

Organoid Unsupervised Exploration

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Loading packages

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

# parameter
print("parameter input:")

## [1] "parameter input"

print(params$data)

## [1] "data/processed/PhenotypeSpectrum/filtered_moderate/umap_absolute_all_drugs_sampled.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/OE0049/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))

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

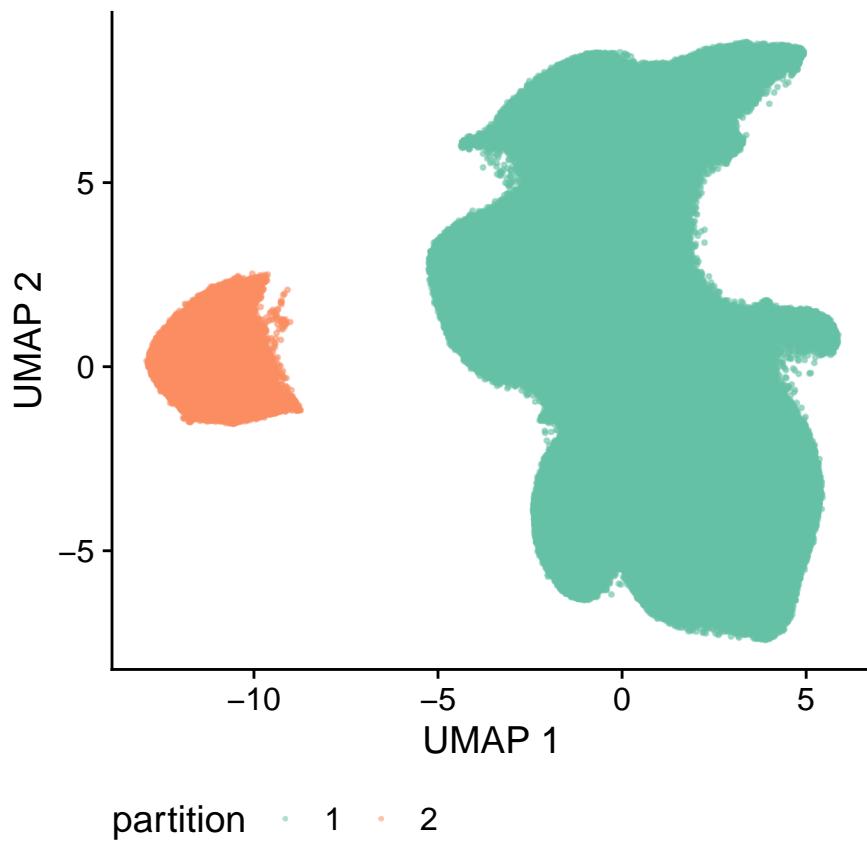
Partition inspection

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()

```



```

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

```

```

## # A tibble: 2 x 3
##   partition     n   ratio
##   <fct>     <int>   <dbl>
## 1 1          278346  0.933
## 2 2          19891  0.0667

```

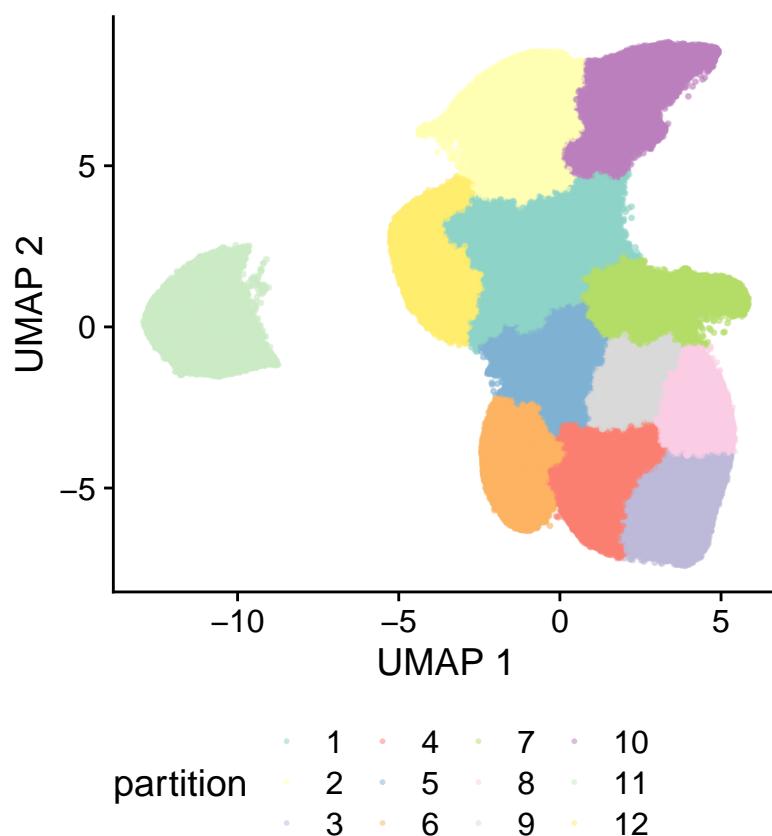
I remove 2 partitions from all main figures for ease of reading. Below, it is easy to toggle the removal of partitions on and off to make sure this filtering step is robust

```

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/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()

