20190701_orthogroup_stat_analysis

July 8, 2020

[1]:
```
import numpy, pandas, datetime, sys, os
import matplotlib, seaborn
import re, math, time, scipy
import sqlite3, IPython.display, sqlalchemy, statsmodels, ete3, svgutils.
 ↪transform
import lxml.etree, gseapy, mygene
import itertools
import igraph
import upsetplot
import random
import subprocess
import importlib
from svgpathtools import svg2paths
from sqlalchemy.types import *
import statsmodels
from statsmodels.sandbox.regression.predstd import wls_prediction_std
from networkx.drawing.nx_agraph import write_dot
from decimal import Decimal

sys.path.append('/Users/kef74yk/Dropbox_w/repos/kftools')
sys.path.append('/Users/kef74yk/Dropbox_w/repos/kftools/kftools')

import kftools
kftools = importlib.reload(kftools)
from kftools import kfplot
from kftools import kfutil
from kftools import kfstat

font_size = 8

%matplotlib inline
pandas.options.display.max_rows=10
pandas.options.display.max_columns=1000
seaborn.set_style("white")
seaborn.set_style("ticks")
matplotlib.rcParams['font.size'] = font_size
#matplotlib.rcParams['font.family'] = 'Helvetica'
```

```
#matplotlib.rc('font',**{'family':'sans-serif','sans-serif':['Helvetica']})
matplotlib.rcParams['svg.fonttype'] = 'none' # none, path, or svgfont

matplotlib.rc('xtick', labelsize=font_size)
matplotlib.rc('ytick', labelsize=font_size)
matplotlib.rc('font', size=font_size)
matplotlib.rc('axes', titlesize=font_size)
matplotlib.rc('axes', labelsize=font_size)
matplotlib.rc('xtick', labelsize=font_size)
matplotlib.rc('ytick', labelsize=font_size)
matplotlib.rc('legend', fontsize=font_size)
matplotlib.rc('figure', titlesize=font_size)
```

[2]:
```
omega_method = 'mapdnds' # 'hyphy' or 'mapdnds'
#l1ou_criterion = 'AICc'
#expression_unit = 'TPM' # 'FPKM', 'TPM'
#intersect_fpkm_tpm = False
sptree_root = 'sp_root'

dir_data = '/Users/kef74yk/Dropbox_p/data/'
wd = os.path.join(dir_data, "04_transcriptome_amalgamation/
 ↪20190701_orthogroup_stat_analysis/out/")
dir_ensembl = os.path.join(dir_data, '/Users/kef74yk/Dropbox_p/db/Ensembl/
 ↪release-91/')
#db_file = os.path.join(dir_ensembl, 'orthogroup/Ensembl.91.orthogroup.
 ↪'+l1ou_criterion+'.db')
db_file = os.path.join(dir_ensembl, 'orthogroup/Ensembl.91.orthogroup.db')
sptree_file = os.path.join(dir_ensembl, 'timetree/species_timetree.nwk')
phylopic_dir = os.path.join(dir_ensembl, 'phylopic/svg_files/')
inkscape='/Applications/Inkscape.app/Contents/Resources/bin/inkscape'
if not (os.path.exists(wd)):
    os.mkdir(wd)
os.chdir(wd)


font_size = 8
max_delta_intron_present=-0.5
pcm_prefixes = ['l1ou_fpkm_','l1ou_tpm_',]
shift_columns =␣
 ↪['l1ou_fpkm_is_shift','l1ou_tpm_is_shift','l1ou_intersect_is_shift']
branch_categories = ['S','D','R']
category_colors = {'S':'#0033cc', 'D':'#cc0000', 'R':'#e59400'}
organs = ['brain','heart','kidney','liver','ovary','testis']
organ_colors = ['#1B9E77','#D95F02','#7570B3','#E7298A','#66A61E','#E6AB02']

organ_colors_dict = dict()
for o,c in zip(organs,organ_colors):
```

```
    organan_colors_dict[o] = c
```

[3]:
```
def attach_neighbor_stats(df, neighbor, columns=[]):
    columns = ['orthogroup','numerical_label',] + columns
    df_tmp = df.loc[:,columns]
    df_tmp.columns = neighbor+'_'+pandas.Series(df_tmp.columns).astype(str)
    right_on = [neighbor+'_orthogroup',neighbor+'_numerical_label']
    df = pandas.merge(df, df_tmp, left_on=['orthogroup',neighbor],␣
 ↪right_on=right_on, how='left')
    df = df.drop(right_on, axis=1)
    return df

def my_distplot(x, df, ax, kde, xlab, norm_hist, x_range):
    seaborn.distplot(df[x], ax=ax, kde=kde, norm_hist=norm_hist, color='black')
    ax.tick_params(axis='both', which='major', direction='in', length=6,␣
 ↪width=1)
    ax.set_xlabel(xlab)
    if norm_hist:
        ax.set_ylabel('Frequency')
    else:
        ax.set_ylabel('Count')
    if (len(x_range)>1)&(type(x_range)!=str):
        ax.set_xlim(x_range[0], x_range[1])

def my_barplot(x, y, ax, xlab, ylab):
    seaborn.barplot(x=x, y=y, ax=ax, color='gray')
    ax.set_xlabel(xlab)
    ax.set_ylabel(ylab)
    ax.tick_params(axis='both', which='major', direction='in', length=6,␣
 ↪width=1)

def add_missing_data(df, index=[], columns=[]):
    try:
        del df.index.name
    except:
        0
    try:
        del df.columns.name
    except:
        0
    for ind in index:
        if not ind in df.index:
            df = pandas.concat([df, pandas.DataFrame(0, index=[ind,],␣
 ↪columns=df.columns)], axis=0)
    for col in columns:
        if not col in df.columns:
```

```
            df = pandas.concat([df, pandas.DataFrame(0, index=df.index,␣
↪columns=[col,])], axis=1)
    df = df.sort_index(axis=0)
    df = df.sort_index(axis=1)
    return df

def add_igraph_legends(svg_file, height, width, texts=[]):
    font_size = 8
    font_family = 'Helvetica'
    fig = svgutils.transform.SVGFigure(str(width)+"pt", str(height)+"pt")
    figs = list()
    figs.append(svgutils.transform.fromfile(svg_file))
    plots = list()
    for i in range(len(figs)):
        plots.append(figs[i].getroot())
    plots[0].moveto(x=0, y=0, scale=1)
    txts = list()
    for i in range(len(texts)):
        txts.append(svgutils.transform.TextElement(x=0, y=font_size*(i+2),␣
↪text=texts[i], size=font_size, weight="normal", font=font_family))
    fig.append(plots)
    fig.append(txts)
    fig.save(svg_file)

def calc_symmetry(pivot_table):
    if not type(pivot_table)==type(pandas.DataFrame()):
        pivoto_table = pivot_table * (numpy.eye(pivot_table.shape[0],␣
↪pivot_table.shape[1])==0)
        pivot_table = pandas.DataFrame(pivot_table)
    pivot_table = pivot_table.fillna(0)
    organs = list(set(pivot_table.index.tolist()).intersection(set(pivot_table.
↪columns.tolist())))
    dif = 0
    for i in itertools.combinations(organs, 2):
        if i[0]!=i[1]:
            dif = dif + numpy.abs(pivot_table.loc[i[0],i[1]] - pivot_table.
↪loc[i[1],i[0]])
    symmetry = 1 - (dif/pivot_table.sum().sum())
    return(symmetry)

def integrate_pcm_stats(df, pcm_prefix, drop=False):
    num_og_before = 0
    df['pcm_method'] = ''
    for pp in pcm_prefix:
        pp_columns = df.columns[df.columns.str.startswith(pp)]
        for ppc in pp_columns:
            new_column = ppc.replace(pp, '')
```

```
            if not (new_column in df.columns):
                df[new_column] = df[ppc]
            else:
                df.loc[df[new_column].isnull(), new_column] = df.
