

# Organoid Unsupervised Exploration

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Loading packages

```
library(ggplot2)
library(dplyr)
library(tidyr)
library(magrittr)
library(purrr)
library(readr)
library(here)
library(ggrastr)
library(cowplot)
library(princurve)
library(scico)
library(gggridges)

# parameter
print("parameter input:")

## [1] "parameter input:"
```

```
print(params$data)
```

```
## [1] "data/processed/PhenotypeSpectrum/umap_absolute_all_drugs_sampled.Rds"
```

```
print(params$sample)
```

```
## [1] "data/processed/PhenotypeSpectrum/umap_absolute_all_drugs_tidy_Paclitaxel.Rds"
```

loading input data and annotation. Note that on the central cluster, with access to the complete data table, the definition of the input can easily be changed. For remote work, the subsampled dataset “umap\_drugs\_sampled.Rds” is the default choice.

```
# I wish I could solve my path problems with the here() package, but experienced unreliable behavior
# PATH = "/dkfz/groups/shared/0E0049/B110-Isilon2/promise/"
PATH = paste0(here::here(), "/")

#umap_df <- read_rds(paste0(PATH, "data/processed/PhenotypeSpectrum/umap_absolute_all_drugs_tidy.Rds"))
#umap_df <- read_rds(paste0(PATH, "data/processed/PhenotypeSpectrum/umap_absolute_all_drugs_sampled.Rds"))
umap_df <- read_rds(here::here(params$data))
umap_df_sample <- read_rds(here::here(params$sample))
```

```

organoid_morphology <- read_delim(here::here("references/imaging/visual_classification_organoids.csv"),
  dplyr::select(line = organoid, morphology = visual_inspection_v2)

#organoid_viability <- read_rds(here::here("data/processed/ldc_viability.rds"))

```

## Data cube

```
umap_df %>% dplyr::distinct(drug, line) %>% dplyr::count(line)
```

```

## # A tibble: 12 x 2
##   line     n
##   <chr> <int>
## 1 D004T01    528
## 2 D007T01    528
## 3 D010T01    528
## 4 D013T01    528
## 5 D018T01    528
## 6 D019T01    528
## 7 D020T01    528
## 8 D020T02    528
## 9 D022T01    528
## 10 D027T01   528
## 11 D030T01   528
## 12 D046T01   528

```

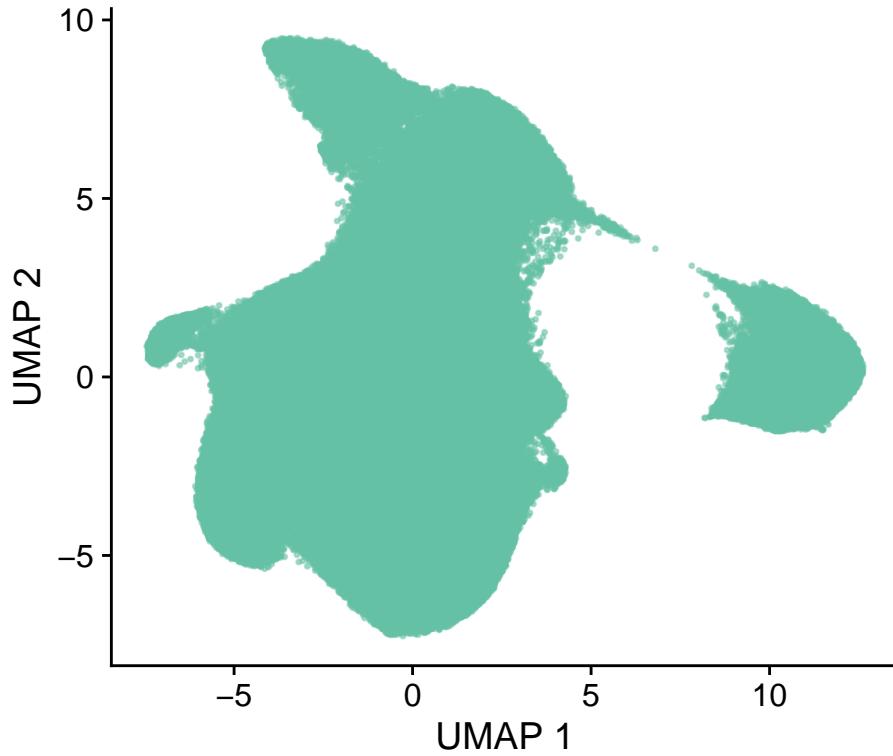
## Partition inspection

We are able to observe 4 partitions in our data. After manual inspection, it becomes cleat that the two smallest partitions are mostly consisting of

```

umap_df %>%
  ggplot(aes(v1, v2, color = factor(partition))) +
  geom_point_rast(alpha = 0.5, size = 0.35) +
  scale_color_brewer(type = "qual", palette = "Set2") +
  theme_cowplot() +
  labs(x = "UMAP 1",
       y = "UMAP 2",
       color = "partition") +
  theme(legend.position = "bottom") +
  coord_fixed()

```



partition • 1

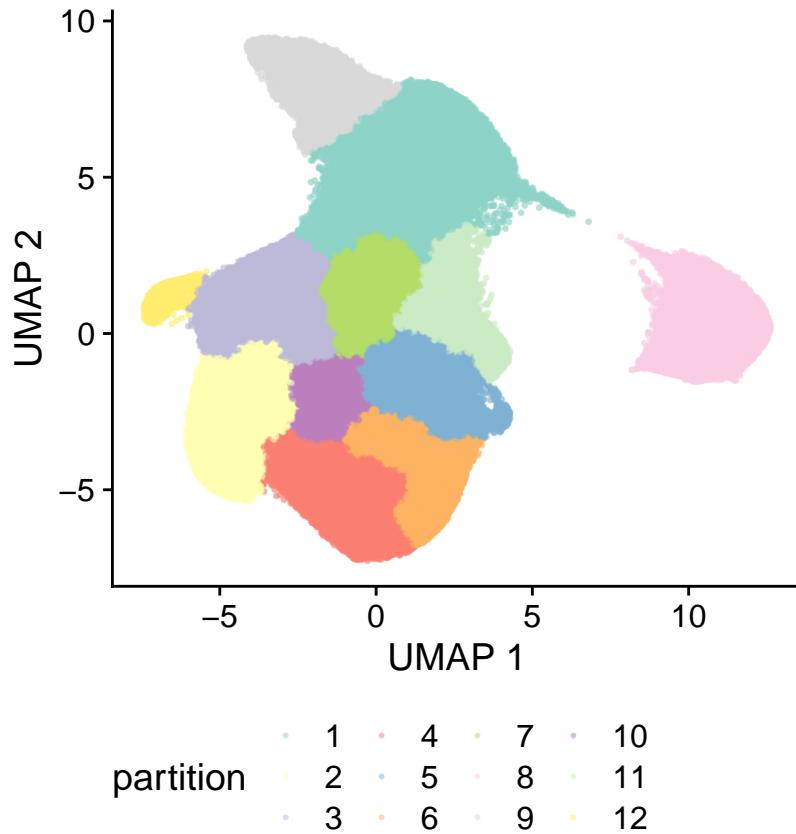
```
umap_df %>%
  dplyr::count(partition) %>%
  mutate(ratio = n/sum(n)) %>%
  arrange(desc(ratio))
```

```
## # A tibble: 1 x 3
##   partition      n ratio
##   <fct>     <int> <dbl>
## 1 1          271308     1
```

I remove 2 partitions from all main figures for ease of reading. Below, it is easy to toggle the removal of partitions on and off to make sure this filtering step is robust

```
gg_cluster <- umap_df %>%
  filter(partition %in% c(1,2)) %>%
  ggplot(aes(v1, v2, color = factor(cluster))) +
  ggrastr::geom_point_rast(alpha = 0.5, size = 0.35) +
  scale_color_manual(values = c(RColorBrewer::brewer.pal(12, "Set3"), "#fb9a99")) +
  cowplot::theme_cowplot() +
  labs(x = "UMAP 1",
       y = "UMAP 2",
       color = "partition") +
  theme(legend.position = "bottom") +
  coord_fixed()

gg_cluster + ggsave(here("reports/figures/imaging/gg_cluster.pdf"), width = 4, height = 4)
```