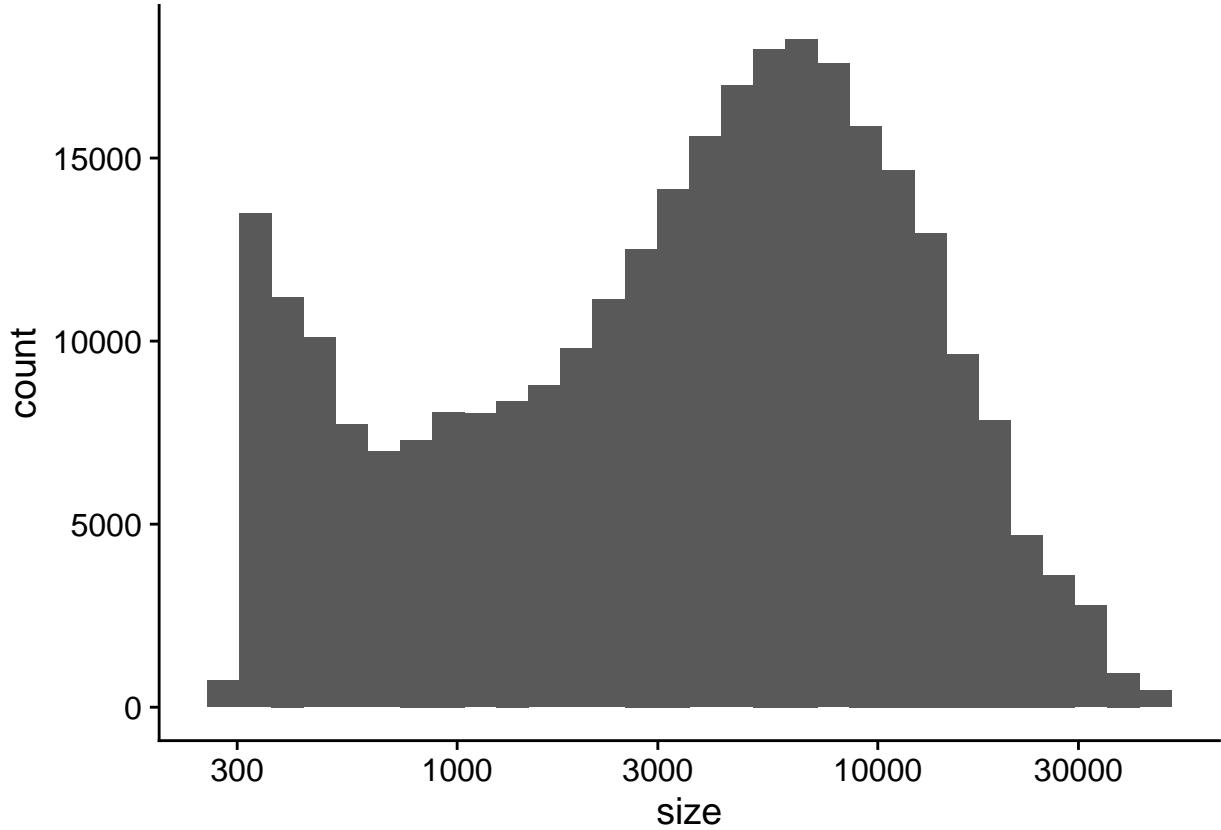
```

```

gg_size_dist_log <- gg_size_dist +
  scale_x_log10()

gg_size_dist_log

```



I add the eCDF.

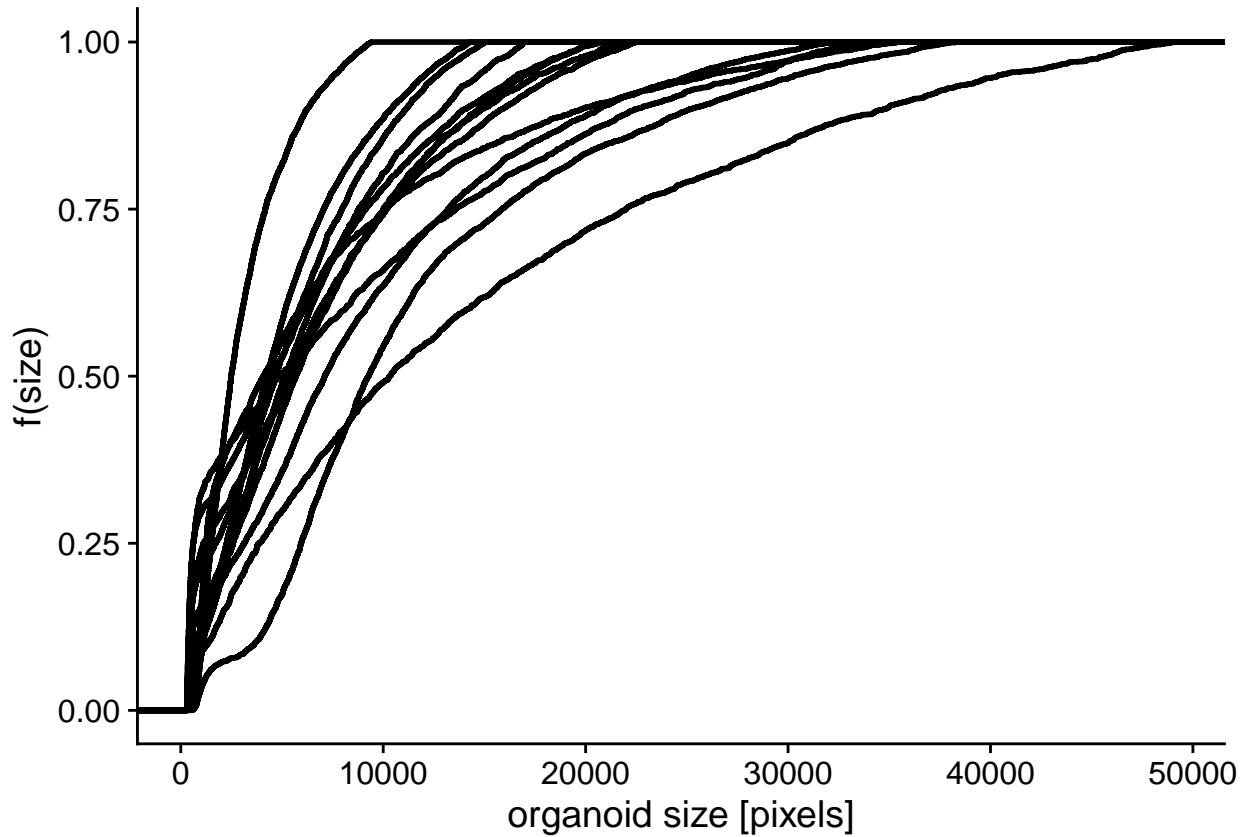
```

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

```



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

```

line_param <- umap_df %>% filter(partition %in% c(1,2)) %>%
  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_factor <- df$line %>% levels()

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 %>%

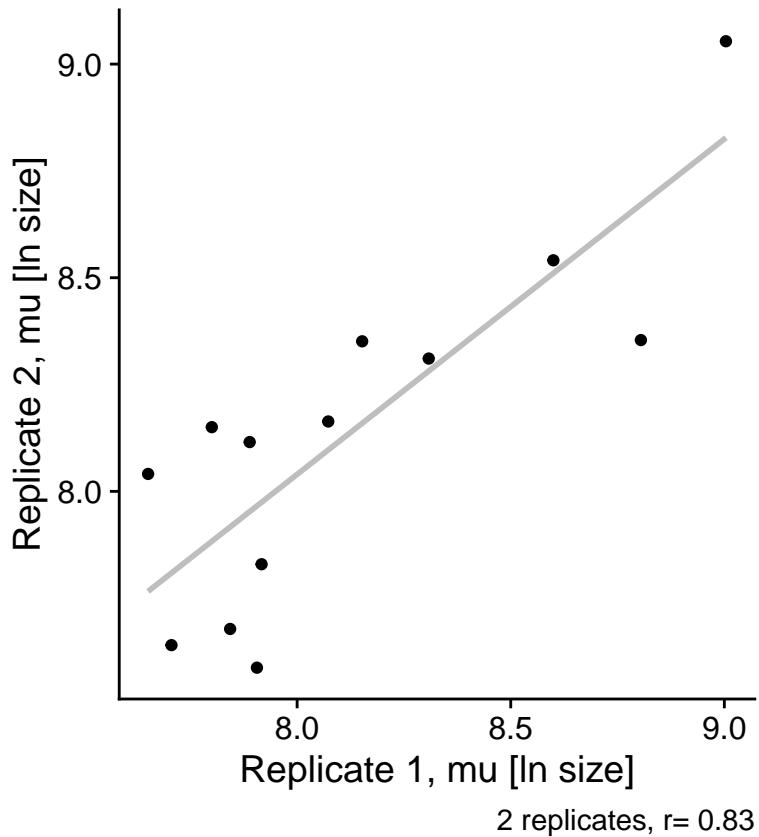
```

```

ggplot(aes('1', '2')) +
  geom_smooth(method = "lm", se = FALSE, color = "grey") +
  geom_point() +
  theme_cowplot() +
  labs(x = "Replicate 1, mu [ln size]",
       y = "Replicate 2, mu [ln size]",
       caption = paste0("2 replicates, r= ", round(r_size, 2))) +
  coord_fixed(ratio = 1)
#geom_abline(slope = 1, color = "grey")

gg_size_replicate

```



```

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 %>% 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) +