 ↪loc[df[new_column].isnull(), ppc]
        if drop:
            df = df.drop(pp_columns, axis=1)
        col = 'regime' if 'regime' in df.columns else 'num_regime'
        df.loc[(~df[col].isnull())&(df['pcm_method']==''),'pcm_method'] = re.
 ↪sub('_$','',pp)
        num_og_after = df.loc[(~df[col].isnull()),'orthogroup'].
 ↪drop_duplicates().shape[0]
        print(pp, ': number of added orthogroups =', num_og_after -␣
 ↪num_og_before)
        num_og_before = num_og_after
    return df

def add_max_mu(df=pandas.DataFrame(), cols=[], new_col=''):
    df[new_col] = df.loc[:,cols].idxmax(axis=1)
    num_null_before = df[new_col].isnull().sum()
    tmp = df.loc[:,cols].values
    row_max = tmp.max(axis=1)
    for i in numpy.arange(tmp.shape[1]):
        tmp[:,i] = tmp[:,i] - row_max
    is_multiple_max = ((tmp==0).sum(axis=1)!=1)
    df.loc[is_multiple_max,new_col] = numpy.nan
    num_null_after = is_multiple_max.sum()
    print(new_col, ':', num_null_after-num_null_before, 'tie max values were␣
 ↪detected')
    return df

def shift_freq_bootstrap(df1, var1='parent_max_organ', var2='max_organ',␣
 ↪down_reg=True, up_reg=True,
                         exclude_self=True, nboot=1000, nsubsample=numpy.inf):
    if exclude_self:
        df1 = df1.loc[(df1[var1]!=df1[var2]),:]
    if df1.shape[0]>nsubsample:
        df1 = df1.loc[numpy.random.choice(df1.index, nsubsample,␣
 ↪replace=False),:]
    df1 = df1.sort_values(axis=0, by=[var1, var2])
    df1 = df1.reset_index()
    N = df1.shape[0]
    print('N after filtering =', N)
    all_organs = pandas.concat([df1[var1],df1[var2]]).dropna().unique()
    all_organs.sort()
    observed = pandas.DataFrame(df1.groupby([var1,var2])['orthogroup'].count())
```

```
    observed = observed.reset_index().pivot(var1, var2)
    colnames = observed.columns.get_level_values(1)
    observed = observed.T.reset_index(drop=True).T
    observed.columns = colnames
    observed = observed.fillna(0)
    observed = add_missing_data(df=observed, index=all_organs,␣
↪columns=all_organs)
    if exclude_self:
        observed_total = observed.sum().sum()
        index_values = observed.index
        column_values = observed.columns
        self_true = numpy.array([ i==c for i in index_values for c in␣
↪column_values ]).reshape([index_values.shape[0],column_values.shape[0]])
    nrep = nboot
    num_var1 = df1[var1].unique().shape[0]
    num_var2 = df1[var2].unique().shape[0]
    axis = [nrep, observed.shape[0], observed.shape[1]]
    bs = numpy.zeros(axis, dtype=numpy.int64)
    replace=False
    for i in numpy.arange(nrep):
        df3 = df1.loc[:,:]
        if replace:
            df3.loc[:,var1] = df3.loc[numpy.random.choice(df3.index, size=df3.
↪shape[0], replace=replace),var1].values
        df3.loc[:,var2] = df3.loc[numpy.random.choice(df3.index, size=df3.
↪shape[0], replace=replace),var2].values
        pivot = pandas.DataFrame(df3.groupby([var1,var2])['orthogroup'].count())
        pivot = pivot.reset_index().pivot(var1, var2)
        pivot.columns = pivot.columns.get_level_values(1)
        if replace:
            if not observed.index.shape[0]==pivot.index.shape[0]:
                organs = list(set(observed.columns.tolist() + observed.index.
↪tolist()))
                missings = [ pcol for pcol in organs if not pcol in pivot.index␣
↪]
                for missing in missings:
                    pivot.loc[missing,:] = 0
            if not observed.columns.shape[0]==pivot.columns.shape[0]:
                organs = list(set(observed.columns.tolist() + observed.index.
↪tolist()))
                missings = [ pcol for pcol in organs if not pcol in pivot.
↪columns.get_level_values(1) ]
                for missing in missings:
                    pivot['orthogroup',missing] = 0
        pivot = add_missing_data(df=pivot, index=all_organs, columns=all_organs)
        pivot = pivot.fillna(0).values
```

```
        if exclude_self:
            pivot[self_true] = 0
            pivot = pivot / pivot.sum().sum() * observed_total
        bs[i,:,:] = pivot
        del df3
    del df1
    col_sum = observed.sum(axis=0)
    row_sum = observed.sum(axis=1)
    col_sum = numpy.expand_dims(col_sum, axis=0)
    row_sum = numpy.expand_dims(row_sum, axis=1)
    col_freq = col_sum / col_sum.sum().sum()
    row_freq = row_sum / row_sum.sum().sum()
    expected = numpy.array(col_freq * row_freq)
    if exclude_self:
        expected[self_true] = 0
    expected = expected / expected.sum().sum() * observed.sum().sum()
    expected = pandas.DataFrame(expected)
    expected.index = observed.index
    expected.columns = observed.columns
    corrected = observed/expected.values
    corrected = add_missing_data(df=corrected, index=all_organs,␣
↪columns=all_organs)
    corrected = corrected.fillna(0)

    return(corrected,observed,expected,bs,N)

def draw_network(corrected, observed, expected, bs, self_arrow=False,␣
↪self_vertex_size=False, show_vertex_stat=False,
                 edge_width=1, hide_nonsig=False, coordinates=None,␣
↪test='random'):
    bs_mean = pandas.DataFrame(bs.mean(axis=0))
    bs_conf95lower = pandas.DataFrame(numpy.percentile(bs, axis=0, q=2.5))
    bs_conf95upper = pandas.DataFrame(numpy.percentile(bs, axis=0, q=97.5))
    bs_conf99lower = pandas.DataFrame(numpy.percentile(bs, axis=0, q=0.5))
    bs_conf99upper = pandas.DataFrame(numpy.percentile(bs, axis=0, q=99.5))
    bs_IQRlower = pandas.DataFrame(numpy.percentile(bs, axis=0, q=25))
    bs_IQRupper = pandas.DataFrame(numpy.percentile(bs, axis=0, q=75))
    for bs in␣
↪[bs_mean,bs_conf95lower,bs_conf95upper,bs_conf99lower,bs_conf99upper,bs_IQRlower,bs_IQRuppe
↪
        bs.index = observed.index
        bs.columns = observed.columns
    g = igraph.Graph(directed=True)
    vertices = pandas.Series(list(set(corrected.index.tolist()+corrected.
