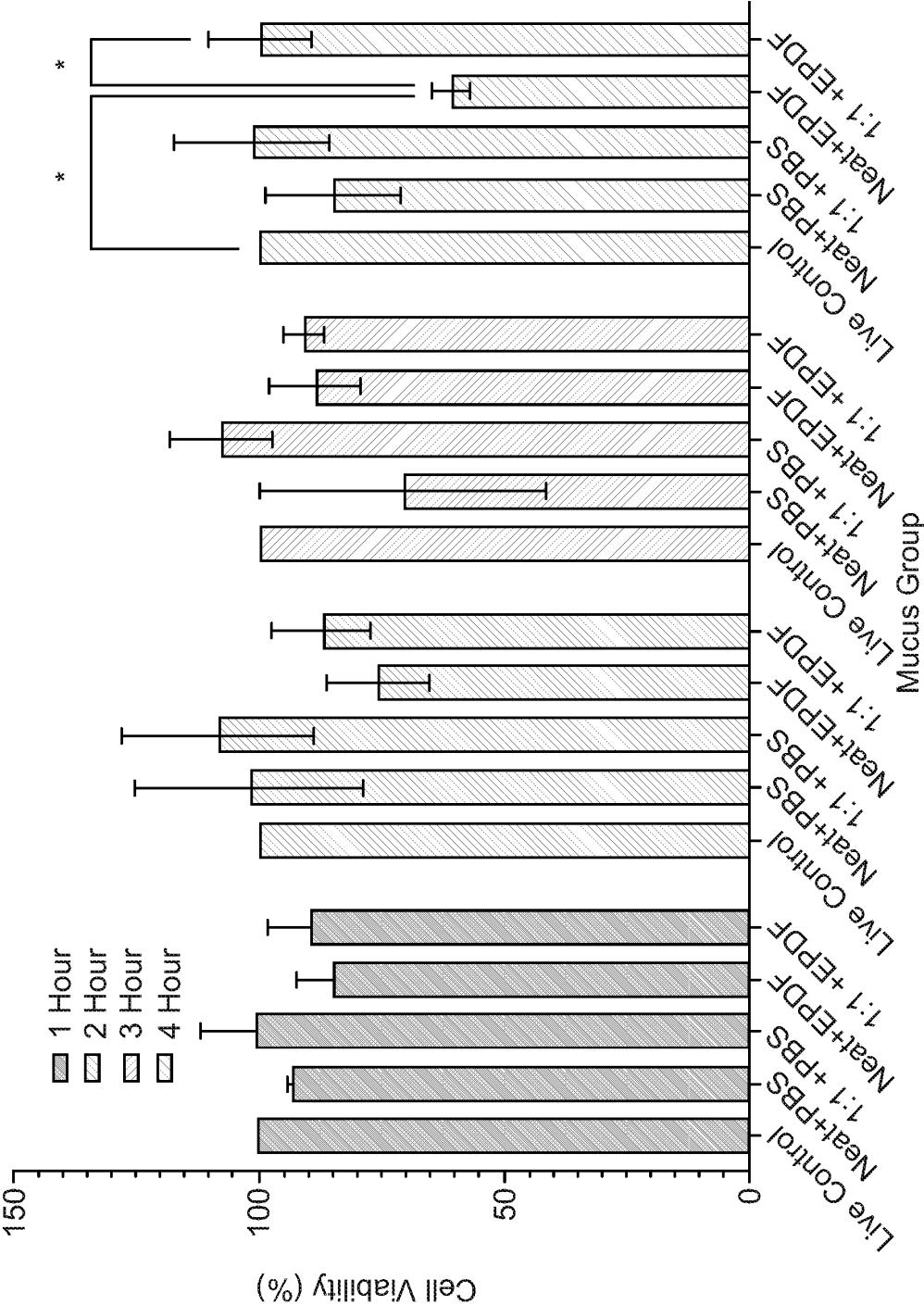
Spearman's Rank correlation analysis of Caco-2 cell P_{app} of 13 APIs permeated through the integrated model, and Human Jejunal P_{eff} .

Fig. 21



Spearman's Rank correlation analysis of Caco-2 cell P_{app} of 8 passively absorbed APIs permeated through the integrated model, and Human Jejunal P_{eff} .

Fig. 22



Caco-2 cell viability of cells incubated with DM (300), either neat or diluted 1:1 prior to dialysis, with PBS or EDPF for 1, 2, 3 or 4 hours.

Fig. 23