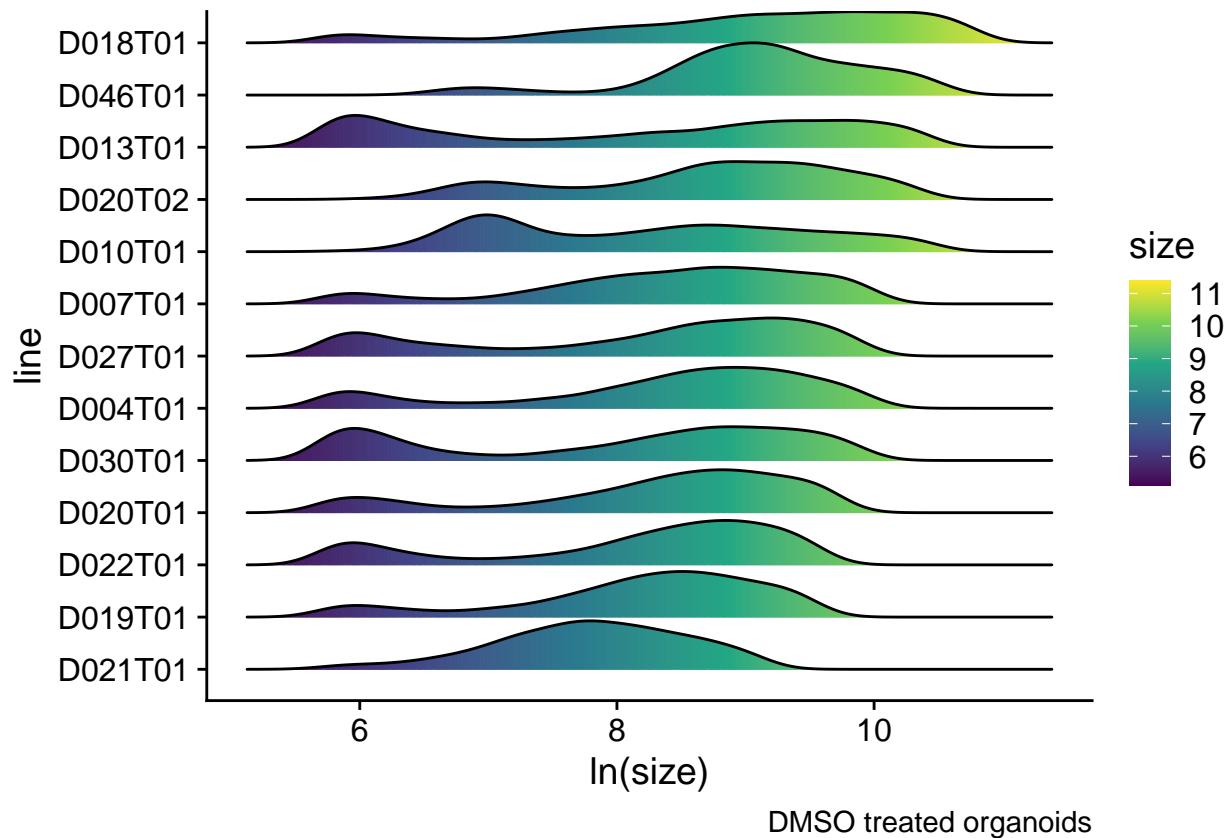
```

```

scale_fill_viridis_c() +
labs(caption = "DMSO treated organoids",
x = "ln(size)",
fill = "size") +
theme(legend.position = "bottom") +
theme_cowplot()

gg_size_dist_morph_ridge

```



```

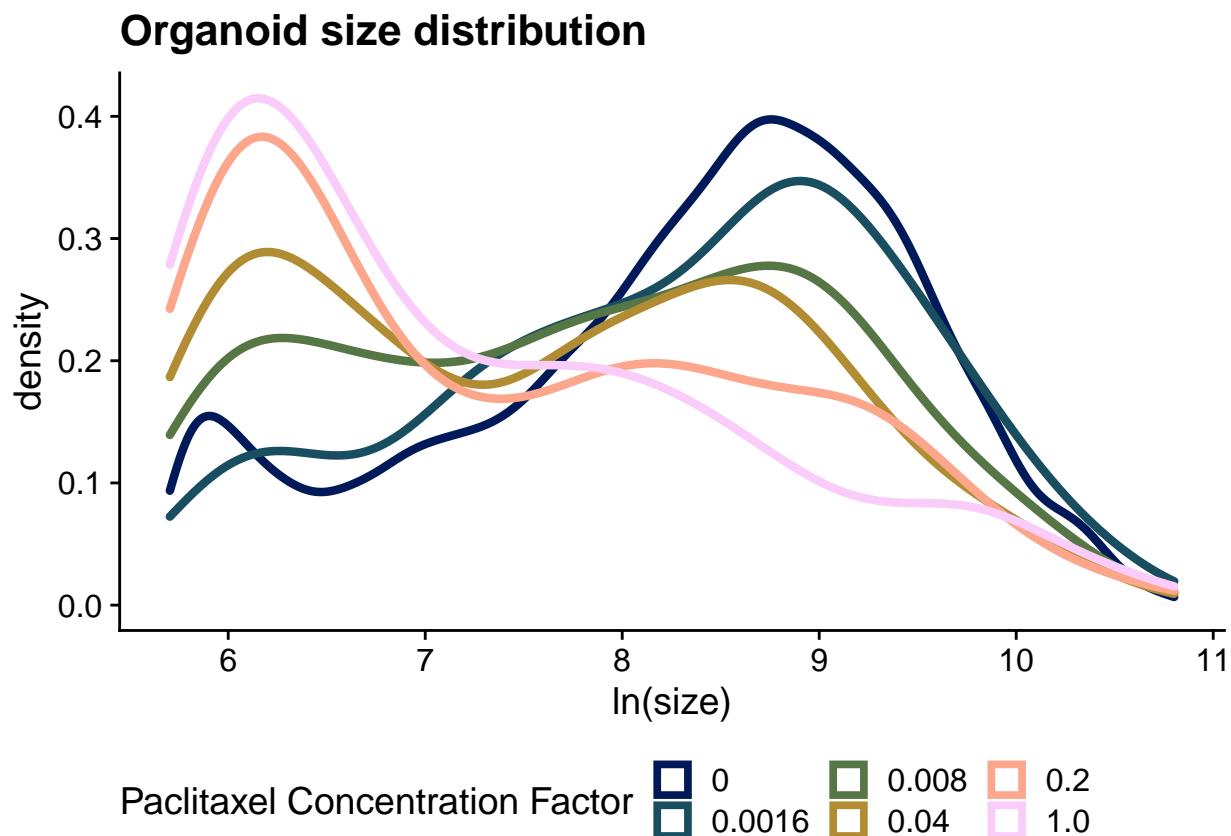
umap_size <- function(umap){
  umap %>%
  #filter(Size < 1000) %>%
  ggplot(aes(v1, v2, color = size_log)) +
  geom_point_rast(alpha = 0.5, size = 0.35) +
  scale_color_viridis_c() +
  theme_cowplot() +
  labs(x = "UMAP 1",
       y = "UMAP 2",
       color = "ln(size)") +
  theme(legend.position = "bottom")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

gg_size <- umap_size(umap_df %>% filter(partition %in% c(1,2)))

```

Organoid Size during Drug Treatment