↪columns.tolist())))
    vertex_weights = list()
    vertex_labels = list()
```

```
    vertex_colors = list()
    tissue_colors={'brain':'#1B9E77','heart':'#D95F02','kidney':
↪'#7570B3','liver':'#E7298A','ovary':'#66A61E','testis':'#E6AB02'}
    my_coordinates = list()
    for organ in vertices:
        if (organ in corrected.index)&(organ in corrected.columns):
            vertex_weights.append(corrected.loc[organ,organ])
            n_parent = str(int(observed.loc[organ,:].sum().sum()))
            n_child = str(int(observed.loc[:,organ].sum().sum()))
            organ = organ.replace('-', '\n')
            if show_vertex_stat:
                vertex_labels.append(organ+'\n'+n_parent+':'+n_child)
            else:
                vertex_labels.append(organ)
        else:
            vertex_labels.append(organ)
            vertex_weights.append(1)
            if show_vertex_stat:
                organ = organ.replace('-', '\n')
                vertex_labels.append(organ)
        if organ in tissue_colors.keys():
            vertex_colors.append(tissue_colors[organ])
        else:
            vertex_colors.append('darkgray')
        if coordinates is not None:
            my_coordinates.append(coordinates[organ])
    g.add_vertices(vertices)
    edge_weights = list()
    edge_colors = list()
    edge_labels = list()
    edge_curves = list()
    if test=='rank':
        df_rank = pandas.DataFrame(observed.values.flatten())
        df_rank = df_rank.rank()
        df_rank = numpy.reshape(df_rank.values, newshape=observed.shape)
        df_rank = df_rank - min(observed.shape) # setting baseline by excluding␣
↪diagonal elements
        numpy.fill_diagonal(a=df_rank, val=0)
        df_rank = pandas.DataFrame(df_rank).astype(int)
        df_rank.index = observed.index
        df_rank.columns = observed.columns
        rank_colors = kfutil.get_rgb_gradient(ncol=int(df_rank.max().max()),␣
↪col1=[0,0,1], col2=[1,0,0], colm=[0.5,0.5,0.5])
    for organ1 in corrected.index:
        for organ2 in corrected.columns:
            flag = True if (self_arrow)|(self_vertex_size) else organ1!=organ2
            if flag:
```

```
                organ1id = vertices.loc[vertices==organ1].index.values[0]
                organ2id = vertices.loc[vertices==organ2].index.values[0]
                corrected_value = corrected.loc[organ1,organ2]
                expected_value = expected.loc[organ1,organ2]
                observed_value = observed.loc[organ1,organ2]
                if test=='random':
                    if (observed_value==int(observed_value)):
                        edge_label = str(int(observed_value))+'/'+str(int(numpy.
↪round(expected_value, decimals=0)))
                    else:
                        edge_label = str(numpy.round(observed_value,␣
↪decimals=2))+'/'+str(numpy.round(expected_value, decimals=2))
                    color = igraph.color_name_to_rgba('#808080')
                    if observed.loc[organ1,organ2] < bs_IQRlower.
↪loc[organ1,organ2]:
                        color = igraph.color_name_to_rgba('#808080')
                    if observed.loc[organ1,organ2] < bs_conf95lower.
↪loc[organ1,organ2]:
                        color = igraph.color_name_to_rgba('#40C040')
                    if observed.loc[organ1,organ2] < bs_conf99lower.
↪loc[organ1,organ2]:
                        color = igraph.color_name_to_rgba('#00FF00')
                    if observed.loc[organ1,organ2] > bs_IQRupper.
↪loc[organ1,organ2]:
                        color = igraph.color_name_to_rgba('#808080')
                    if observed.loc[organ1,organ2] > bs_conf95upper.
↪loc[organ1,organ2]:
                        color = igraph.color_name_to_rgba('#C040C0')
                    if observed.loc[organ1,organ2] > bs_conf99upper.
↪loc[organ1,organ2]:
                        color = igraph.color_name_to_rgba('#FF00FF')
                elif test=='chisq':
                    parentY_childY = observed.loc[(observed.index==organ1),␣
↪(observed.columns==organ2)].sum().sum()
                    parentY_childN = observed.loc[(observed.index==organ1),␣
↪(observed.columns!=organ2)].sum().sum()
                    parentN_childY = observed.loc[(observed.index!=organ1),␣
↪(observed.columns==organ2)].sum().sum()
                    parentN_childN = observed.loc[(observed.index!=organ1),␣
↪(observed.columns!=organ2)].sum().sum()
                    cont_table = pandas.DataFrame([[parentY_childY,␣
↪parentY_childN],[parentN_childY, parentN_childN]])
                    chi2_out = scipy.stats.
↪chi2_contingency(observed=cont_table, correction=True)
                    chi2 = chi2_out[0]
                    pvalue = chi2_out[1]
```

```
                    print(organ1, organ2, chi2, pvalue)
                    print('test = chisq. This option is not yet implemented.')
                elif test=='rank':
                    rank = int(df_rank.loc[organ1,organ2])
                    rgb = rank_colors[rank-1]
                    hex_color = kfutil.rgb_to_hex(rgb[0],rgb[1],rgb[2])
                    color = igraph.color_name_to_rgba(hex_color)
                    edge_label = ''
                g.add_edges([(organ1id,organ2id),])
                if edge_width=='observed':
                    edge_weight = 0.5
                    if observed_value >= 10:
                        edge_weight = 1
                    if observed_value >= 100:
                        edge_weight = 2
                else:
                    edge_weight = edge_width
                edge_weights.append(edge_weight)
                edge_colors.append(color)
                edge_labels.append(edge_label)
                edge_curve = -0.05
                if (organ1 not in corrected.columns)|(organ2 not in corrected.
↪index):
                    edge_curve = 0
                edge_curves.append(edge_curve)
    if hide_nonsig:
        for i in range(len(edge_labels)):
            if edge_colors[i]==igraph.color_name_to_rgba('#808080'):
                edge_labels[i] = ''
    visual_style = {}
    visual_style["vertex_size"] = [ v*20 for v in vertex_weights ] if␣
↪self_vertex_size else 26#27
    visual_style["vertex_label"] = vertex_labels
    visual_style["vertex_color"] = vertex_colors
    visual_style["vertex_label_color"] = 'black'
    visual_style["vertex_label_size"] = 8 if show_vertex_stat else 8
    visual_style["edge_width"] = edge_weights
    visual_style["edge_arrow_size"] = 0.5
    visual_style["edge_label"] = edge_labels
    visual_style["edge_label_size"] = 6
    visual_style["edge_label_color"] = edge_colors
    visual_style["edge_color"] = edge_colors
    visual_style["edge_curved"] = edge_curves
    #random.seed(22) #15 #6 #9
    if coordinates is None:
        layout = g.layout("circular")#"kk"
    else:
```

```
        layout = my_coordinates
    return(g,layout,visual_style)

def ols_annotations(x, y, data=None, ax=None, color='black', font_size=8,␣
↪textxy=[0.05,0.95], textva='top',
                    method='quantreg', stats=['N','slope','slope_p']):
    import statsmodels.api as sm
    import statsmodels.formula.api as smf
    if data is None:
        data = pandas.DataFrame({'X':x,'Y':y})
        x = 'X'
        y = 'Y'
    data = data.sort_values(x)
    if method=='ols':
        X = sm.add_constant(data.loc[:,x])
        Y = data.loc[:,y]
        mod = sm.OLS(Y, X)
        res = mod.fit()
    elif method=='quantreg':
        mod = smf.quantreg(y+' ~ '+x, data)
        res = mod.fit(q=0.5)
    N = data.shape[0]
    slope = res.params[x]
    slope_p = res.pvalues[x]
    rsquared = res.rsquared_adj
    rsquared_p = res.f_pvalue
    text = ''
    for stat in stats:
        if stat=='N':
            text += 'N = {:,}\n'.format(N)
        if stat=='slope':
            text += 'slope = {}\n'.format('%.2f'%Decimal(slope))
        if stat=='slope_p':
            text += 'P = {}\n'.format('%.2E'%Decimal(slope_p))
        if stat=='rsquared':
            text += 'R2 = {}\n'.format('%.2f'%Decimal(rsquared))
        if stat=='rsquared_p':
            text += 'P = {}\n'.format('%.2E'%Decimal(rsquared_p))
    ax.text(textxy[0], textxy[1], text, transform=ax.transAxes, va=textva,␣
↪color=color, fontsize=font_size)
    xmin = data.loc[:,x].min()
    xmax = data.loc[:,x].max()
    ax.plot(data[x].values[[0,N-1]], res.predict()[[0,N-1]], color=color)

def get_quantile(observed, bs):
    q = observed.copy()
    q.loc[:,:] = numpy.nan
```

```
    for i in range(q.shape[0]):
        for c in range(q.shape[1]):
            gt_count = (observed.iloc[i,c]>bs[:,i,c]).sum()
            ge_count = (observed.iloc[i,c]>=bs[:,i,c]).sum()
            corrected_rank = (gt_count + ge_count)/2
            q.iloc[i,c] = corrected_rank/bs.shape[0]
    return q

def get_quantile_fdr(quantile, fdr_threshold=0.001, tail='both'):
    q2 = quantile.copy()
    if tail=='both':
        q2[q2<0.5] = 1-q2[q2<0.5]
    f = q2.values.flat
    decimals = 0
    thresholds = numpy.array([])
    for d in numpy.arange(1,10):
        start = 1-(10**(-float(d-1)))
        end = 1-(10**(-float(d)))
        step = (10**(-float(d-1)))/1000
        tmp = numpy.arange(start, end, step)
        thresholds = numpy.concatenate((thresholds, tmp))
        if all(f==numpy.round(f, decimals=d)):
            decimals = d
            break
    if decimals!=0:
        print('Inferred number of permutations:', 10**decimals)
    else:
        print('Number of permutations could not be inferred.')