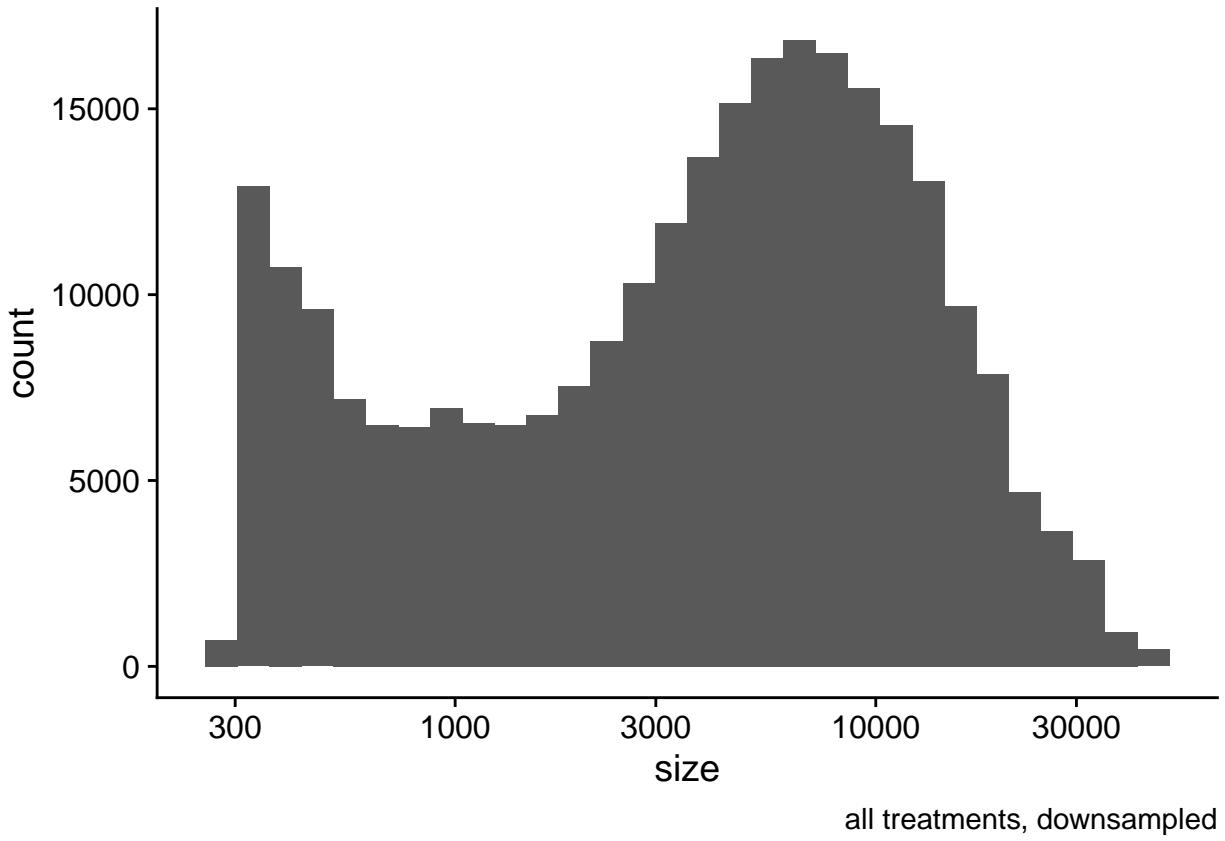
## Organoid Size Distributions

I plot a size-distribution.

```
gg_size_dist <- umap_df %>%
  filter(partition %in% c(1,2)) %>%
  ggplot(aes(size)) +
  geom_histogram() +
  theme_cowplot() +
  labs(caption = "all treatments, downsampled")

gg_size_dist_log <- gg_size_dist +
  scale_x_log10()

gg_size_dist_log + ggsave(here("reports/figures/imaging/gg_size_dist.pdf"), width = 4, height = 4)
```

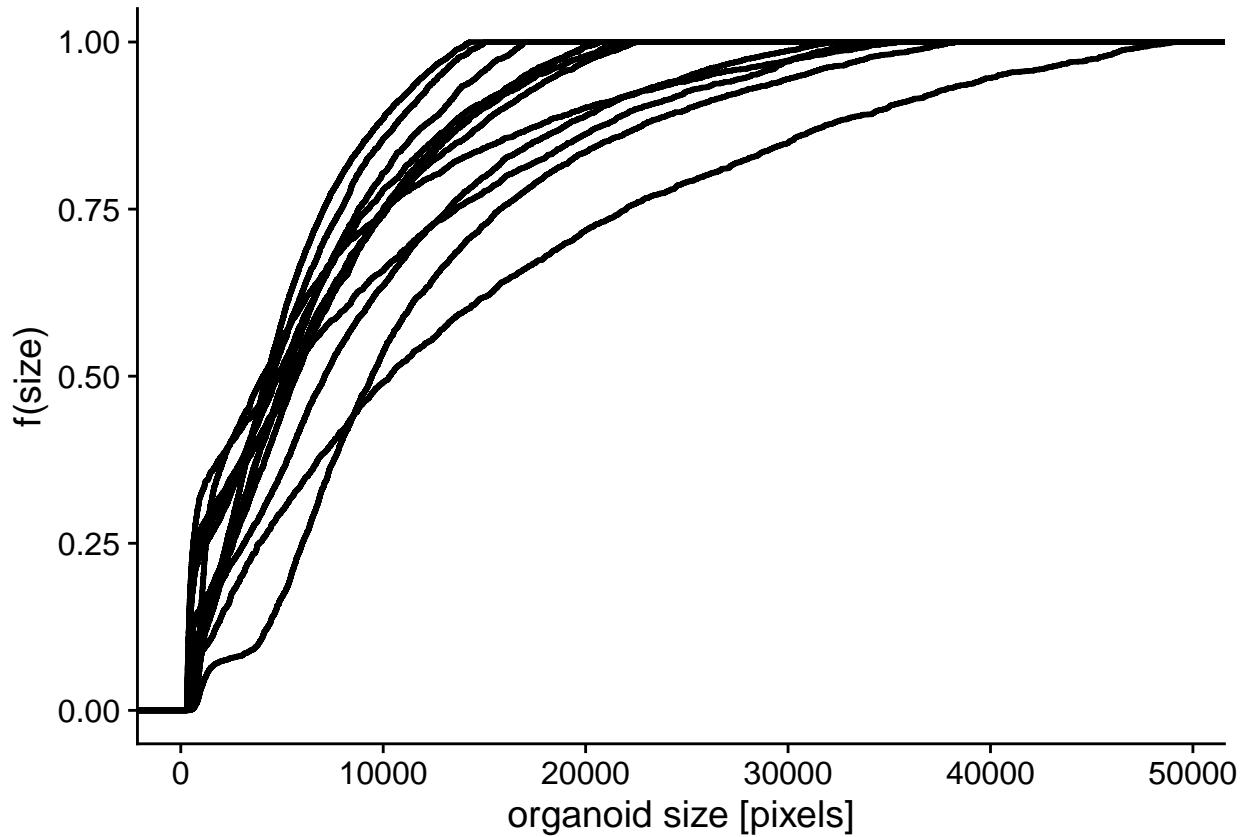


I add the eCDF.

```
df <- umap_df %>% filter(partition %in% c(1,2))

gg_ecdf <- ggplot(df %>% filter(drug == "DMSO")) +
  stat_ecdf(aes(x = size, group = line),
            geom = "step", size = 1) +
  #scale_color_manual(values = c("#00AFBB", "#E7B800")) +
  labs(y = "f(size)",
       x = "organoid size [pixels]") +
  theme_cowplot()

gg_ecdf
```



```
# variance_explained %>% ggplot(aes(PC, var_explained)) + geom_point() + geom_vline(xintercept = 25) + ...

# element wise multiplication
mat = components %>% dplyr::select(-X1) %>% as.matrix() %>% .[,1:25] %>% matrix(ncol = 25)
vector = sqrt(variance_explained$eigenvalue) %>% .[1:25]
df = mat * vector

index = df %>% abs() %>% rowSums() %>% tibble(max = ., index = 1:length(.)) %>% arrange(desc(max)) %>% ...

pheatmap::pheatmap(mat = annotated_PC %>% dplyr::select(name, PC1:PC25) %>% .[index,] %>% remove_rownames
                  annotation_row = annotated_PC %>% dplyr::select(name, class, channel) %>% .[index,]
                  cluster_cols = FALSE)
```

For more details about distributions, please refer to \*reports/Phenotypespectrum/'xyz'\_dist.pdf\*.

```
line_param <- umap_df %>% filter(partition %in% c(1,2)) %>%
  #filter(drug == "DMSO") %>%
  nest(-line, -replicate) %>%
  mutate(fit = map(data, ~ fitdistrplus::fitdist(.x$size, "lnorm")),
         param = map(fit, ~ .x$estimate %>% broom::tidy()))

df <- line_param %>% unnest(param) %>%
  filter(names == "meanlog") %>%
  group_by(line) %>%
```

```

mutate(mean_meanlog = mean(x)) %>%
arrange(mean_meanlog) %>%
ungroup() %>%
mutate(line = factor(line, levels = .\$line %>% unique()))

organoid_size_fit <- df %>% dplyr::select(line, replicate, names, x, mean_meanlog)
organoid_size_fit %>% saveRDS(here::here("data/processed/morphology/organoid_size.Rds"))
organoid_size_fit <- readRDS(here::here("data/processed/morphology/organoid_size.Rds"))

organoid_size_factor <- organoid_size_fit$line %>% levels()
df <- organoid_size_fit

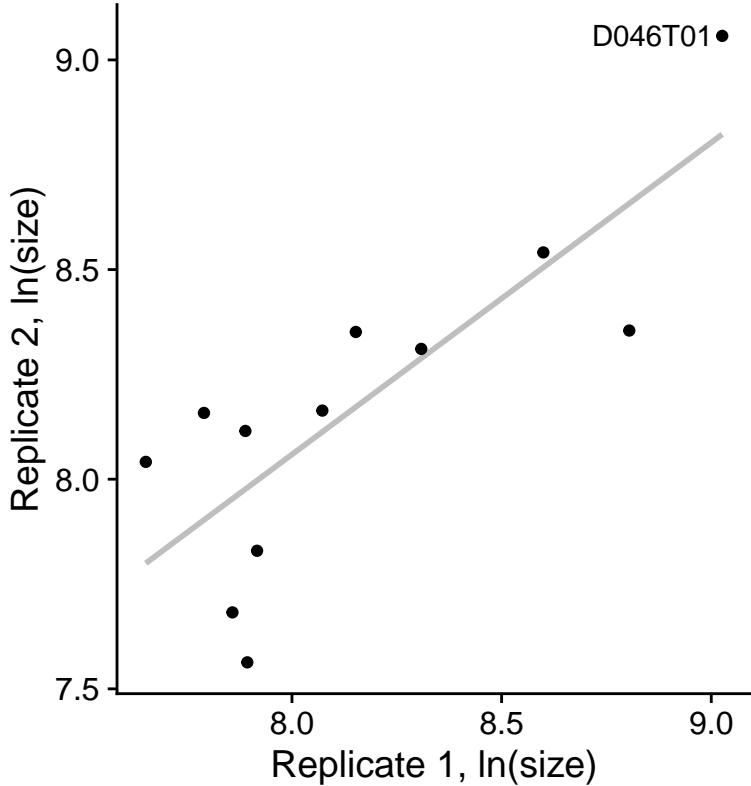
df <- df %>%
  dplyr::select(line, replicate, x) %>%
  # tidyr::pivot_wider(names_from = replicate,
  #                     values_from = x)
  tidyr::spread(key = replicate, value = x)

r_size = df %>% ungroup() %>% dplyr::select(-line) %>% as.matrix %>% cor() %>% min()

gg_size_replicate <- df %>%
  ggplot(aes('1', '2')) +
  geom_smooth(method = "lm", se = FALSE, color = "grey") +
  geom_point() +
  ggrepel::geom_text_repel(data = df %>% filter(line %in% c("D021T01", "D046T01")), aes(label = line)) +
  theme_cowplot() +
  labs(x = "Replicate 1, ln(size)",
       y = "Replicate 2, ln(size)",
       caption = paste0("all treatments, downsampled, 2 replicates, r= ", round(r_size, 2))) +
  coord_fixed(ratio = 1)
#geom_abline(slope = 1, color = "grey")

gg_size_replicate