```
drug_size <- umap_df %>% filter(partition %in% c(1,2)) %>% filter(drug == "DMSO" | drug == "Paclitaxel") %>%  
  mutate(concentration = ifelse(drug == "DMSO", 0, concentration)) %>%  
  #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
```



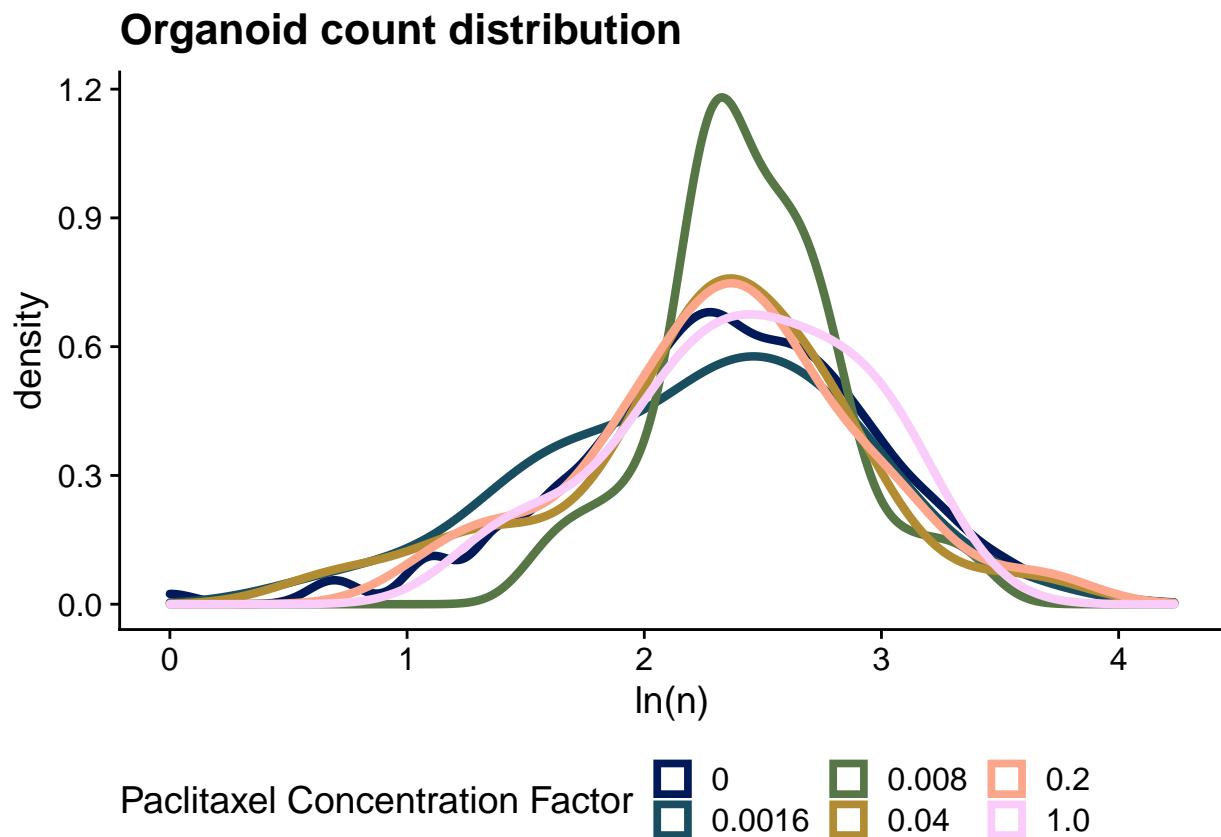
```
drug_count <- drug_size %>%  
  dplyr::count(concentration, line, replicate, well)  
  
ggdrug_count <- ggplot(drug_count) +
```

```

geom_density(aes(x = log(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 = "ln(n)")

ggdrug_count

```



```

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

df <- umap_df %>%
  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 %>% 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 %>%

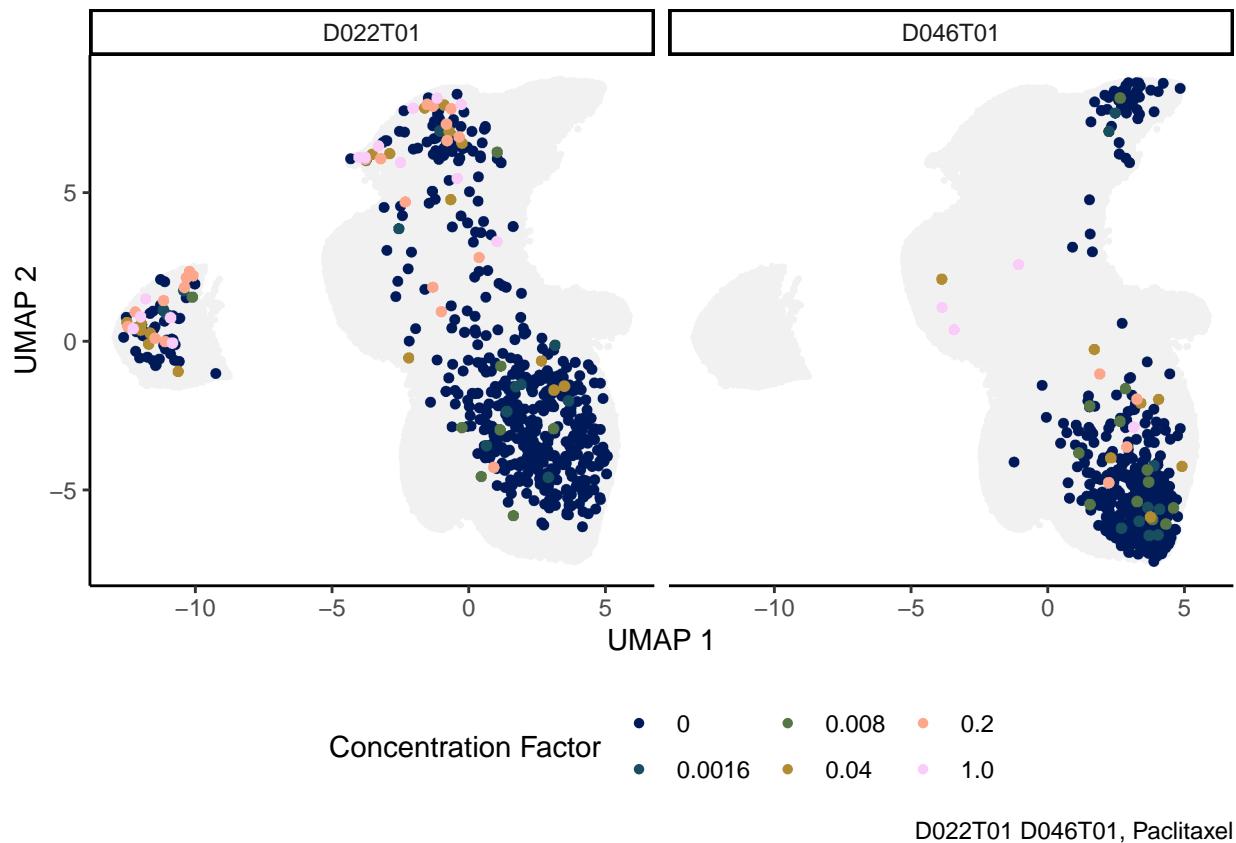
```

```

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") +
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", "D055T01")