    num_data = q2.shape[0] * q2.shape[1]
    for i in numpy.arange(len(thresholds)):
        fdr = ((1-thresholds[i])*num_data)/((f > thresholds[i]).sum())
        if fdr<fdr_threshold:
            quantile_threshold = thresholds[i]
            print('FDR={}, Quantile threshold={}'.format(fdr,␣
↪quantile_threshold))
            break
        assert i<(len(thresholds)-1), 'No quantile threshold satisfied FDR␣
↪threshold.'
    fdrs = q2 > quantile_threshold
    return fdrs

def draw_network2(observed, quantile, fdrs, self_arrow=False,␣
↪self_vertex_size=False, show_vertex_stat=False, no_obs=True,
                  edge_width=False, edge_width_weight=None, hide_nonsig=False,␣
↪vertex_dict=None, coordinates=None,
                 show_edge_color=True, scaled_edge_curve=False,␣
↪relative_freq_edge_width=False, no_fp=False, sig_color='bluered'):
```

```
    g = igraph.Graph(directed=True)
    if sig_color=='bluered':
        high_color = '#FF0000'
        low_color = '#0000FF'
    elif sig_color=='greenpink':
        high_color = '#FF00FF'
        low_color = '#00FF00'
    if vertex_dict is None:
        vertices = pandas.Series(list(set(observed.index.tolist()+observed.
↪columns.tolist())))
        vertex_colors = 'darkgray'
    else:
        vertices = pandas.Series(vertex_dict['vertex'])
        vertex_colors = pandas.Series(vertex_dict['color'])
    vertex_weights = list()
    vertex_labels = list()
    my_coordinates = list()
    for v in vertices:
        if (v in observed.index)&(v in observed.columns):
            vertex_weights.append(observed.loc[v,v])
            n_parent = str(int(observed.loc[v,:].sum().sum()))
            n_child = str(int(observed.loc[:,v].sum().sum()))
            v = v.replace('-', '\n')
            if show_vertex_stat:
                vertex_labels.append(v+'\n'+n_parent+':'+n_child)
            else:
                vertex_labels.append(v)
        else:
            vertex_labels.append(v)
            vertex_weights.append(1)
            if show_vertex_stat:
                v = v.replace('-', '\n')
                vertex_labels.append(v)
        if coordinates is not None:
            my_coordinates.append(coordinates[v])
    g.add_vertices(vertices)
    edge_weights = list()
    edge_colors = list()
    edge_labels = list()
    edge_curves = list()
    for v1 in observed.index:
        for v2 in observed.columns:
            flag = True if (self_arrow)|(self_vertex_size) else v1!=v2
            if (no_fp)&(v1 in ['F','P'])&(v2 in ['F','P']):
                flag = False
            if flag:
                v1id = vertices.loc[vertices==v1].index.values[0]
```

```
                v2id = vertices.loc[vertices==v2].index.values[0]
                observed_value = observed.loc[v1,v2]
                edge_label = str(int(observed_value))
                color = igraph.color_name_to_rgba('#808080')
                if (fdrs.loc[v1,v2])&(quantile.loc[v1,v2]<0.5):
                    color = igraph.color_name_to_rgba(low_color)
                else:
                    if (not no_obs)&(observed.loc[v1,v2]==0):
                        continue
                if (fdrs.loc[v1,v2])&(quantile.loc[v1,v2]>0.5):
                    color = igraph.color_name_to_rgba(high_color)
                g.add_edges([(v1id,v2id),])
                edge_weight = 0.5
                if edge_width=='discrete':
                    if observed_value >= 10:
                        edge_weight = 1
                    if observed_value >= 100:
                        edge_weight = 2
                elif edge_width=='identity':
                    edge_weight = observed_value+1
                elif edge_width=='log':
                    edge_weight = numpy.log2(observed_value+1)
                edge_weights.append(edge_weight)
                edge_colors.append(color)
                edge_labels.append(edge_label)
                edge_curve = -0.2 if (len(vertices) < 5) else -0.01
                if (v1 not in observed.columns)|(v2 not in observed.index):
                    edge_curve = 0
                if scaled_edge_curve:
                    v1coordinate = my_coordinates[v1id]
                    v2coordinate = my_coordinates[v2id]
                    euclidean_dist = numpy.linalg.norm(numpy.
↪array(v1coordinate)-numpy.array(v2coordinate))
                    edge_curve = edge_curve * ((1+euclidean_dist)*2)
                edge_curves.append(edge_curve)
    if hide_nonsig:
        for i in range(len(edge_labels)):
            if edge_colors[i]==igraph.color_name_to_rgba('#808080'):
                edge_labels[i] = ''
    if relative_freq_edge_width:
        edge_weights = [ ew/sum(edge_weights)*20 for ew in edge_weights ]
    visual_style = {}
    visual_style["vertex_size"] = [ v*20 for v in vertex_weights ] if␣
↪self_vertex_size else 26
    visual_style["vertex_label"] = vertex_labels
    visual_style["vertex_color"] = vertex_colors
    visual_style["vertex_label_color"] = 'black'
```

```
    visual_style["vertex_label_size"] = 8 if show_vertex_stat else 8
    visual_style["edge_width"] = edge_weights
    visual_style["edge_arrow_size"] = 0.5
    visual_style["edge_label"] = edge_labels
    visual_style["edge_label_size"] = 6
    visual_style["edge_label_color"] = edge_colors if show_edge_color else␣
 ↪'black'
    visual_style["edge_color"] = edge_colors if show_edge_color else 'black'
    visual_style["edge_curved"] = edge_curves
    #random.seed(22) #15 #6 #9
    if coordinates is None:
        layout = g.layout("circular")#"kk"
    else:
        layout = my_coordinates
    return(g,layout,visual_style)
```

[4]:
```
print('start:', "{0:%Y-%m-%d %H:%M:%S}".format(datetime.datetime.today()))

conn = sqlalchemy.create_engine("sqlite:///"+db_file)
#b = pandas.read_sql_query(sql="SELECT * from branch", con=conn,␣
 ↪index_col=None, coerce_float=True)
#t = pandas.read_sql_query(sql="SELECT * from tree", con=conn, index_col=None,␣
 ↪coerce_float=True)
b = pandas.read_sql_query(sql="SELECT * from branch", con=conn, index_col=None,␣
 ↪coerce_float=True)
t = pandas.read_sql_query(sql="SELECT * from tree", con=conn, index_col=None,␣
 ↪coerce_float=True)

conn.dispose()

tissues = ['brain','heart','kidney','liver','ovary','testis']

#b = integrate_pcm_stats(b, pcm_prefix)
#t = integrate_pcm_stats(t, pcm_prefix)

b.loc[:,'l1ou_intersect_is_shift'] = (b['l1ou_fpkm_is_shift'].fillna(0).