```



all treatments, downsampled, 2 replicates,  $r= 0.81$

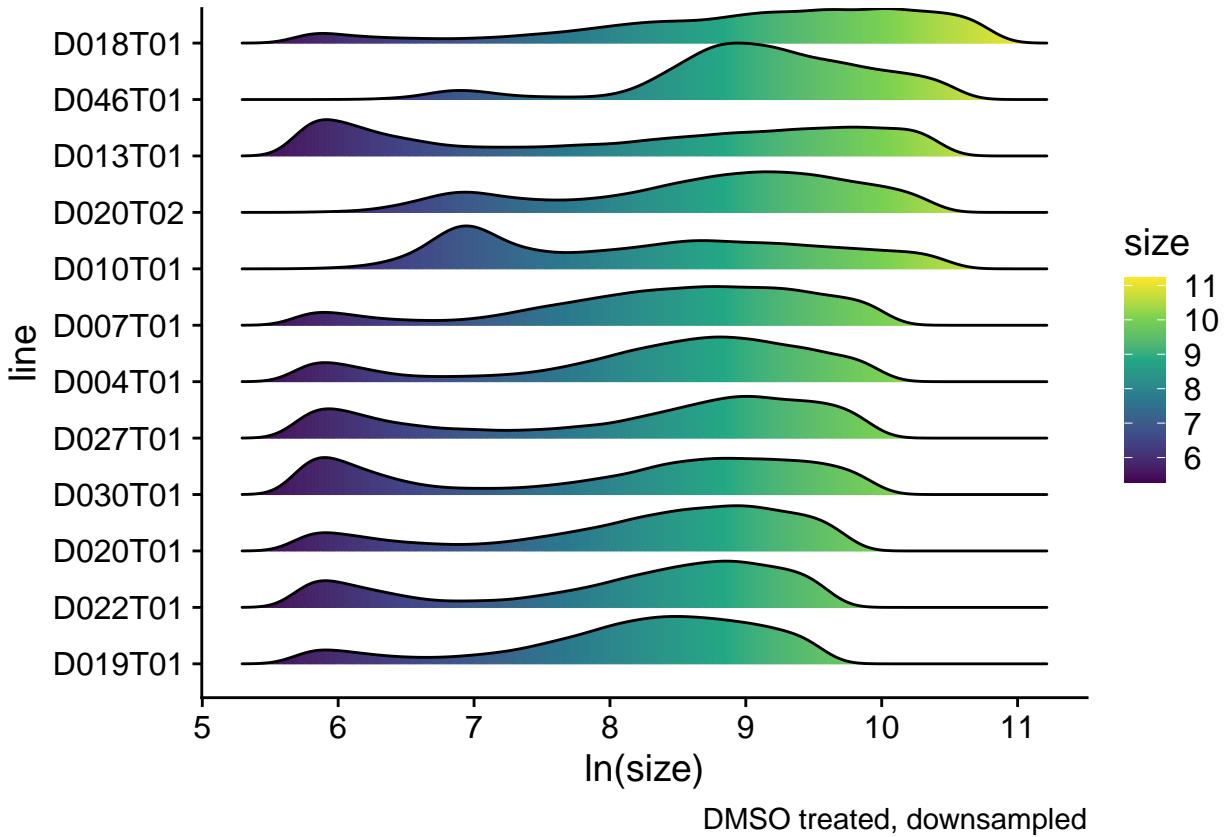
```

organoid_size_factor_09 <- umap_df %>% filter(partition %in% c(1,2)) %>% group_by(line) %>%
  summarise(x = quantile(size_log, 0.9)) %>%
#summarise(x = mean(size_log)) %>%
  arrange(x) %>% .$line

gg_size_dist_morph_ridge <- umap_df_sample %>% filter(partition %in% c(1,2)) %>% filter(drug == "DMSO") %
  mutate(line = factor(line, levels = organoid_size_factor_09)) %>%
  ggplot() +
  geom_density_ridges_gradient(aes(y = line, x = size_log, fill = stat(x)), scale = 1) +
#geom_density(aes(x = size_log, group = replicate, color = morphological_class)) +
#facet_wrap(~ line) +
  scale_fill_viridis_c() +
  labs(caption = "DMSO treated organoids",
       x = "ln(size)",
       fill = "size") +
  theme(legend.position = "bottom") +
  theme_cowplot() +
  labs(caption = "DMSO treated, downsampled")

gg_size_dist_morph_ridge

```



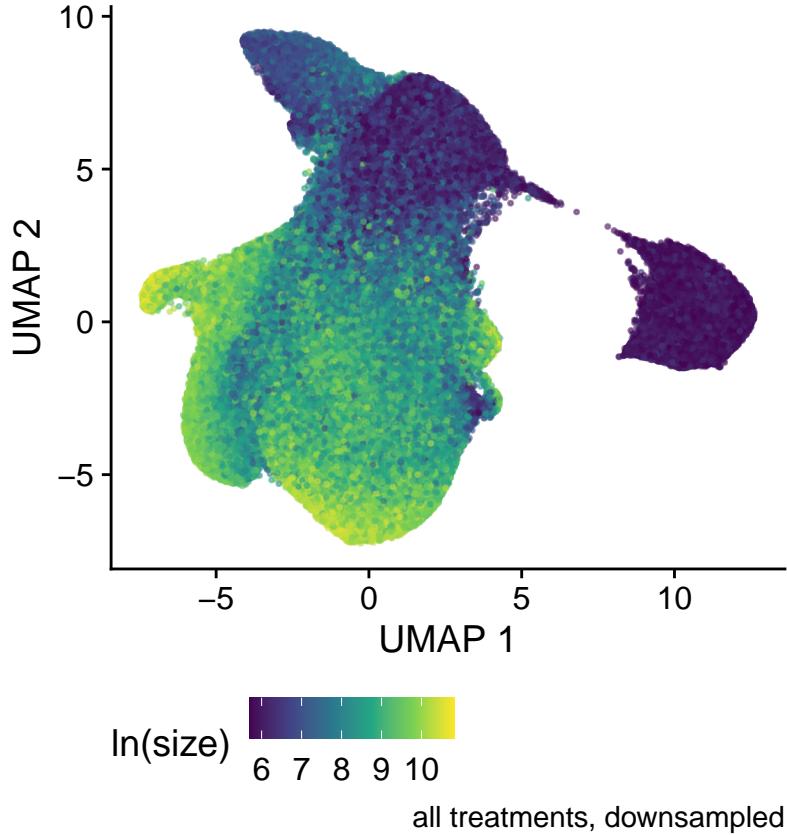
```

umap_size <- function(umap){
  umap %>%
    #filter(Size < 1000) %>%
    ggplot(aes(v1, v2, color = size_log)) +
    geom_point_rast(alpha = 0.5, size = 0.35) +
    scale_color_viridis_c() +
    theme_cowplot() +
    labs(x = "UMAP 1",
         y = "UMAP 2",
         color = "ln(size)") +
    theme(legend.position = "bottom") +
    coord_fixed()
}

gg_size <- umap_size(umap_df) +
  labs(caption = "all treatments, downsampled")

gg_size + ggsave(paste0(PATH, "reports/figures/imaging/gg_size_all.pdf"))

```

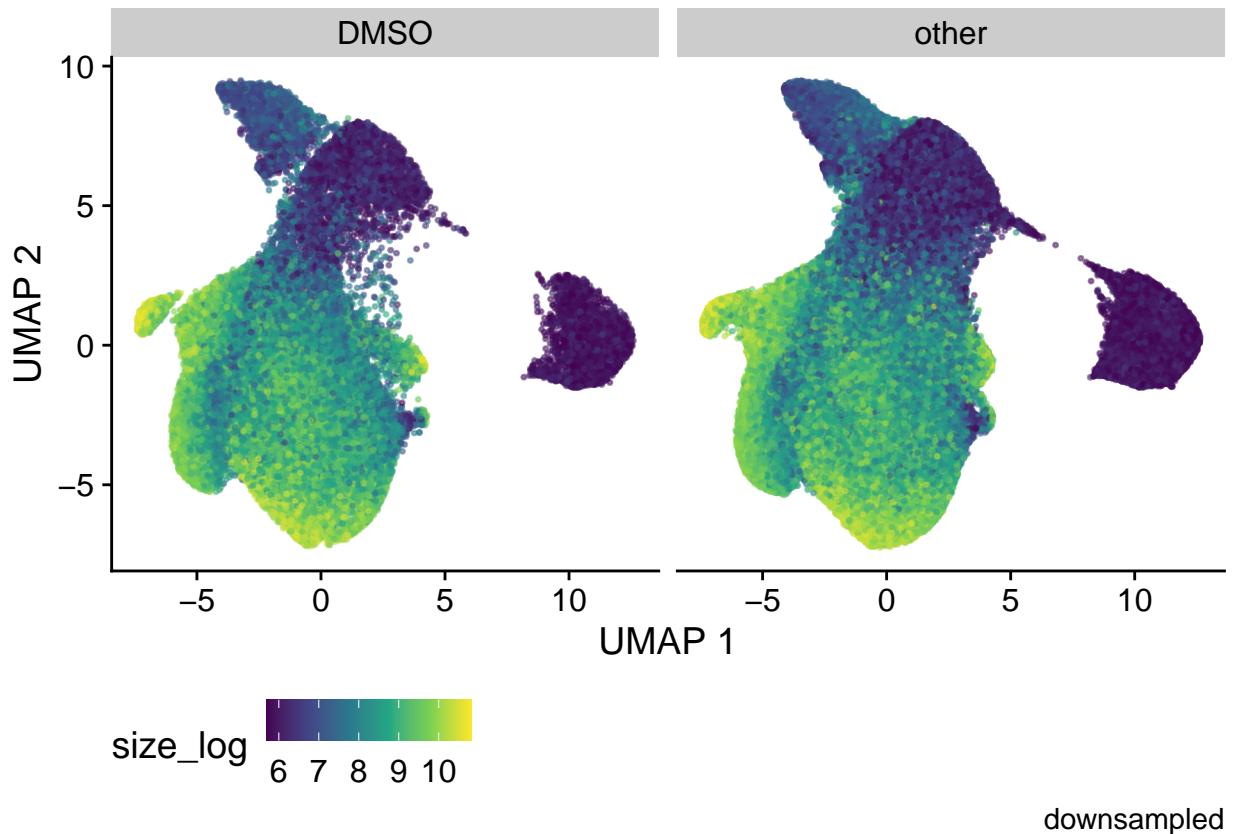


In general, DMSO treated organoid lines cover the same latent space than drug treated organoids. This is likely influenced by the large number of untreated organoids in the dataset.

```
df <- umap_df

gg_size_supp <- df %>%
  mutate(drug = if_else(drug == "DMSO", "DMSO", "other")) %>%
  ggplot(aes(v1, v2, color = size_log)) +
  geom_point_rast(alpha = 0.5, size = 0.35) +
  scale_color_viridis_c() +
  theme_cowplot() +
  labs(x = "UMAP 1",
       y = "UMAP 2") +
  theme(legend.position = "bottom") +
  facet_wrap(~ drug) +
  labs(caption = "downsampled")

gg_size_supp + ggsave(paste0(PATH, "reports/figures/imaging/gg_size_all.pdf"))
```