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

```

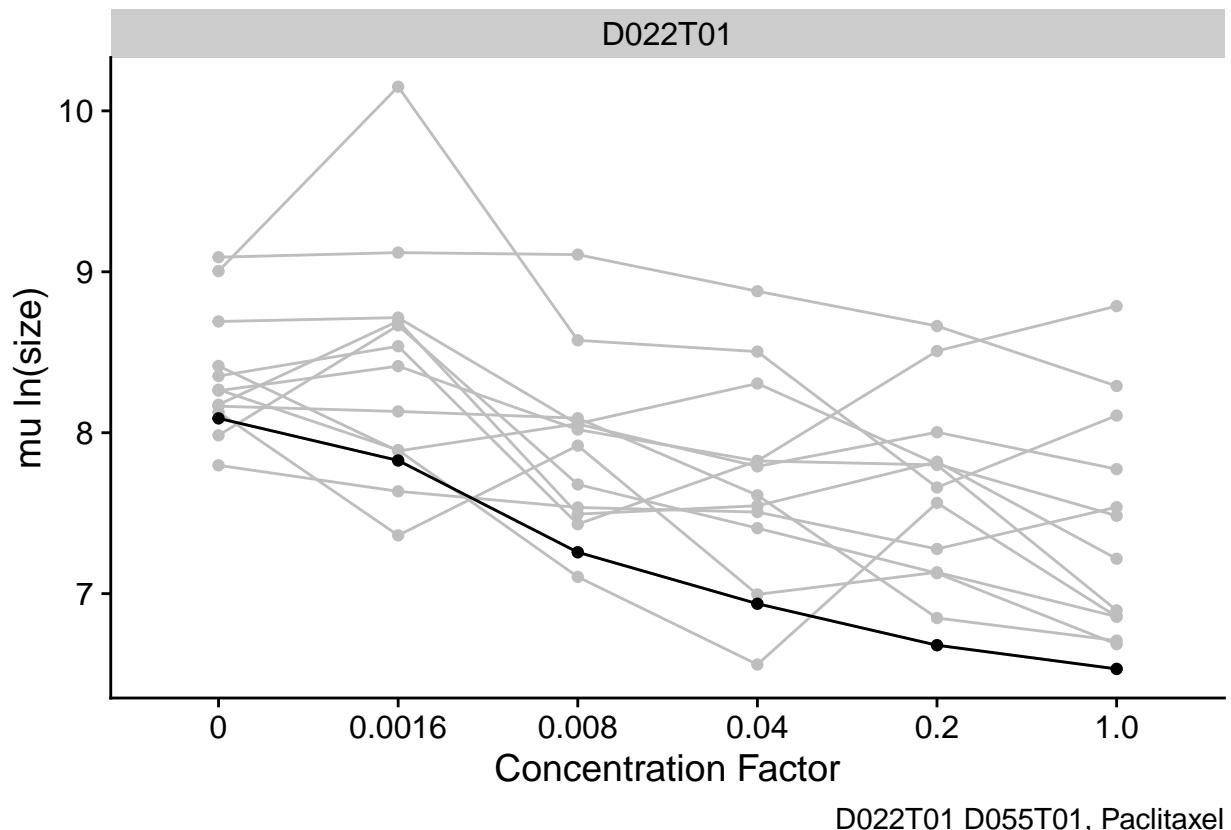
```

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, main){
  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",
       title = main,
       color = "p(dead)") +
  theme(legend.position = "bottom") +
  guides(fill = guide_colourbar(barwidth = 0.5, barheight = 10))
}

p1 <- umap_ldc(unmap_sampled_h, "Harmony normalised, All data")
p2 <- umap_ldc(unmap_sampled, "Raw Data, All data")
p3 <- umap_ldc(unmap_sampled_dmso_h, "Harmony normalised, DMSO")
p4 <- umap_ldc(unmap_sampled_dmso, "Raw Data, DMSO")

plot_grid(
  p1, p2,
  p3, p4,
  labels = "AUTO", ncol = 2
) + ggsave(paste0(PATH, "notebooks/PhenotypeSpectrum/gg_ldc_panel.pdf"),
            width = 8,
            height = 8)

p2 + ggsave(paste0(PATH, "notebooks/PhenotypeSpectrum/gg_ldc.pdf"), width = 4, height = 4)

```

Organoid Heterogeneity

I plot 2 organoid lines treated with DMSO control

```

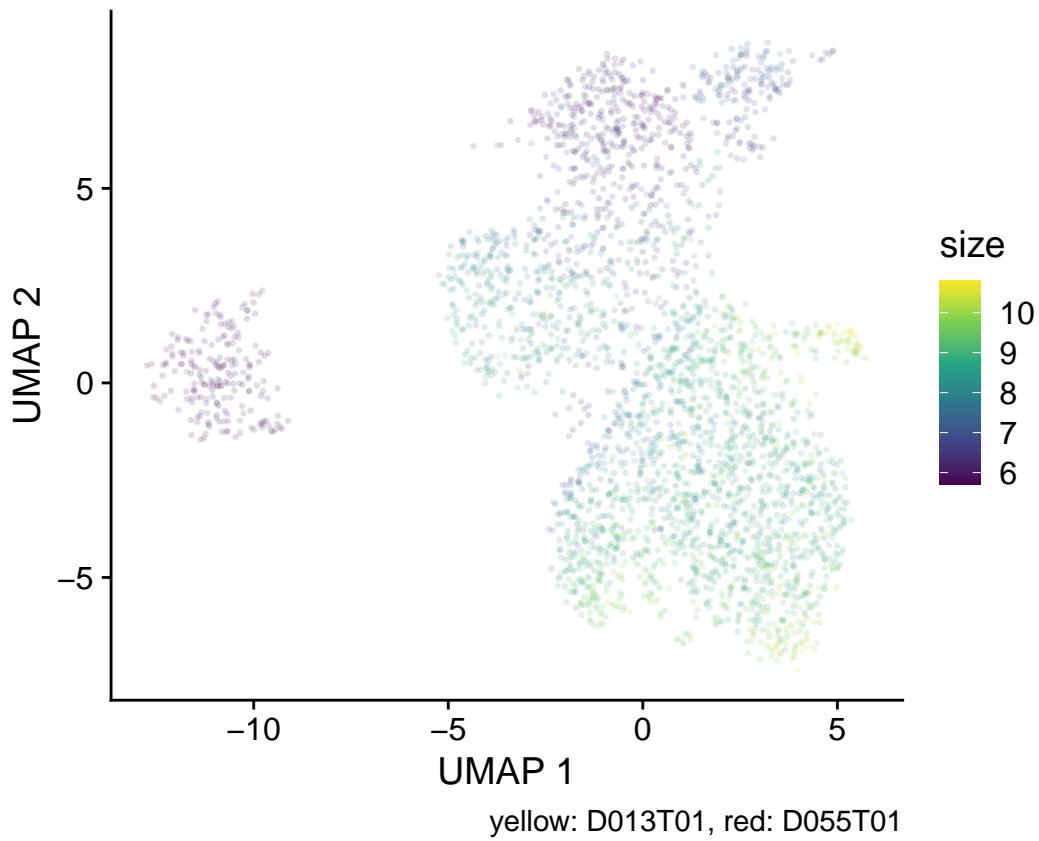
set.seed(234)