 ↪astype(bool))&(b['l1ou_tpm_is_shift'].fillna(0).astype(bool))
b.loc[b.parent==0,'so_event_parent'] = 'No'
b.loc[(b.spnode_coverage=='root')&(b.so_event_parent=='S'),'so_event_parent'] =␣
 ↪'No'
b['chromosome'] = b.loc[:,['A','X','Y']].idxmax(axis=1)

for pp in pcm_prefixes:
    mus = [ pp+'mu_'+o for o in␣
 ↪['brain','heart','kidney','liver','ovary','testis'] ]
    b[pp+'max_mu'] = b.loc[:,mus].max(axis=1)
```

```
    b[pp+'second_max_mu'] = numpy.sort(b.loc[:,mus].values)[:,-2]
    b[pp+'max_second_mu_ratio'] = b[pp+'max_mu'] - b[pp+'second_max_mu']
    pc = mus + [pp+'tau',␣
 ↪pp+'max_mu',pp+'second_max_mu',pp+'max_second_mu_ratio',pp+'is_shift',]
    b = attach_neighbor_stats(df=b, neighbor='parent', columns=pc)
    b = attach_neighbor_stats(df=b, neighbor='sister', columns=[pp+'is_shift',])

for ext in ['_omega','_dn','_ds']:
    cols = b.columns[b.columns.str.endswith(ext)]
    for col in cols:
        b['log_'+col] = numpy.log(b[col])
b = attach_neighbor_stats(df=b, neighbor='parent',␣
 ↪columns=['l1ou_intersect_is_shift','chromosome','age','support_iqtree'])
sc =␣
 ↪['delta_intron_present','hyphy_omega','mapdnds_omega','log_hyphy_omega','log_mapdnds_omega'
b = attach_neighbor_stats(df=b, neighbor='sister', columns=sc)
b.loc[(b.spnode_coverage.isnull()),'spnode_coverage'] = sptree_root

for pcm_prefix in pcm_prefixes:
    for tis in tissues:
        b[pcm_prefix+'delta_mu_'+tis] = b[pcm_prefix+'mu_'+tis] -␣
 ↪b['parent_'+pcm_prefix+'mu_'+tis]
        b.loc[b.parent==0,pcm_prefix+'delta_mu_'+tis] = 0

    for prefix in ['mu_','delta_mu_']:
        targets = [ pcm_prefix+prefix+o for o in tissues ]
        b[pcm_prefix+prefix+'max'] = b.loc[:,targets].idxmax(axis=1)
        b[pcm_prefix+prefix+'max'] = b[pcm_prefix+prefix+'max'].str.
 ↪replace(pcm_prefix+prefix,'')
        b.loc[b.loc[:,targets].sum(axis=1)==0,pcm_prefix+prefix+'max'] = 'no'

    prefixes =␣
 ↪[pcm_prefix+'delta_mu_',pcm_prefix+'mu_','parent_'+pcm_prefix+'mu_',]
    newcols =␣
 ↪[pcm_prefix+'max_upregulation',pcm_prefix+'max_organ','parent_'+pcm_prefix+'max_organ']
    for prefix,newcol in zip(prefixes, newcols):
        cols = [ prefix+o for o in tissues ]
        b = add_max_mu(df=b, cols=cols, new_col=newcol)
        b[newcol] = b[newcol].str.replace(prefix,'')

is_parent_dup = b.so_event_parent=='D'
is_retrotransposition = (b.delta_intron_present<=max_delta_intron_present)
is_sister_retrotransposition = (b.
 ↪sister_delta_intron_present<=max_delta_intron_present)
is_lower_delta_intron_present = (b.delta_intron_present<=b.
 ↪sister_delta_intron_present)
```

```
is_higher_dnds = (b[omega_method+'_omega']>=b['sister_'+omega_method+'_omega'])
b['branch_category'] = numpy.nan
b.loc[(~is_parent_dup),'branch_category'] = 'S'
b.
 ↪loc[(~is_retrotransposition)&(~is_sister_retrotransposition)&(is_parent_dup),'branch_catego
 ↪= 'D'
b.
 ↪loc[(is_retrotransposition)&(is_lower_delta_intron_present)&(is_parent_dup),'branch_categor
 ↪= 'R'
b.loc[(b.so_event_parent.isnull()),'branch_category'] = numpy.nan

b = attach_neighbor_stats(df=b, neighbor='parent', columns=['branch_category',])
b = attach_neighbor_stats(df=b, neighbor='sister',␣
 ↪columns=['branch_category','spnode_coverage'])

for sc in shift_columns:
    conditions = True
    conditions = (conditions)&(b['spnode_coverage']!=sptree_root).fillna(False)
    conditions = (conditions)&(b['sister_spnode_coverage']!=sptree_root).
 ↪fillna(False)
    conditions = (conditions)&((b[sc]==1).fillna(False)|(b['sister_'+sc]==1).
 ↪fillna(False))
    conditions = (conditions)&~((b[sc]==1).fillna(False)&(b['sister_'+sc]==1).
 ↪fillna(False))
    conditions = (conditions)&~((b['sister_branch_category']=='R')&(b[sc]==1).
 ↪fillna(False))
    conditions =␣
 ↪(conditions)&~((b['branch_category']=='R')&(b['sister_'+sc]==1).
 ↪fillna(False))
    conditions = (conditions)&(b.branch_category!='No')
    b.loc[:,sc+'_pair'] = conditions

t = t.loc[(~t['l1ou_tpm_alpha_brain'].isnull())&(~t['l1ou_fpkm_alpha_brain'].
 ↪isnull()),:]
b = b.loc[(~b['l1ou_tpm_mu_brain'].isnull())&(~b['l1ou_fpkm_mu_brain'].
 ↪isnull()),:]
b = b.loc[:,~b.columns.str.contains('phylogeneticem')]
t = t.loc[:,~t.columns.str.contains('phylogeneticem')]

print('Number of orthogroups in the tree table:', t['orthogroup'].unique().
 ↪shape[0])
print('Number of orthogroups in the branch table:', b['orthogroup'].unique().
 ↪shape[0])

criterion = 'l1ou_fpkm_alpha_brain'
is_leaf = (b['so_event']=='L')
```

```
analyzed_orthogroups = t.loc[(~t[criterion].isnull()),'orthogroup']
num_analyzed_orthogroups = analyzed_orthogroups.shape[0]
is_analyzed = (b['orthogroup'].isin(analyzed_orthogroups))

spp = b.loc[(is_leaf)&(is_analyzed),'node_name'].str.replace('_',' ', 1).str.
 ↪replace('_.*','').unique()
num_spp = spp.shape[0]
num_genes = b.loc[(is_leaf)&(is_analyzed),:].shape[0]
mean_num_gene_per_sp = num_genes / num_spp
num_human_genes = b.loc[(is_leaf)&(is_analyzed)&(b['node_name'].str.