## Organoid Size during Drug Treatment

```

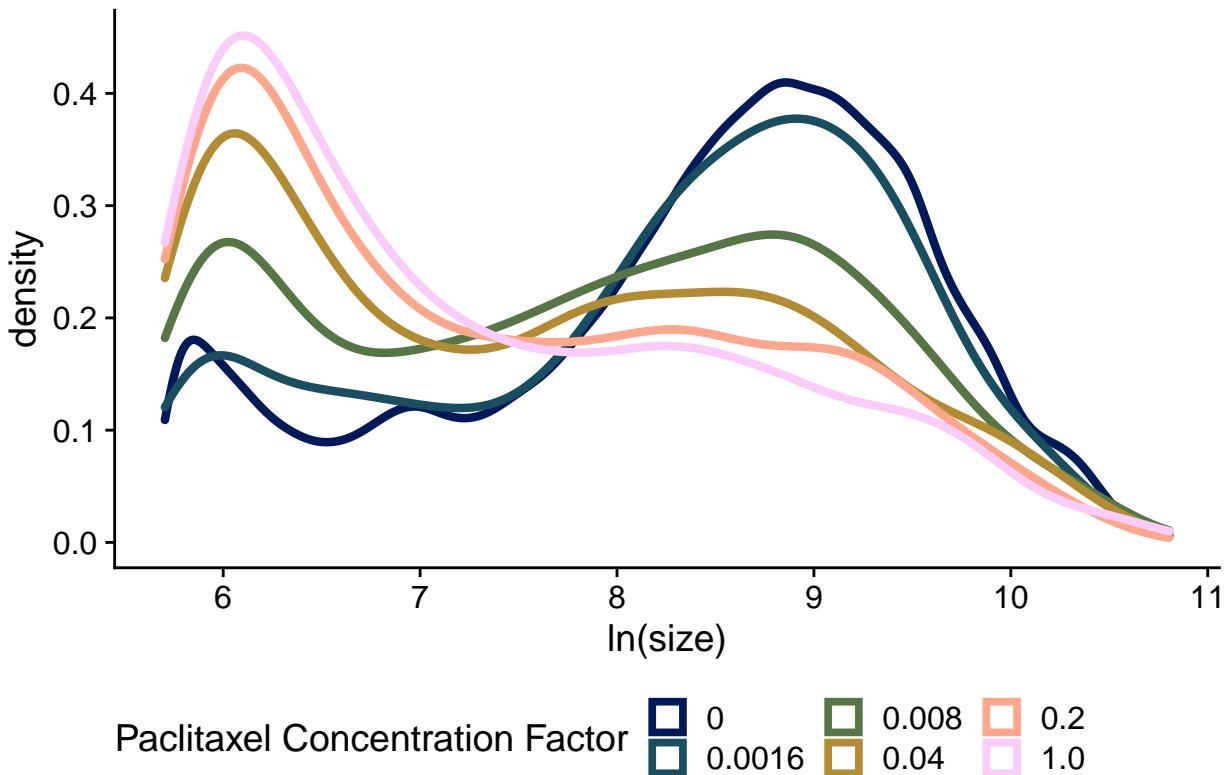
drug_size <- umap_df_sample %>% filter(partition %in% c(1,2)) %>% filter(drug == "DMSO" | drug == "Paclitaxel") %>% filter(morphological_class == "disorganized") %>% filter(morphological_class != "other") %>% mutate(concentration = factor(concentration, levels = c("0", "0.0016", "0.008", "0.04", "0.2", "1.0")))

ggdrug_size <- ggplot(drug_size) +
  geom_density(aes(x = log(size), group = concentration, color = concentration), size = 1.5) +
  scico::scale_color_scico_d() +
  theme_cowplot() +
  #scale_x_continuous(limits = c(0, 15000)) +
  theme(legend.position = "bottom") +
  labs(color = "Paclitaxel Concentration Factor",
       title = "Organoid size distribution",
       x = "ln(size)")

ggdrug_size

```

## Organoid size distribution

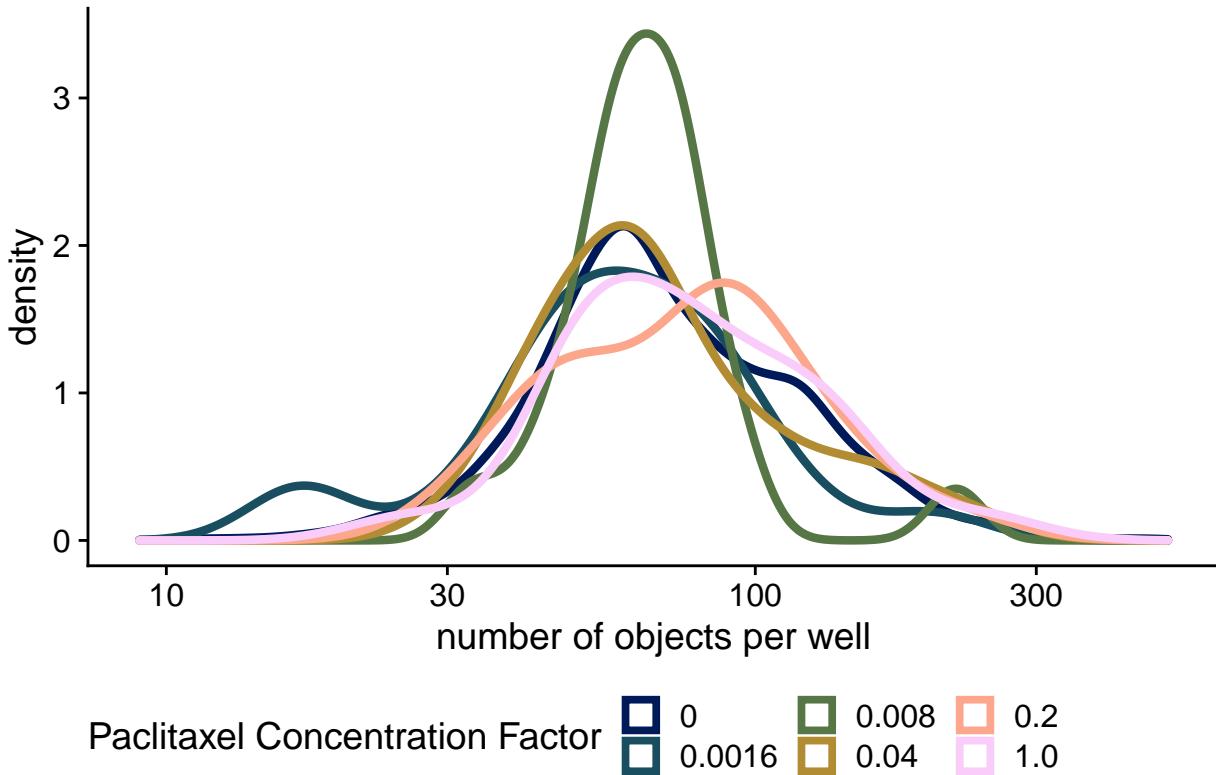


```
drug_count <- drug_size %>%
  dplyr::count(concentration, line, replicate, well)

ggdrug_count <- ggplot(drug_count) +
  geom_density(aes(x = n, group = concentration, color = concentration), size = 1.5) +
  scico::scale_color_scico_d() +
  theme_cowplot() +
  theme(legend.position = "bottom") +
  labs(color = "Paclitaxel Concentration Factor",
       title = "Organoid count distribution",
       x = "number of objects per well") +
  scale_x_log10()

ggdrug_count
```