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 == "D055T01" & well == "D24" & plate == "D055T01P007L02", 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
```



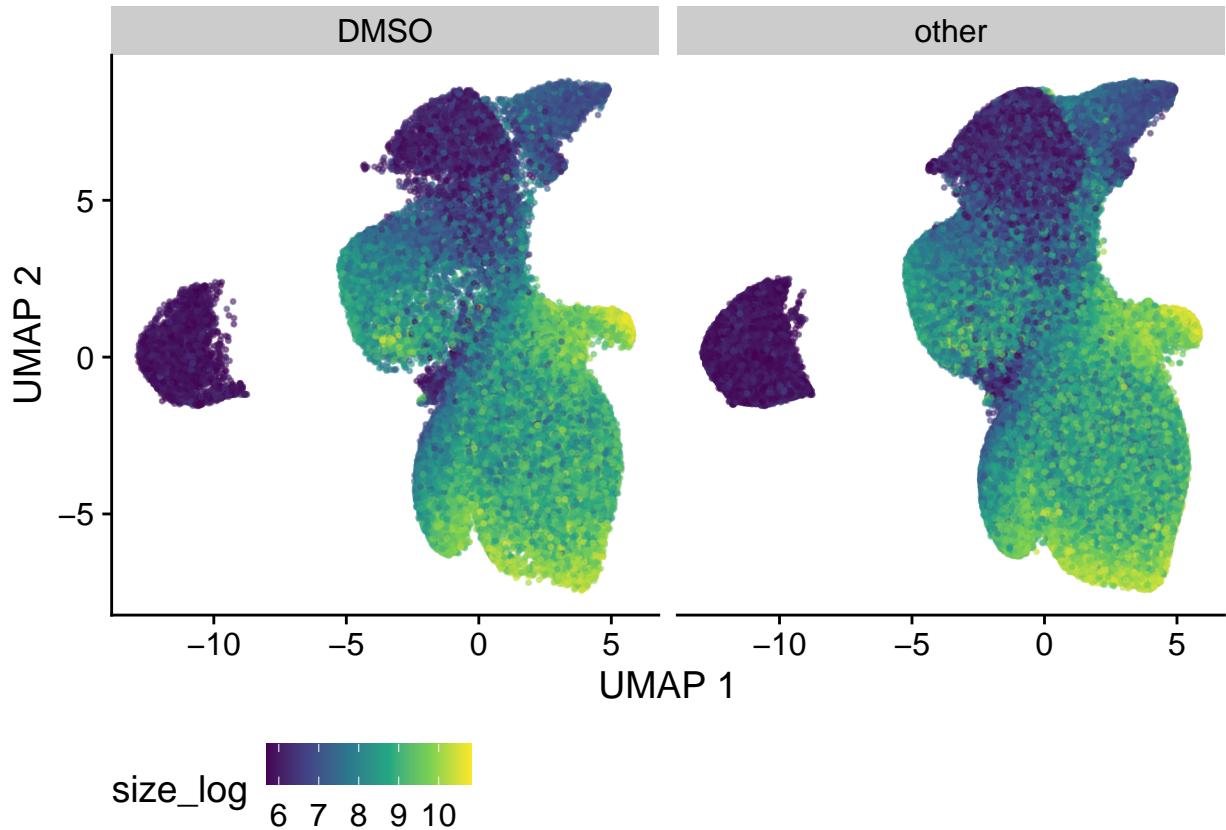
In general, DMSO treated organoid lines cover the same latent space than drug treated organoids. This is likely influenced by the large number of untreated organoids in the dataset.

```
set.seed(123)

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

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)

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



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", "D027T01", "D018T01") #c("D055T01", "D007T01", "D021T01", "D019T01", "D021T01")
#loi <- umap_df$line %>% unique()

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

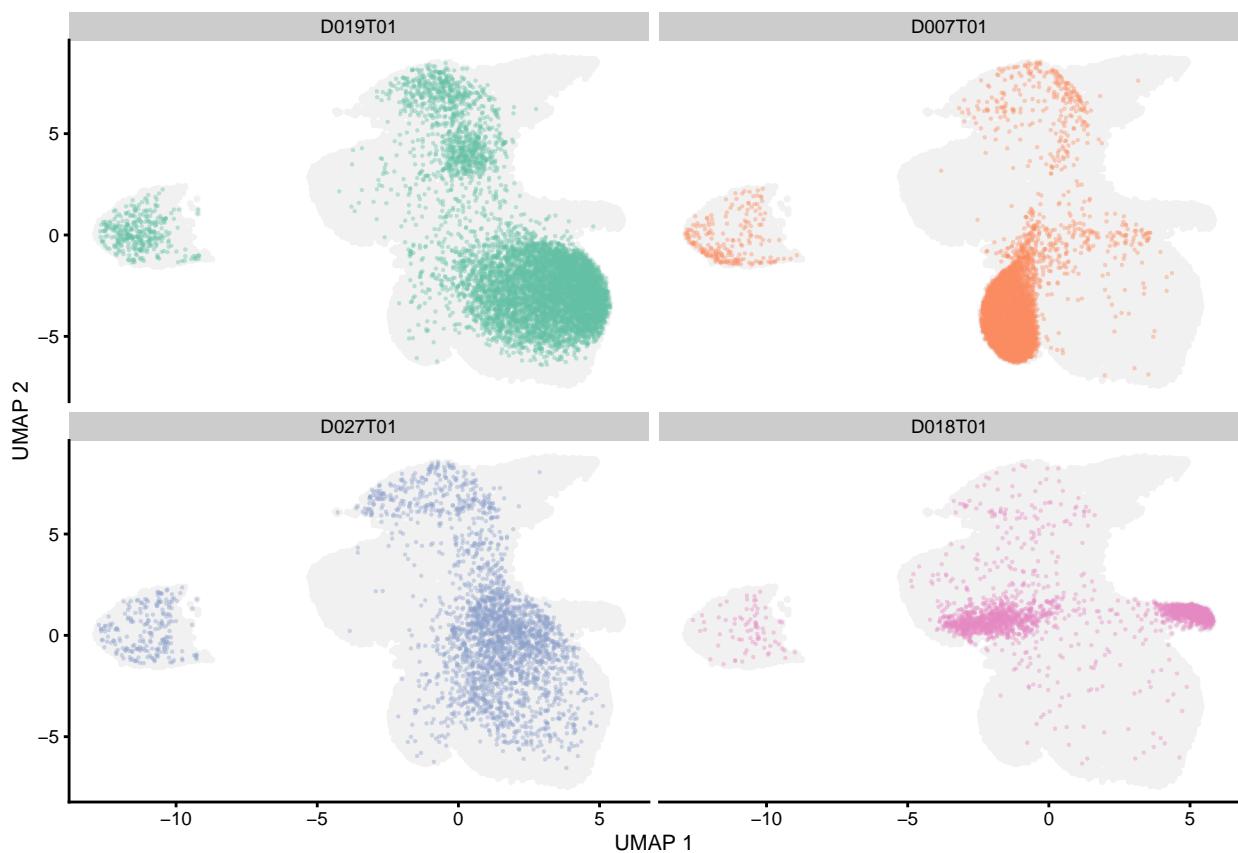
gg_line <- df %>% dplyr::select(-line) %>%
  ggplot(aes(v1, v2)) +
  geom_point_rast(alpha = 1, size = 0.35, color = "#f1f1f1") +
  geom_point_rast(data = umap_df %>%
    filter(drug == "DMSO") %>%
    # filter(line %in% c("D021T01")) %>%
    filter(line %in% loi) %>%
    mutate(line = factor(line, levels = 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/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),