 ↪startswith('Homo')),:].shape[0]

print('The number of species analyzed:', num_spp)
print('The number of orthogroups analyzed:', num_analyzed_orthogroups)
print('The average number of genes per species:', mean_num_gene_per_sp)
print('The number of analyzed genes:', num_genes)
print('The number of analyzed human genes:', num_human_genes)

sci_names = b['spnode_coverage'].drop_duplicates()
for sn in sci_names:
    if len(sn)>4:
        is_gene = (b['node_name'].str.startswith(sn)) &␣
 ↪(~b['l1ou_fpkm_mu_brain'].isnull())
        is_introned_gene = (is_gene) & (b['num_intron']>=1)
        is_intronless_gene = (is_gene) & (b['num_intron']==0)
        print(sn, '# gene:', is_gene.sum(), '# intron-containing:',␣
 ↪is_introned_gene.sum(), '# intronless:', is_intronless_gene.sum())

is_root = (b['spnode_coverage']=='root')
is_shift = (b['l1ou_intersect_is_shift']==1)
num_all_shift = (~is_root&is_shift).sum()
print('Number of all shifts:', num_all_shift)
for event in b['branch_category'].unique():
    is_event = (b['branch_category']==event)
    num_branch = ((~is_root)&(is_event)).sum()
    num_shift = ((~is_root)&is_event&is_shift).sum()
    print('Number of {} branches: {}'.format(event, num_branch))
    print('Number of {} shifts: {} or {}%'.format(event, num_shift, num_shift/
 ↪num_all_shift*100))

TEC_cutoff = 0.5
num_higher_tec = (b.loc[is_shift,'l1ou_fpkm_mu_complementarity']>=TEC_cutoff).
 ↪sum()
print('Number of highly complementary shifts: {} or {}%. TEC threshold = {}'.
 ↪format(num_higher_tec, num_higher_tec/num_all_shift, TEC_cutoff))
```

```
print('Number of trees dated with non-RDS constraint: {}'.
 ↪format((t['dating_method']!='RDS').sum()))

tmp = b.loc[:,['orthogroup','mapdnds_omega','hyphy_omega']].replace([numpy.inf,␣
 ↪-numpy.inf], numpy.nan).dropna()
sout = scipy.stats.spearmanr(tmp['mapdnds_omega'], tmp['hyphy_omega'])
pout = scipy.stats.pearsonr(tmp['mapdnds_omega'], tmp['hyphy_omega'])
print('All: Omega correlation between mapdNdS and Hyphy: {}'.format(sout))
print('All: Omega correlation between mapdNdS and Hyphy: {}'.format(pout))

print('end:', "{0:%Y-%m-%d %H:%M:%S}".format(datetime.datetime.today()))

c = 'orthogroup'
is_nonc = [ col!=c for col in t.columns ]
nonc = t.columns[is_nonc].tolist()
t = t.loc[:,[c,] + nonc]
t = t.sort_values(by=c, axis=0)
t.to_csv('orthogroup_statistics.tsv', sep='\t', index=False)
```

```
start: 2020-07-08 10:54:12
```

```
/Users/kef74yk/anaconda3/lib/python3.6/site-packages/pandas/core/series.py:679:
RuntimeWarning: divide by zero encountered in log
  result = getattr(ufunc, method)(*inputs, **kwargs)
```

```
l1ou_fpkm_max_upregulation : 584780 tie max values were detected
l1ou_fpkm_max_organ : 0 tie max values were detected
parent_l1ou_fpkm_max_organ : 0 tie max values were detected
l1ou_tpm_max_upregulation : 583600 tie max values were detected
l1ou_tpm_max_organ : 0 tie max values were detected
parent_l1ou_tpm_max_organ : 0 tie max values were detected
Number of orthogroups in the tree table: 15280
Number of orthogroups in the branch table: 15280
The number of species analyzed: 21
The number of orthogroups analyzed: 15280
The average number of genes per species: 15474.666666666666
The number of analyzed genes: 324968
The number of analyzed human genes: 20873
Bos_taurus # gene: 17022 # intron-containing: 15673 # intronless: 1349
Callithrix_jacchus # gene: 16432 # intron-containing: 15526 # intronless: 906
Canis_lupus # gene: 16219 # intron-containing: 14775 # intronless: 1444
Chinchilla_lanigera # gene: 15053 # intron-containing: 14604 # intronless: 449