## Organoid count distribution



```

set.seed(234)
loi = c("D022T01", "D046T01")

df <- umap_df_sample %>%
  filter(partition %in% c(1,2)) %>%
  filter(drug == "DMSO" | drug == "Paclitaxel") %>%
  mutate(concentration = ifelse(drug == "DMSO", 0, concentration)) %>%
  filter(line == loi)

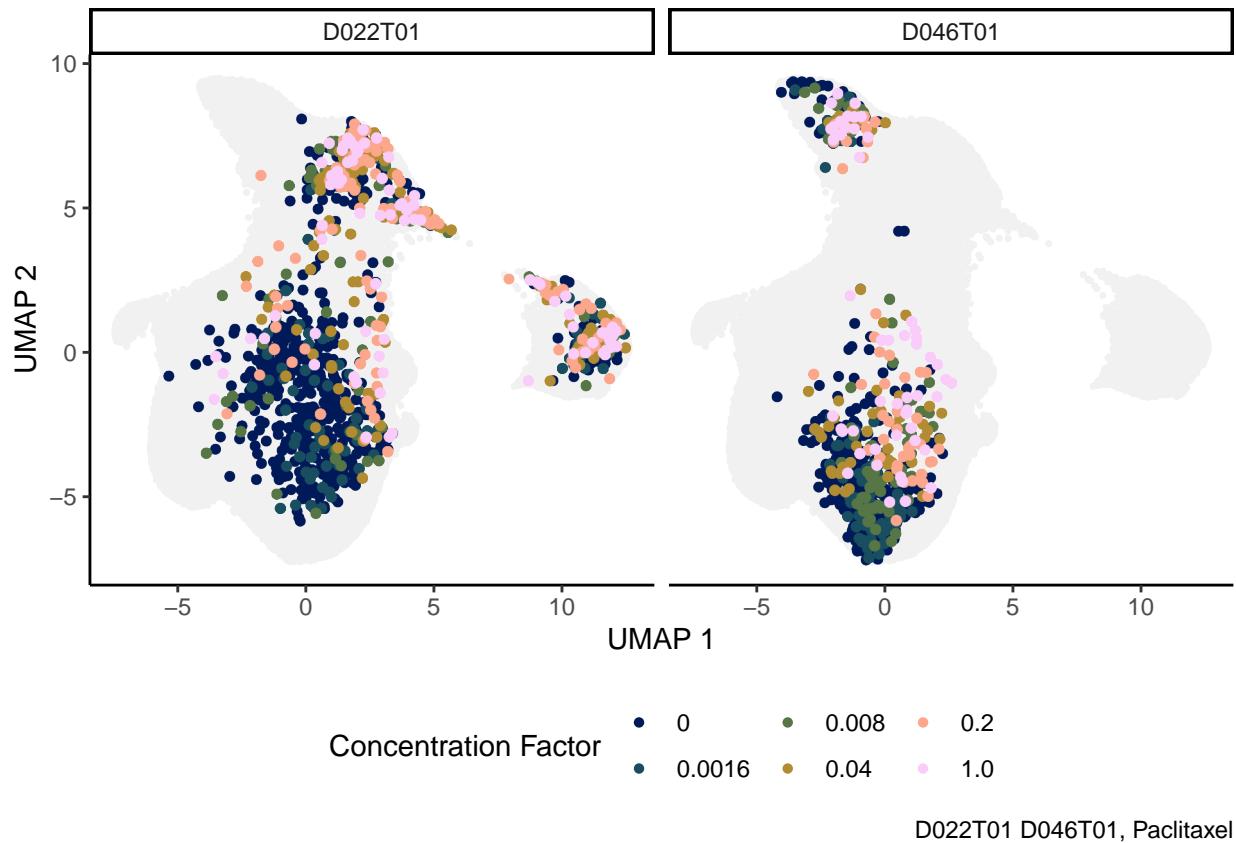
gg_drug <- umap_df_sample %>% filter(partition %in% c(1,2)) %>%
  dplyr::select(-line, -concentration) %>%
  ggplot(aes(v1, v2)) +
  geom_point_rast(alpha = 1, size = 0.35, color = "#f1f1f1") +
  geom_point_rast(data = df %>%
    group_by(concentration) %>%
    sample_n(1000, replace = TRUE),
    aes(color = concentration), alpha = 1, size = 1.5, shape=16) +
  #facet_wrap(~ concentration, ncol = 1) +
  #scale_color_brewer(type = "seq", palette = "YlOrRd") +
  #geom_density2d(color = "black") +
  theme_classic() +
  labs(x = "UMAP 1",
       y = "UMAP 2",
       caption = paste0(paste(loi, collapse=" "), ", Paclitaxel"),
       color = "Concentration Factor") +
  theme(legend.position = "bottom")
  
```

```

scico::scale_color_scico_d() +
facet_wrap(~ line, ncol = 2) +
theme(legend.position = "bottom") +
#theme_cowplot(font_size = 8) +
theme(legend.position = "bottom")

gg_drug

```



```

loi <- c("D022T01", "D046T01")

drug_size_param <- drug_size %>%
  nest(-concentration, -line) %>%
  mutate(fit = map(data, ~ fitdistrplus::fitdist(.x$size, "lnorm")),
         param = map(fit, ~ .x$estimate %>% broom::tidy()))

df <- drug_size_param %>% unnest(param) %>%
  filter(names == "meanlog") %>%
  mutate(concentration = factor(concentration, levels = c("0", "0.0016", "0.008", "0.04", "0.2", "1.0")))

gg_size_drug <- df %>%
  filter(line %in% loi) %>%
  #mutate(concentration = as.numeric(as.character(concentration))) %>%
  ggplot(aes(concentration, x)) +
  geom_point(color = "grey") +
  geom_line(data = df %>% dplyr::rename(line_h = line), aes(group = line_h), color = "grey") +

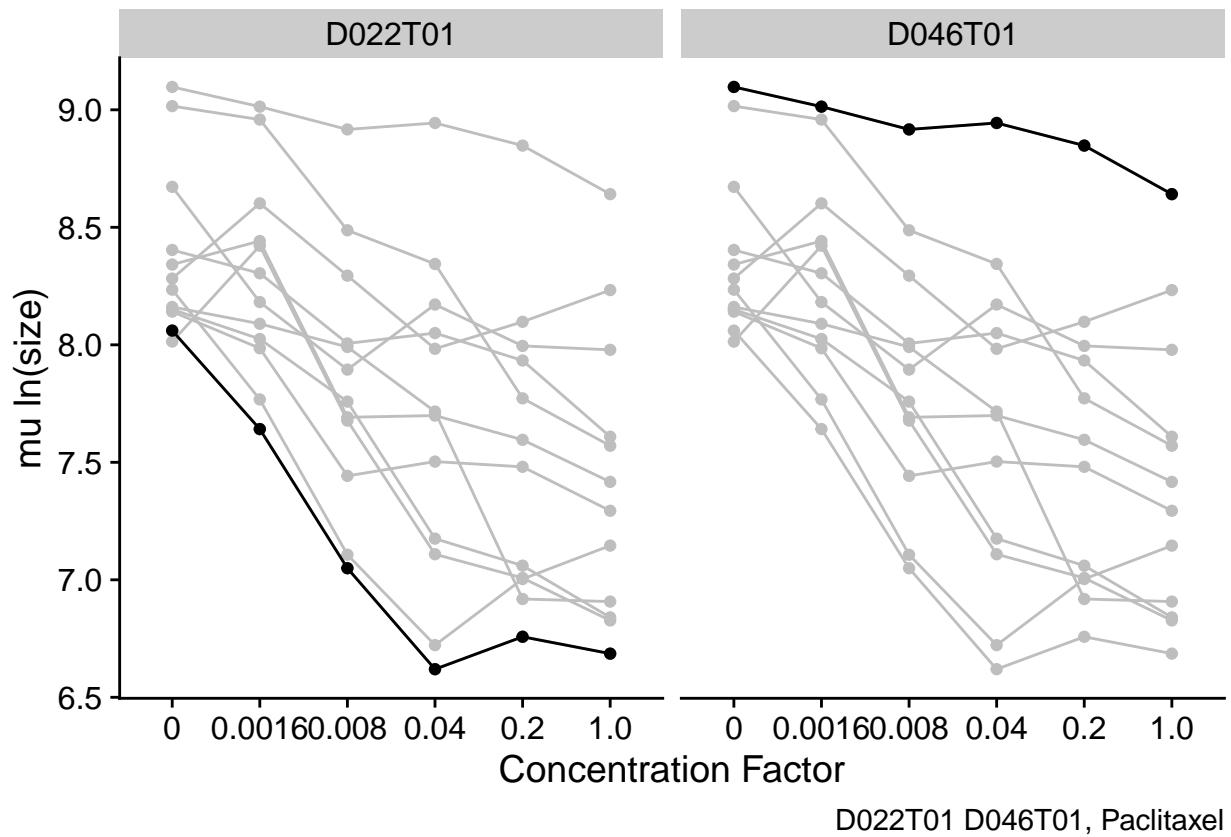
```

```

geom_point(data = df %>% dplyr::rename(line_h = line), color = "grey") +
geom_point(color = "black") +
geom_line(aes(group = line), color = "black") +
labs(y = 'mu ln(size)', ,
x = "Concentration Factor",
caption = paste0(paste(loi, collapse=" "), ", Paclitaxel")) +
facet_wrap(~ line) +
theme_cowplot()

gg_size_drug

```



## TODO

```

umap_ldc <- function(umap){
  umap %>%
  #filter(Size < 1000) %>%
  ggplot(aes(v1, v2, color = prob_dead)) +
  geom_point_rast(alpha = 0.5, size = 0.35) +
  scale_color_scico(palette = 'lajolla') + #lajolla #vik0
  theme_cowplot() +
  labs(x = "UMAP 1",
       y = "UMAP 2",
       color = "p(dead)") +
  theme(legend.position = "bottom") +
  guides(fill = guide_colourbar(barwidth = 0.5, barheight = 10))
}

```

```
gg_ldc <- umap_ldc(umap_df %>% filter(partition %in% c(1,2)))

gg_ldc
```

## Organoid Heterogeneity

I plot 2 organoid lines treated with DMSO control

```
set.seed(234)

df <- umap_df %>% filter(partition %in% c(1,2)) %>%
  mutate(cystic = if_else(line == "D013T01" & well == "D24" & plate == "D013T01P001L02", TRUE, FALSE))
  mutate(compact = if_else(line == "D046T01" & well == "D24" & plate == "D046T01P007L02", TRUE, FALSE))

gg_cys_comp <- df %>%
  sample_frac(0.01) %>%
  ggplot(aes(v1, v2, color = size_log)) +
  #scale_color_brewer(type = "qual", palette = 2) +
  geom_point_rast(alpha = 0.1, size = 0.35) +
  geom_point_rast(color = "#F4B400", alpha = 1, size = 0.5, data = df %>% filter(cystic == TRUE)) +
  geom_point_rast(color = "#DB4437", alpha = 1, size = 0.5, data = df %>% filter(compact == TRUE)) +
  scale_color_viridis_c() +
  labs(color = "size",
       caption = "yellow: D013T01, red: D055T01",
       x = "UMAP 1",
       y = "UMAP 2") +
  theme_cowplot() +
  coord_fixed()

gg_cys_comp
```