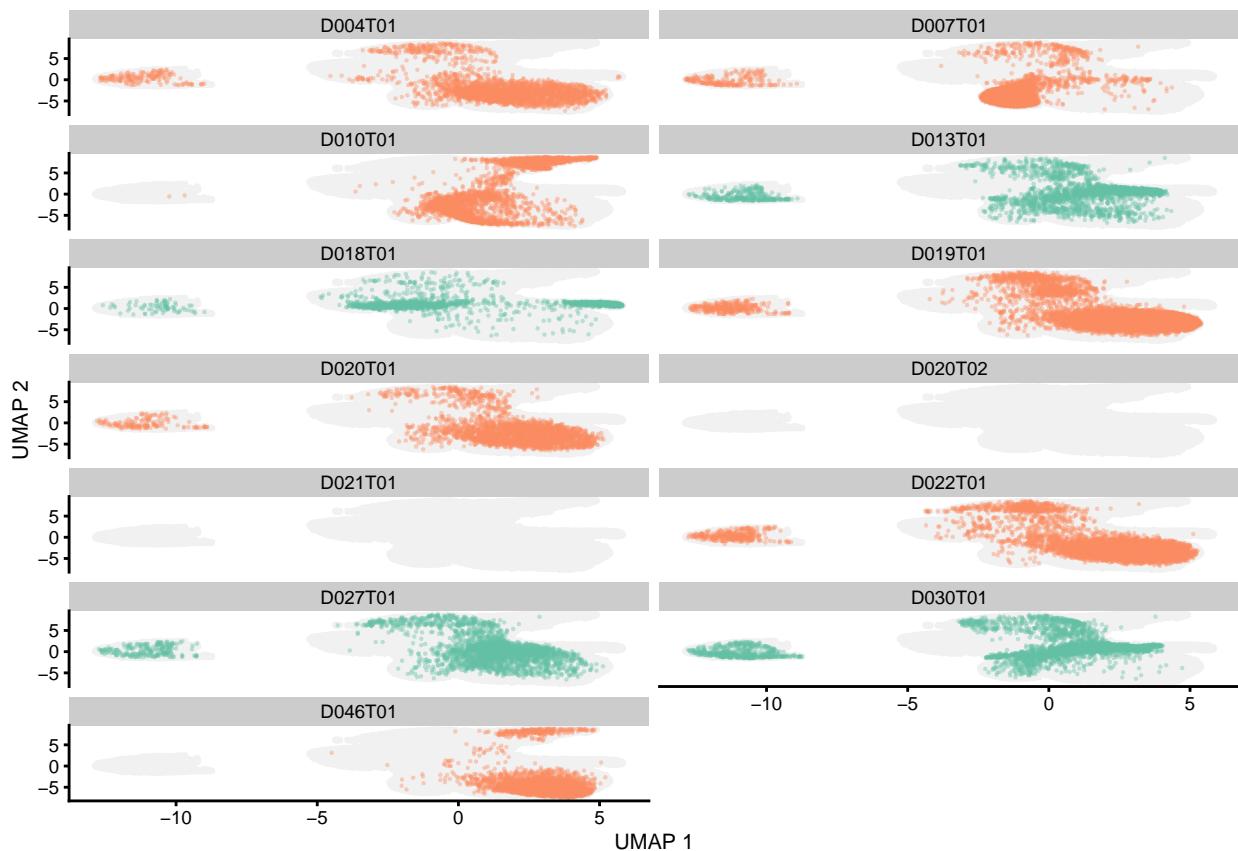
```

```

#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 = "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_morph + ggsave(paste0(PATH, "reports/figures/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")), # %>%

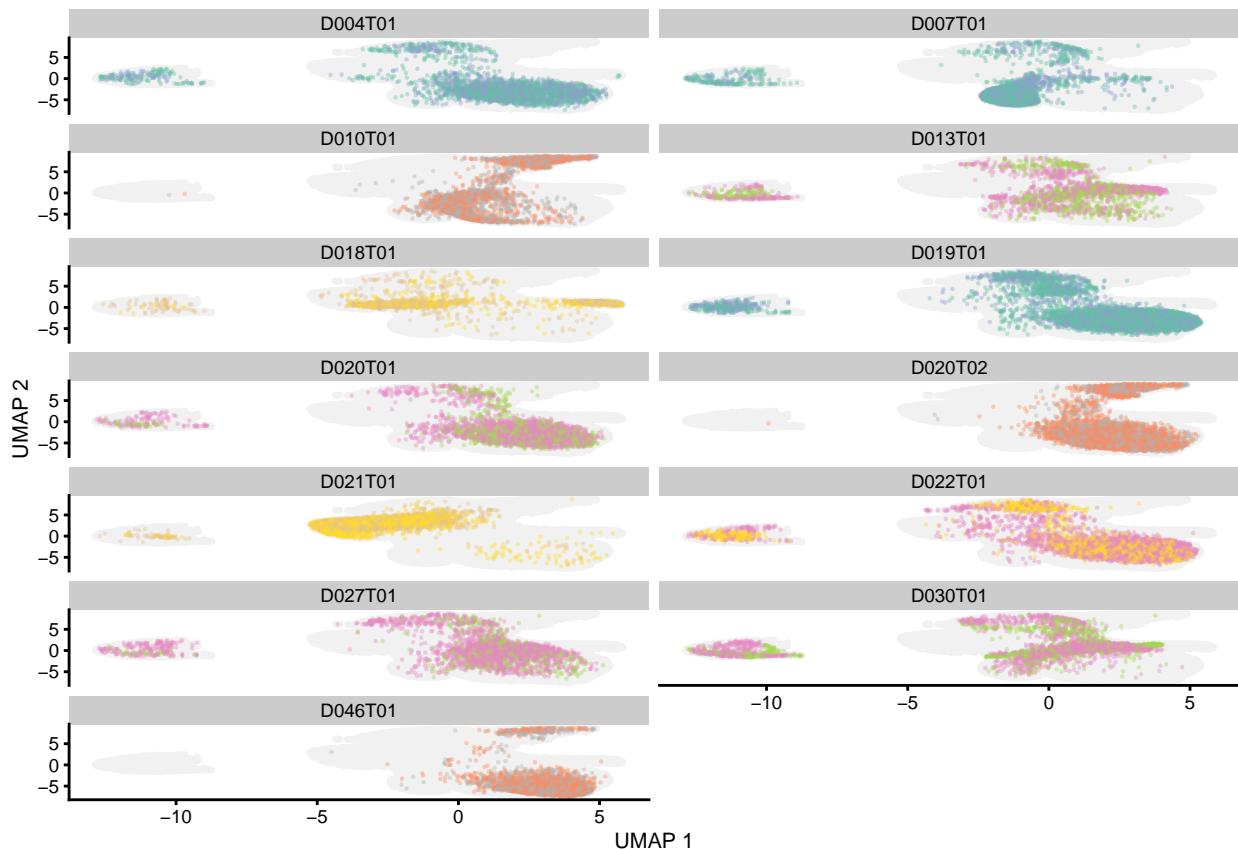
```

```

#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 =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_screen_id + ggsave(paste0(PATH, "reports/figures/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)

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/gg_actin.pdf"), width = 4, height = 4)

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 = "Nuclear staining intensity") +
theme(legend.position = "bottom") +
ggsave(paste0(PATH, "reports/figures/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")

```