Homo_sapiens # gene: 20873 # intron-containing: 19990 # intronless: 883
Macaca_mulatta # gene: 15771 # intron-containing: 14935 # intronless: 836
Mus_musculus # gene: 19946 # intron-containing: 18970 # intronless: 976
Oryctolagus_cuniculus # gene: 15108 # intron-containing: 13539 # intronless:
1569
```

```
Ovis_aries # gene: 15765 # intron-containing: 14504 # intronless: 1261
Rattus_norvegicus # gene: 18573 # intron-containing: 16778 # intronless: 1795
Sus_scrofa # gene: 16871 # intron-containing: 15745 # intronless: 1126
Anolis_carolinensis # gene: 12971 # intron-containing: 12029 # intronless: 942
Astyanax_mexicanus # gene: 15235 # intron-containing: 14319 # intronless: 916
Danio_rerio # gene: 19628 # intron-containing: 18794 # intronless: 834
Gallus_gallus # gene: 13023 # intron-containing: 12229 # intronless: 794
Oreochromis_niloticus # gene: 17734 # intron-containing: 16955 # intronless: 779
Ornithorhynchus_anatinus # gene: 7467 # intron-containing: 7025 # intronless:
442
sp_root # gene: 0 # intron-containing: 0 # intronless: 0
Oryzias_latipes # gene: 13633 # intron-containing: 13181 # intronless: 452
Xenopus_tropicalis # gene: 13566 # intron-containing: 12774 # intronless: 792
Monodelphis_domestica # gene: 15424 # intron-containing: 13854 # intronless:
1570
Gadus_morhua # gene: 8654 # intron-containing: 8313 # intronless: 341
Number of all shifts: 19636
Number of S branches: 556240
Number of S shifts: 11762 or 59.90018333672846%
Number of D branches: 72476
Number of D shifts: 6480 or 33.00061112242819%
Number of R branches: 2985
Number of R shifts: 1107 or 5.637604400081483%
Number of nan branches: 0
Number of nan shifts: 0 or 0.0%
Number of highly complementary shifts: 18583 or 0.9463740069260542%. TEC
threshold = 0.5
Number of trees dated with non-RDS constraint: 5642
All: Omega correlation between mapdNdS and Hyphy:
SpearmanrResult(correlation=0.7278447626412824, pvalue=0.0)
All: Omega correlation between mapdNdS and Hyphy: (-3.159100507681842e-06,
0.9980921341552754)
end: 2020-07-08 10:55:25
```

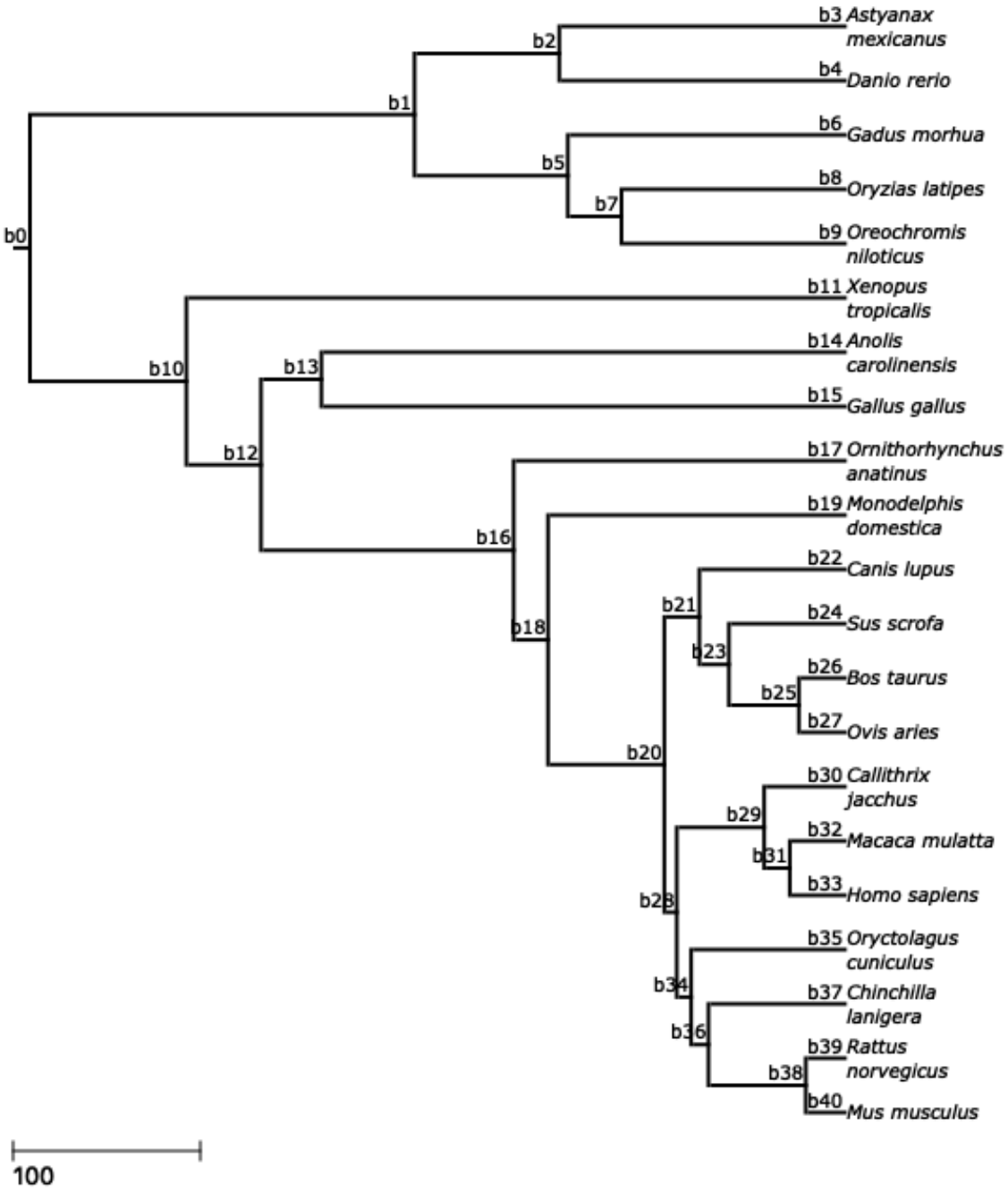
[5]:
```python
# prepare sptree
sptree = ete3.PhyloNode(sptree_file, format=3)
sptree.ladderize()
node_id = 0
for node in sptree.traverse(strategy='preorder'):
    node.name = node.name.replace("\'", "")
    node.id = 'b'+str(node_id)
    node_id += 1
    if node.is_root():
        node.name = sptree_root
b['branch_id'] = 0
for node in sptree.traverse(strategy='preorder'):
    b.loc[(b['spnode_coverage']==node.name),'branch_id'] = node.id
```

```
def my_layout(node):
    size_s = 6
    size_m = 10
    size_phylopic = 25
    nodeStyle = ete3.NodeStyle()
    nodeStyle["hz_line_width"] = nodeStyle["vt_line_width"] = 2
    nodeStyle["size"] = 0
    if node.is_root():
        node.dist=10
    if node.is_leaf():
        if len(node.name)>15:
            leaf_name = node.name.replace('_', '\n')
        else:
            leaf_name = node.name.replace('_', ' ')
        leafnameFace = ete3.TextFace(leaf_name, ftype="Verdana", fsize=size_m,␣
↪fgcolor="black", fstyle="italic", tight_text=False)
        ete3.add_face_to_node(face=leafnameFace, node=node, column=1,␣
↪aligned=True, position="aligned")
    # branch_id
    text_branch = str(node.id)
    branchFace = ete3.TextFace(text_branch, fsize=size_m, fgcolor="black")
    branchFace.margin_bottom = branchFace.margin_right = branchFace.margin_top␣
↪= branchFace.margin_left = 2
    ete3.add_face_to_node(face=branchFace, node=node, column=1, aligned=False,␣
↪position="float")