## Organoid line differences

I create a single plot showing the two extreme organoid lines and their distribution within the embedding.

```
set.seed(123)

loi <- c("D019T01", "D007T01", "D030T01", "D018T01") #c("D055T01", "D007T01", "D021T01", "D019T01", "D020T01")
#loi <- umap_df$line %>% unique()

df <- umap_df %>%
  filter(drug == "DMSO") %>%
  filter(partition %in% c(1,2))

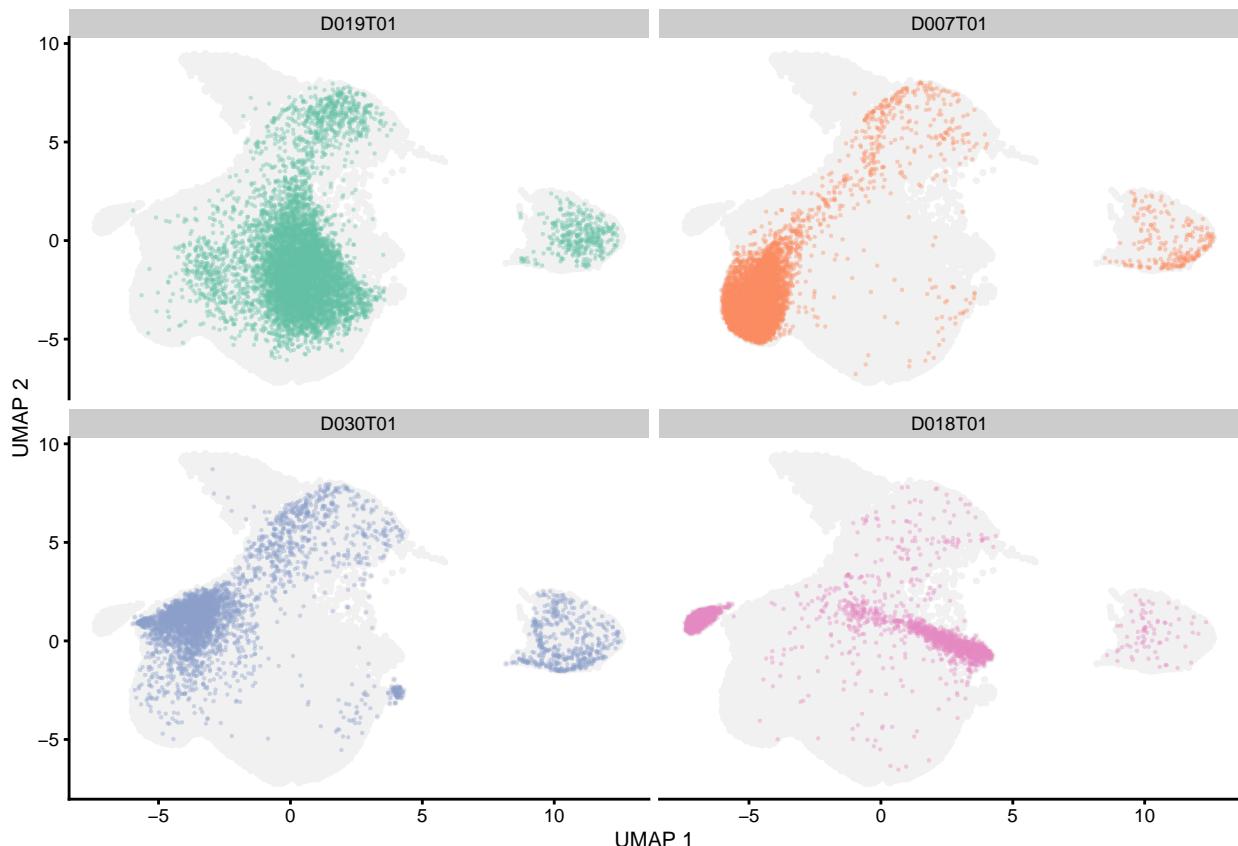
gg_line <- df %>% dplyr::select(-line) %>%
  ggplot(aes(v1, v2)) +
  geom_point_rast(alpha = 1, size = 0.35, color = "#f1f1f1") +
```

```

geom_point_rast(data = umap_df %>%
  filter(drug == "DMSO") %>%
  # filter(line %in% c("D021T01")) %>%
  filter(line %in% loi) %>%
  mutate(line = factor(line, levels = loi)), #>%
  #sample_frac(0.1),
  #mutate(line = factor(line, levels = c("D021T01"))),
  aes(color = line), alpha = .4, size = 0.35, shape=16) +
facet_wrap(~ line, ncol = 2) +
scale_color_brewer(type = "qual", palette = "Set2") +
#scale_color_manual(values = c(c("#D80D12", "#461C01", "#9a4c91", "#70BE6F", "#24345E"))) +
#geom_density2d(color = "black") +
theme_classic() +
labs(x = "UMAP 1",
y = "UMAP 2") +
#caption = "control treated organoids" +
theme_cowplot(font_size = 8) +
theme(legend.position = "nothing")

gg_line + ggsave(paste0(PATH, "reports/figures/imaging/gg_size_all.pdf"), width = 4, height = 4)

```



```

df <- umap_df %>%
  left_join(organoid_morphology %>% mutate(line = paste0(line, "01"))) %>%
  filter(drug == "DMSO") %>%
  filter(partition %in% c(1,2))

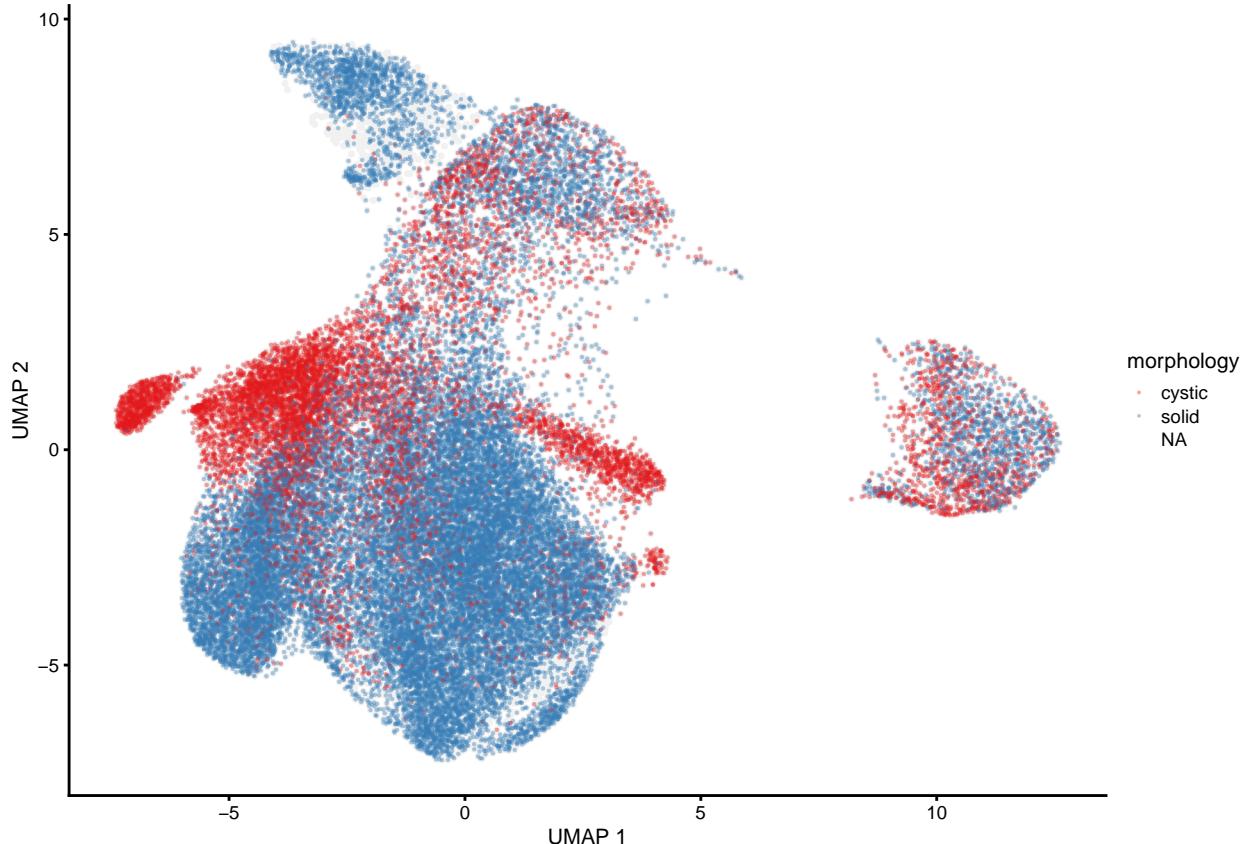
```

```

gg_morph <- df %>% dplyr::select(-line) %>%
  ggplot(aes(v1, v2)) +
  geom_point_rast(alpha = 1, size = 0.35, color = "#f1f1f1") +
  geom_point_rast(data = umap_df %>% left_join(organoid_morphology %>% mutate(line = paste0(line, "01"))),
                  filter(drug == "DMSO"), #%>%
  #sample_frac(0.1),
  #mutate(line = factor(line, levels = c("D021T01"))),
  aes(color = morphology), alpha = .4, size = 0.35, shape=16) +
  #facet_wrap(~ line, ncol =2) +
  scale_color_brewer(type = "qual", palette = "Set1") +
  #scale_color_manual(values = c(c("#D80D12", "#461C01", "#9a4c91", "#70BE6F", "#24345E"))) +
  #geom_density2d(color = "black") +
  theme_classic() +
  labs(x = "UMAP 1",
       y = "UMAP 2")+
  #caption = "control treated organoids" +
  theme_cowplot(font_size = 8)

gg_morph + ggsave(paste0(PATH, "reports/figures/imaging/gg_morphology.pdf"), width = 4, height = 4)