```

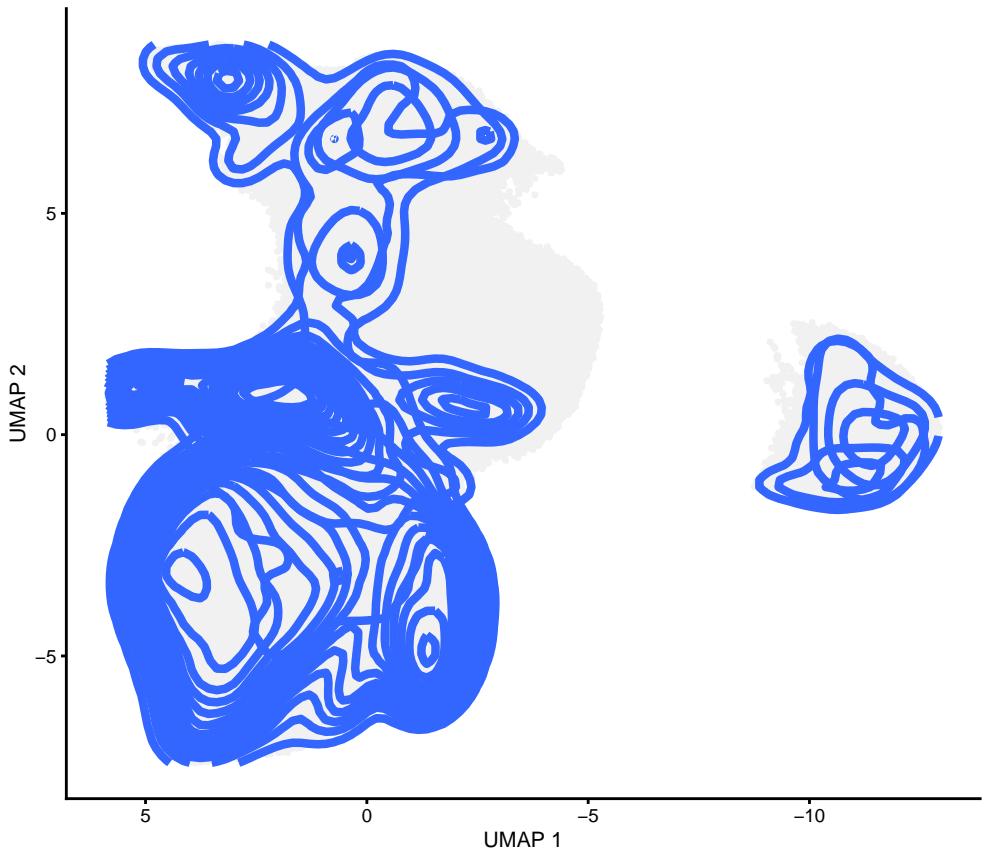
dense_l <- organoid_morphology %>% filter(morphology == "solid") %>%.line %>% paste0(., "01")

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

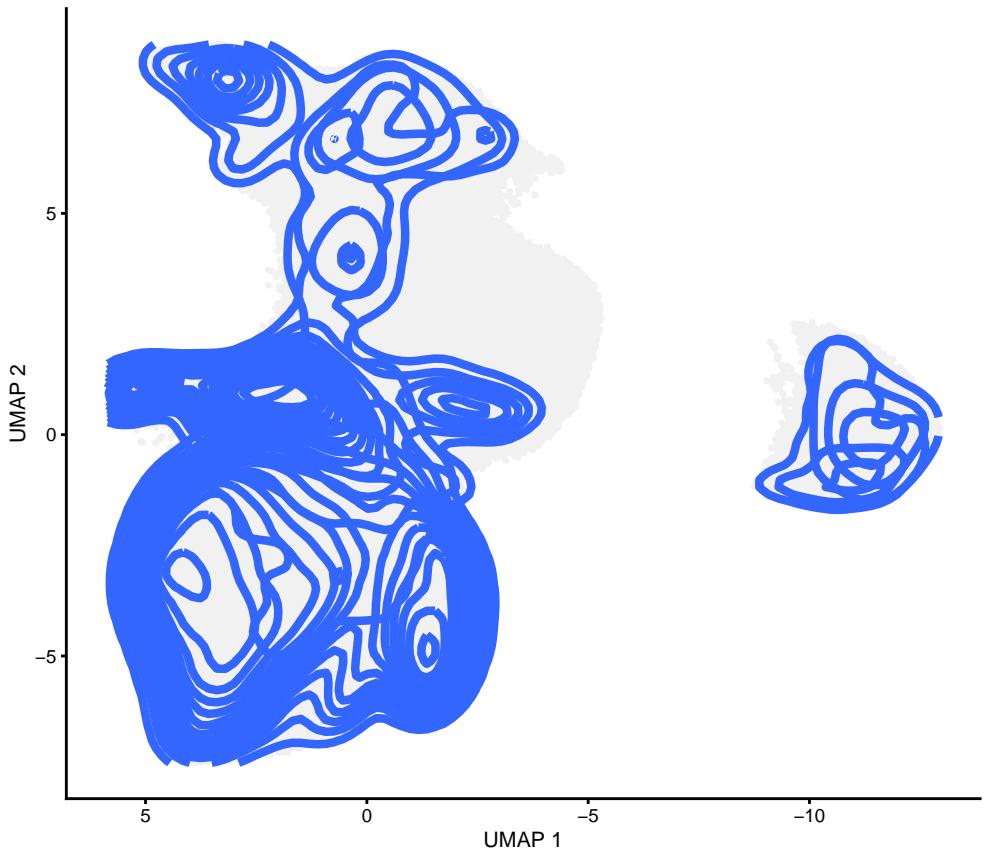
```



Plot Export

```
#gg_size_dist + ggsave(paste0(PATH, "reports/figures/gg_size_dist.pdf"))
#gg_size_dist_log + ggsave(paste0(PATH, "reports/figures/gg_size_dist_log.pdf"))
#gdrug_size + ggsave(paste0(PATH, "reports/figures/gg_drug_dist_size_log.pdf"))
#gg_ecdf + ggsave(paste0(PATH, "reports/figures/gg_size_dist_ecdf.pdf"))
#gg_size_dist_morph_ridge + ggsave(paste0(PATH, "reports/figures/gg_size_dist_morph_ridge.pdf"), width = 3.65, height = 4)

# ggdrug_count + ggsave(paste0(PATH, "reports/figures/gg_drug_dist_n_log.pdf"))
# gg_drug + ggsave(paste0(PATH, "reports/figures/gg_drug.pdf"), width = 8, height = 4)
# gg_size_drug + ggsave(paste0(PATH, "reports/figures/gg_trametinib_size_dose.pdf"), width = 3.65, height = 4)
gg_cystic + ggsave(paste0(PATH, "reports/figures/gg_cystic.pdf"), width = 4, height = 4)
```



```

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-p0.3.8.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    printrcurve_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      isoband_0.2.1
## [17] pillar_1.4.4     glue_1.4.1      withr_2.2.0      fitdistrplus_1.1-1
## [21] RColorBrewer_1.1-2 lifecycle_0.2.0   plyr_1.8.6       stringr_1.4.0
## [25] munsell_0.5.0    gtable_0.3.0    evaluate_0.14    labeling_0.3
## [29] knitr_1.28       Cairo_1.5-12    viper_0.4.5      fansi_0.4.1
## [33] broom_0.5.6     Rcpp_1.0.4.6    scales_1.1.1     backports_1.1.7
## [37] farver_2.0.3     hms_0.5.3      digest_0.6.25    stringi_1.4.6
## [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

```