```



```

df <- umap_df %>%
  left_join(organoid_morphology %>% mutate(line = paste0(line, "01")))) %>%
  filter(drug == "DMSO") %>%
  filter(partition %in% c(1,2))

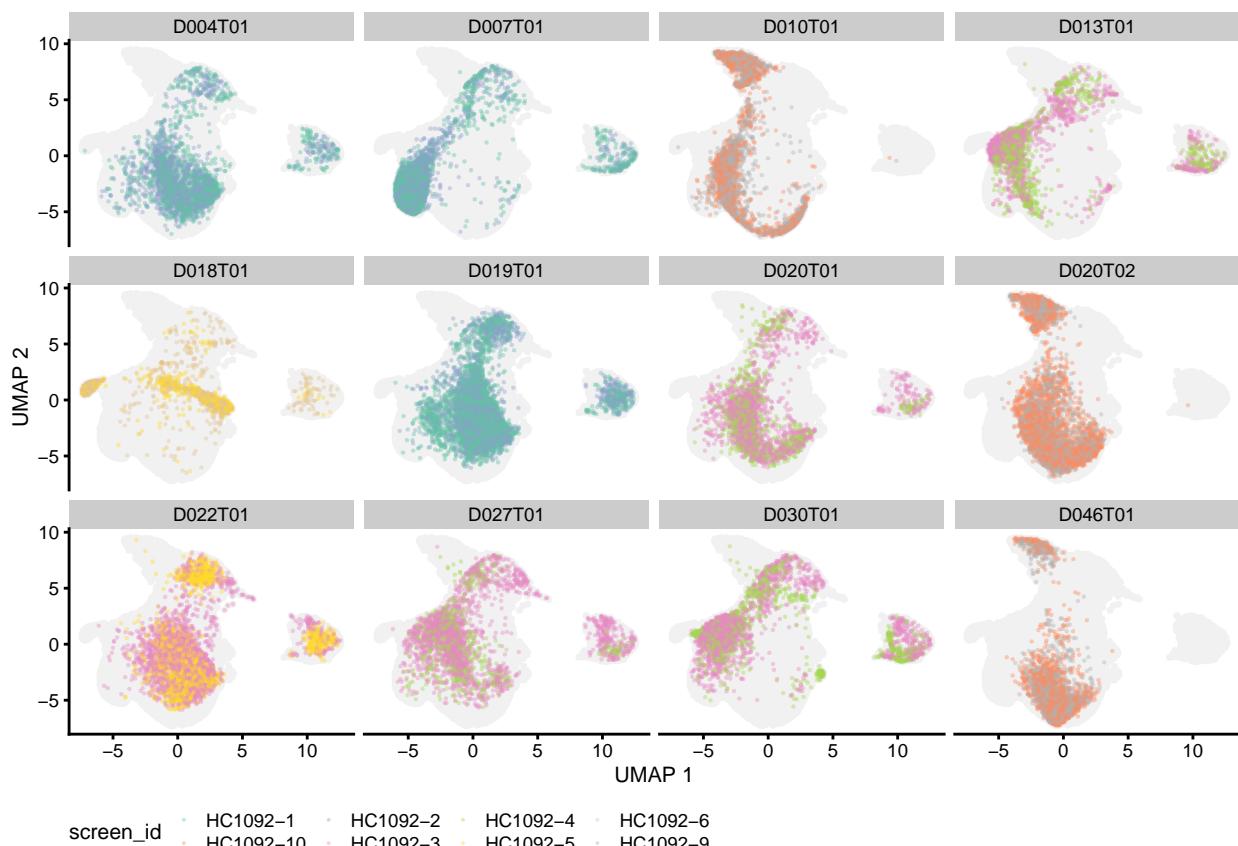
```

```

gg_screen_id <- df %>% dplyr::select(-line) %>%
  ggplot(aes(v1, v2)) +
  geom_point_rast(alpha = 1, size = 0.35, color = "#f1f1f1") +
  geom_point_rast(data = umap_df %>% left_join(organoid_morphology %>% mutate(line = paste0(line, "01"))),
                  filter(drug == "DMSO"), #%>%
  #sample_frac(0.1),
  #mutate(line = factor(line, levels = c("D021T01"))),
  aes(color = screen_id), alpha = .4, size = 0.35, shape=16) +
  facet_wrap(~ line, ncol =4) +
  scale_color_brewer(type = "qual", palette = "Set2") +
  #scale_color_manual(values = c(c("#D80D12", "#461C01", "#9a4c91", "#70BE6F", "#24345E"))) +
  #geom_density2d(color = "black") +
  theme_classic() +
  labs(x = "UMAP 1",
       y = "UMAP 2")+
  #caption = "control treated organoids" +
  theme_cowplot(font_size = 8) +
  theme(legend.position = "bottom")

gg_screen_id + ggsave(paste0(PATH, "reports/figures/imaging/gg_screen_id.pdf"), width = 4, height = 4)

```



## Dye Intensity

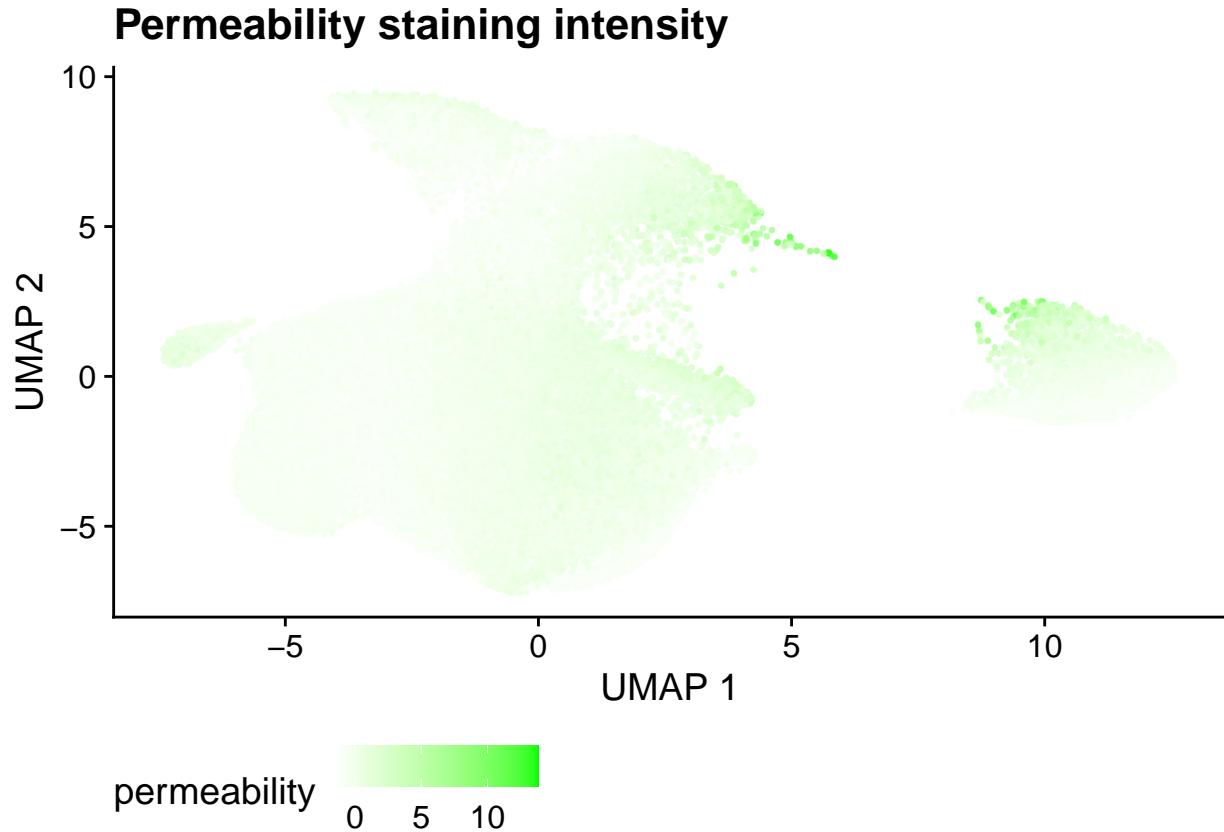
```
umap_sample %>%
  ggplot(aes(actin, fill = screen_id)) +
  geom_density(alpha = 0.5) +
  scale_fill_brewer(type = 'qual') +
  facet_wrap(~ line) +
  theme_cowplot()
```

```
df %>%
  ggplot(aes(permeability, fill = screen_id)) +
  geom_density(alpha = 0.5) +
  scale_fill_brewer(type = 'qual') +
  facet_wrap(~ line) +
  theme_cowplot()
```

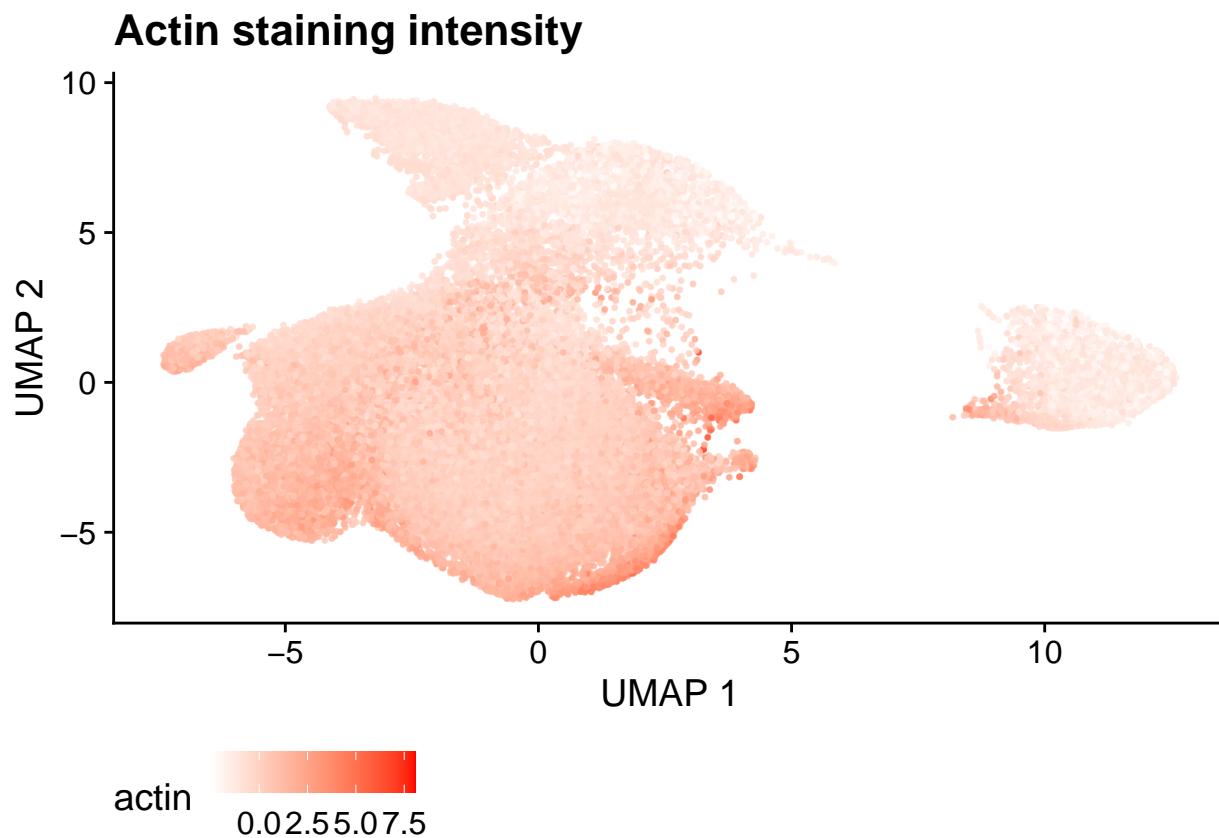
```
df %>%
  ggplot(aes(dapi, fill = screen_id)) +
  geom_density(alpha = 0.5) +
  scale_fill_brewer(type = 'qual') +
  facet_wrap(~ line) +
  theme_cowplot()
```

```
set.seed(123)

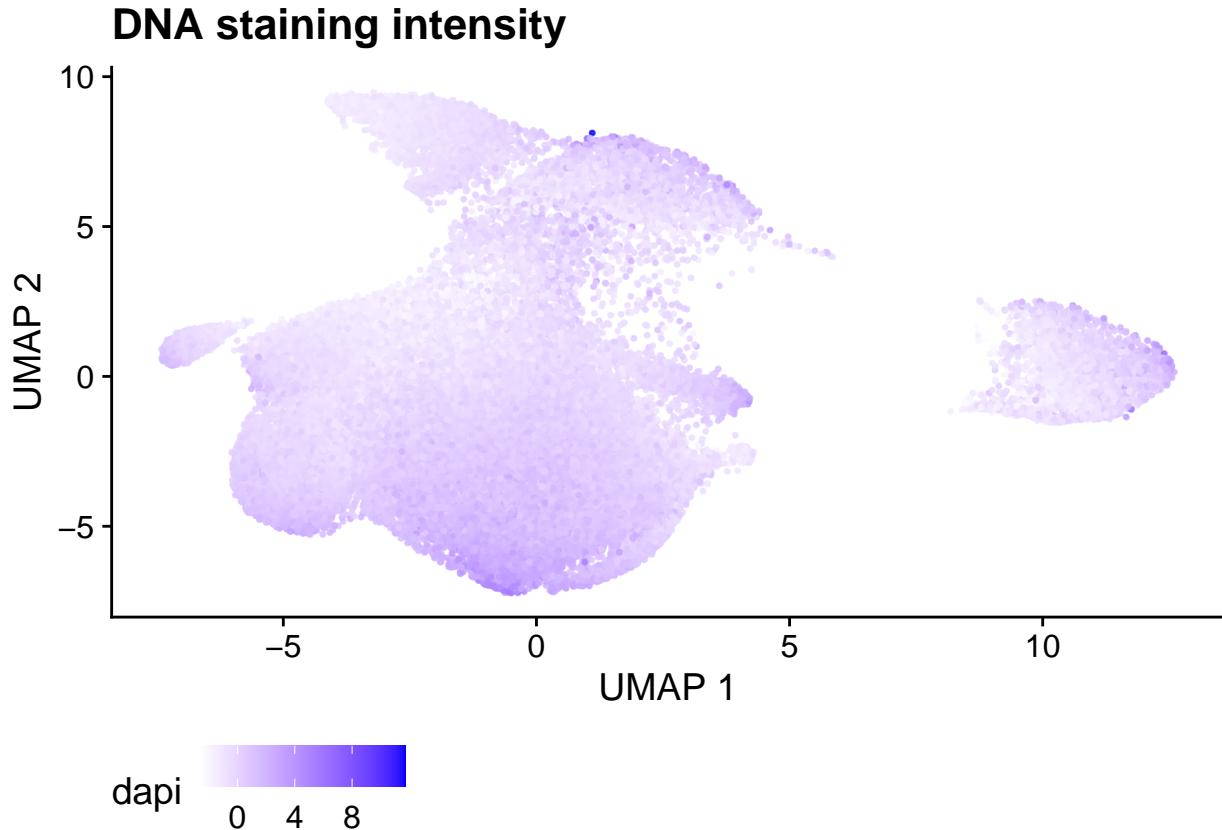
umap_df %>%
  filter(drug == "DMSO") %>%
  #sample_n(10000) %>%
  ggplot(aes(v1, v2, color = permeability)) +
  geom_point_rast(alpha = 0.75, size = 0.35) +
  scale_colour_gradient(low = "white", high = "green") +
  theme_cowplot() +
  labs(x = "UMAP 1",
       y = "UMAP 2",
       title = "Permeability staining intensity") +
  theme(legend.position = "bottom") +
  ggsave(paste0(PATH, "reports/figures/imaging/gg_permeability.pdf"), width = 4, height = 4)
```



```
umap_df %>%
  filter(drug == "DMSO") %>%
  #sample_n(10000) %>%
  ggplot(aes(v1, v2, color = actin)) +
  geom_point_rast(alpha = 0.75, size = 0.35) +
  scale_colour_gradient(low = "white", high = "red") +
  theme_cowplot() +
  labs(x = "UMAP 1",
       y = "UMAP 2",
       title = "Actin staining intensity") +
  theme(legend.position = "bottom") +
  ggsave(paste0(PATH, "reports/figures/imaging/gg_actin.pdf"), width = 4, height = 4)
```



```
umap_df %>%
  filter(drug == "DMSO") %>%
  #sample_n(10000) %>%
  ggplot(aes(v1, v2, color = dapi)) +
  geom_point_rast(alpha = 0.75, size = 0.35) +
  scale_colour_gradient(low = "white", high = "blue") +
  theme_cowplot() +
  labs(x = "UMAP 1",
       y = "UMAP 2",
       title = "DNA staining intensity") +
  theme(legend.position = "bottom") +
  ggsave(paste0(PATH, "reports/figures/imaging/gg_dapi.pdf"), width = 4, height = 4)
```



I am focusing on cystic vs solid organoid lines

```
#UMAP Cystic (Lines 18, 13, 27, 30) vs. Solid (others) treated with DMSO, for Figure 1 / matching expression

set.seed(123)

cystic_l <- organoid_morphology %>% filter(morphology == "cystic") %>% .$.line %>% paste0(., "01")
dense_l <- organoid_morphology %>% filter(morphology == "solid") %>% .$.line %>% paste0(., "01")

df <- umap_df %>%
  filter(drug == "DMSO") %>%
  filter(partition %in% c(1,2)) %>%
  mutate(morphology = case_when(line %in% cystic_l ~ "cystic",
                                line %in% dense_l ~ "solid",
                                TRUE ~ "other"))

gg_cystic <- umap_df %>%
  ggplot(aes(v1, v2)) +
  geom_point_rast(alpha = 1, size = 0.35, color = "#f1f1f1") +
  # geom_point_rast(data = df %>%
  #   filter(morphology == "cystic") %>%
  #   sample_frac(0.05),
  #   aes(color = morphology), alpha = .4, size = 0.35, shape=16) +
  geom_density_2d(data = df %>% #geom_density_2d_filled
```

```

filter(morphology != "other"), # %>%
# sample_frac(0.05)
aes(fill = morphology), size = 1.5) +
#scale_color_brewer(type = "qual", palette = "Set2") +
#scale_fill_manual(values = c("#0571b0", "#ca0020")) +
scale_color_manual(values = c("#0571b0", "#ca0020")) +
#geom_density2d(color = "black") +
theme_classic() +
labs(x = "UMAP 1",
y = "UMAP 2") +
#caption = "control treated organoids" +
theme_cowplot(font_size = 8) +
#theme(legend.position = "nothing") +
coord_fixed() +
scale_x_reverse()

```

gg\_cystic

## Plot Export

```

plot_grid(plot_grid(gg_size_dist_morph_ridge, gg_size_replicate, labels = c('A', 'B'), label_size = 12,
gg_size,
plot_grid(gg_line, gg_cystic, labels = c('D', 'E'), label_size = 12, ncol = 2),
labels = c(' ', 'C', ' '), label_size = 12, ncol = 1) +
ggsave(paste0(PATH, "reports/panels/panel_size_dist.pdf"), width = 8, height = 16)

```

```

plot_grid(plot_grid(ggdrug_size, ggdrug_count, labels = c('A', 'B'), label_size = 12),
gg_drug,
gg_size_drug,
labels = c(' ', 'C', 'D'), label_size = 12, ncol = 1) +
ggsave(paste0(PATH, "reports/panels/panel_size_drug.pdf"), width = 8, height = 12)

```

gg\_size\_supp

sessionInfo()

```

## R version 4.0.0 (2020-04-24)
## Platform: x86_64-pc-linux-gnu (64-bit)
## Running under: Ubuntu 20.04.2 LTS
##
## Matrix products: default
## BLAS/LAPACK: /usr/lib/x86_64-linux-gnu/openblas-pthread/libopenblas-r0.3.8.so
##
## locale:
## [1] LC_CTYPE=en_US.UTF-8          LC_NUMERIC=C
## [3] LC_TIME=en_US.UTF-8          LC_COLLATE=en_US.UTF-8
## [5] LC_MONETARY=en_US.UTF-8       LC_MESSAGES=C
## [7] LC_PAPER=en_US.UTF-8          LC_NAME=C

```

```

## [9] LC_ADDRESS=C           LC_TELEPHONE=C
## [11] LC_MEASUREMENT=en_US.UTF-8 LC_IDENTIFICATION=C
##
## attached base packages:
## [1] stats      graphics   grDevices utils     datasets   methods    base
##
## other attached packages:
## [1] ggridges_0.5.2  scico_1.1.0   princurve_2.1.4 cowplot_1.0.0
## [5] ggrastr_0.2.3   here_0.1     readr_1.3.1    purrr_0.3.4
## [9] magrittr_1.5     tidyverse_1.1.0 dplyr_1.0.0    ggplot2_3.3.1
##
## loaded via a namespace (and not attached):
## [1] beeswarm_0.2.3    tidyselect_1.1.0  xfun_0.14       lattice_0.20-41
## [5] splines_4.0.0     colorspace_1.4-1  vctrs_0.3.1     generics_0.0.2
## [9] viridisLite_0.3.0 htmltools_0.4.0  mgcv_1.8-31     yaml_2.2.1
## [13] utf8_1.1.4       survival_3.1-12  rlang_0.4.6     pillar_1.4.4
## [17] glue_1.4.1        withr_2.2.0      fitdistrplus_1.1-1 RColorBrewer_1.1-2
## [21] lifecycle_0.2.0   plyr_1.8.6      stringr_1.4.0    munsell_0.5.0
## [25] gtable_0.3.0     evaluate_0.14   labeling_0.3     knitr_1.28
## [29] Cairo_1.5-12     vipor_0.4.5     fansi_0.4.1     broom_0.5.6
## [33] Rcpp_1.0.4.6     scales_1.1.1    backports_1.1.7  farver_2.0.3
## [37] hms_0.5.3        digest_0.6.25   stringi_1.4.6   ggrepel_0.8.2
## [41] grid_4.0.0        rprojroot_1.3-2  cli_2.0.2       tools_4.0.0
## [45] tibble_3.0.1      crayon_1.3.4   pkgconfig_2.0.3 MASS_7.3-51.5
## [49] Matrix_1.2-18    ellipsis_0.3.1  ggbeeswarm_0.6.0 assertthat_0.2.1
## [53] rmarkdown_2.2      R6_2.4.1       nlme_3.1-147   compiler_4.0.0

```