    ete3.add_face_to_node(face=ete3.TextFace('', fsize=size_m), node=node,␣
↪column=1, aligned=False, position="float")
    #  phylopic images
    if False:
    #if node.is_leaf():
        phylopic_file = [ file for file in os.listdir(phylopic_dir) if file.
↪startswith(node.name) ][0]
        paths, attributes = svg2paths(phylopic_dir+phylopic_file)
        for i in range(len(paths)):
            if i==0:
                xmin, xmax, ymin, ymax = paths[i].bbox()
            else:
                my_xmin, my_xmax, my_ymin, my_ymax = paths[i].bbox()
                xmin = my_xmin if my_xmin < xmin else xmin
                xmax = my_xmax if my_xmax > xmax else xmax
                ymin = my_ymin if my_ymin < ymin else ymin
                ymax = my_ymax if my_ymax > ymax else ymax
        width=None
        height=None
        if (ymax-ymin)>(xmax-xmin):
```

```
            height=size_phylopic
        else:
            width=size_phylopic
        phylopicFace = ete3.SVGFace(phylopic_dir+phylopic_file, width=width,␣
↪height=height)
        ete3.add_face_to_node(face=phylopicFace, node=node, column=2,␣
↪aligned=True, position="aligned")
    node.set_style(nodeStyle)

treeStyle = ete3.TreeStyle()
treeStyle.layout_fn = my_layout
treeStyle.scale = 1
treeStyle.min_leaf_separation = 29
treeStyle.show_leaf_name = False
treeStyle.scale_length = 100
#treeStyle.optimal_scale_level = "mid"
treeStyle.complete_branch_lines_when_necessary  = False
treeStyle.allow_face_overlap = False
#sptree.render(file_name="annotated_sptree.pdf", tree_style=treeStyle, h=None,␣
↪w=4.2, units="in", dpi=1200)
#sptree.render(file_name="annotated_sptree.svg", tree_style=treeStyle, h=None,␣
↪w=4.2, units="in", dpi=1200)
sptree.render(file_name="annotated_sptree.pdf", tree_style=treeStyle, h=None,␣
↪w=3.0, units="in")
sptree.render(file_name="annotated_sptree.svg", tree_style=treeStyle, h=None,␣
↪w=3.0, units="in")
sptree.render("%%inline", tree_style=treeStyle)
```

[5]:



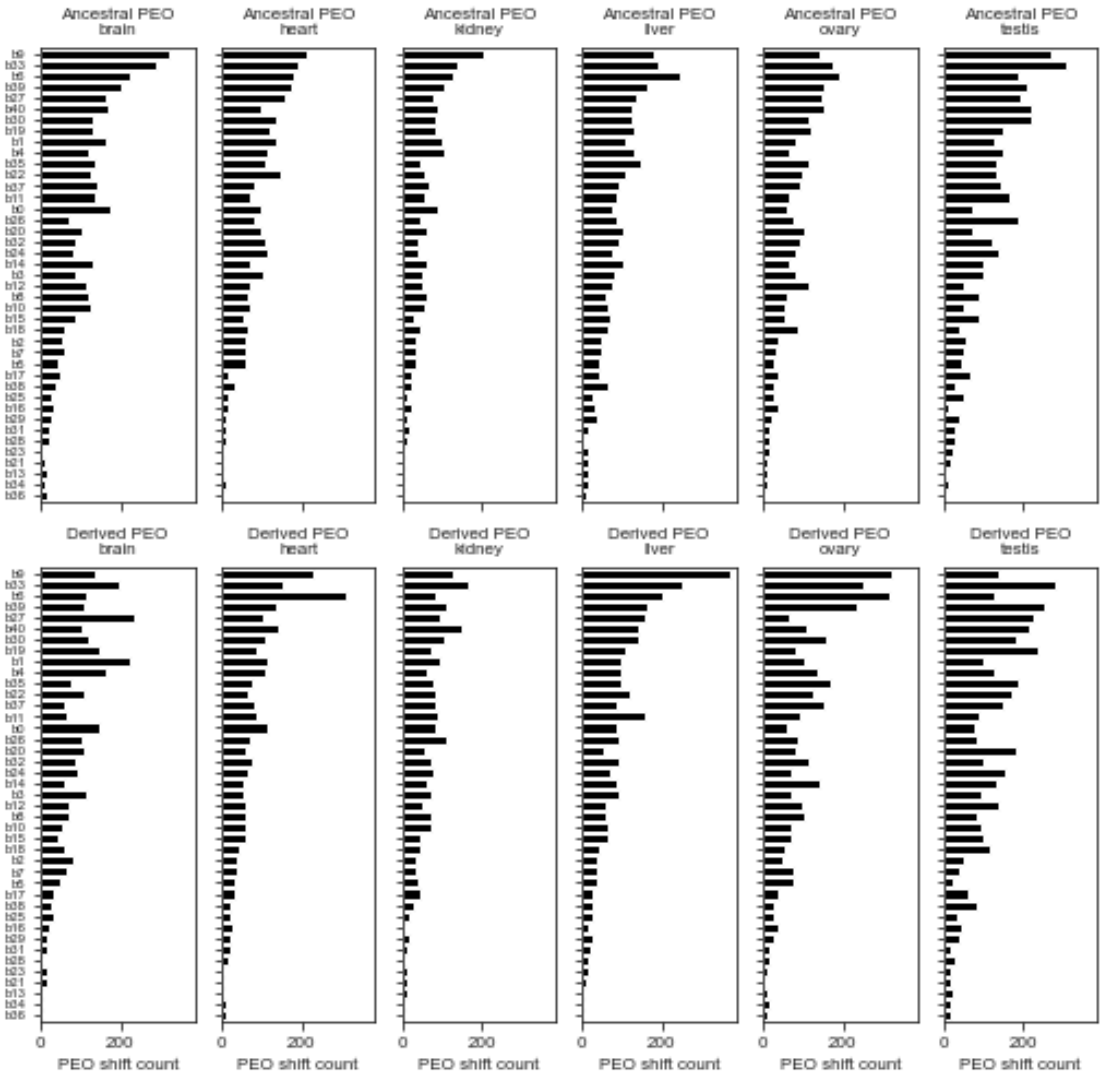
[6]:
```
for pp in pcm_prefixes:
    fig,axes = matplotlib.pyplot.subplots(nrows=2, ncols=len(organs),␣
 ↪figsize=(7.2, 7), sharex=True)
```

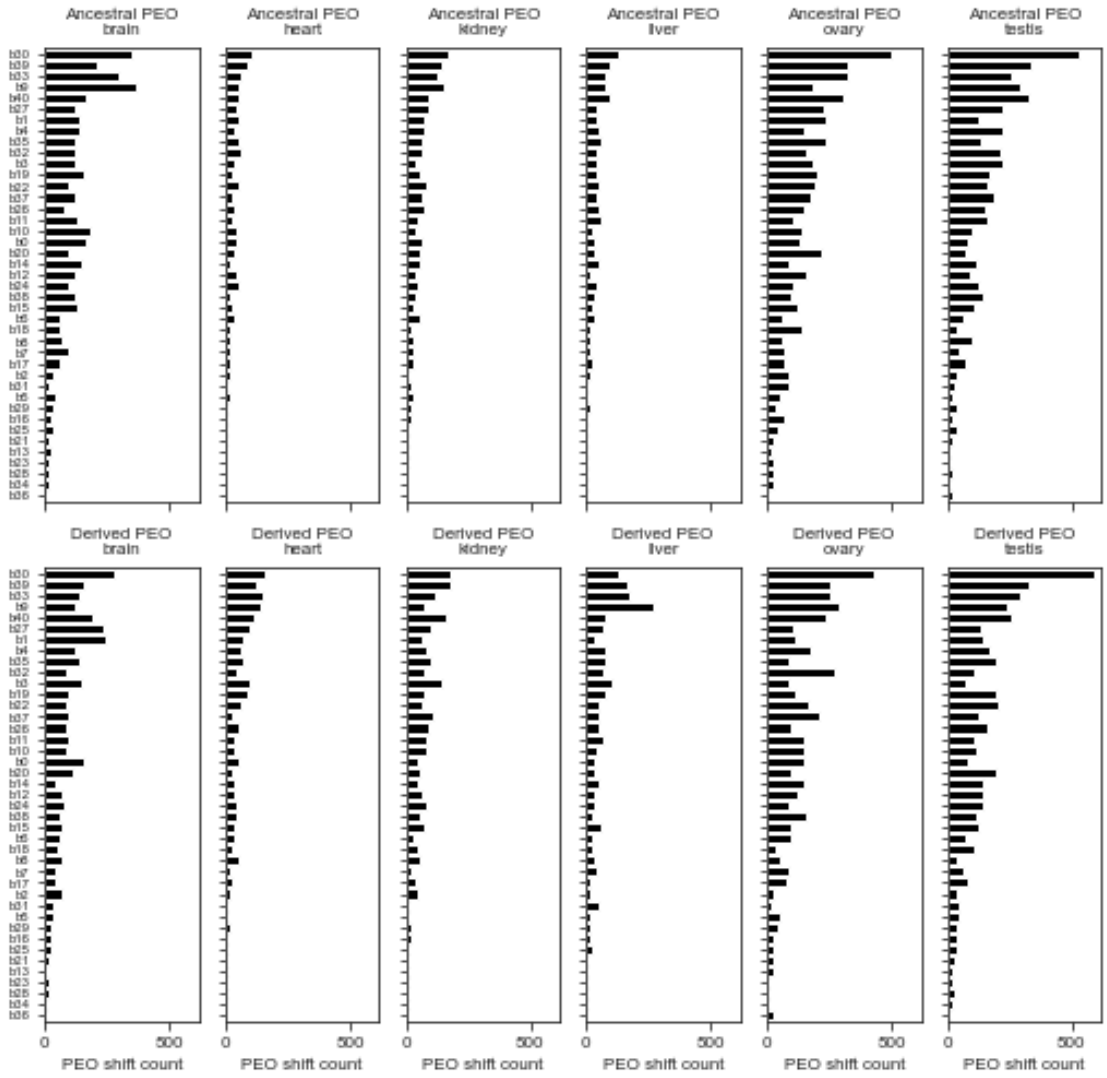
```
    is_shift = (b[pp+'is_shift']==1)
    is_peo_shift = (b['parent_'+pp+'max_organ']!=b[pp+'max_organ'])
    is_target = (is_shift)&(is_peo_shift)

    #is_specific = (b[pp+'delta_tau']>0.5)
    #is_target = (is_target)&(is_specific)

    tmp = b.loc[is_target,:]
    #tmp['o2o'] = tmp['parent_'+pp+'max_organ'] + '_' + tmp[pp+'max_organ']
    index_order = tmp['branch_id'].value_counts()
    for j,col in enumerate(['parent_'+pp+'max_organ',pp+'max_organ']):
        for k,organ in enumerate(organs):
            ax = axes[j,k]
            dat = tmp.loc[(tmp[col]==organ),'branch_id'].value_counts()
            dat = dat.loc[index_order.index]
            seaborn.barplot(x=dat, y=dat.index, color='black', ax=ax)
            if k!=0:
                 ax.set_yticklabels([''] * len(ax.get_yticklabels()),␣
↪fontsize=font_size-2)
            else:
                 ax.set_yticklabels(ax.get_yticklabels(), fontsize=font_size-2)
            if j==1:
                ax.set_title('Derived PEO\n'+organ, fontsize=font_size)
                ax.set_xlabel('PEO shift count', fontsize=font_size)
            else:
                ax.set_title('Ancestral PEO\n'+organ, fontsize=font_size)
                ax.set_xlabel('', fontsize=font_size)

    fig.tight_layout()
    file_base = 'branch_wise_peo_shift_'+pp
    for ext in ['png','pdf','svg']:
        fig.savefig(file_base+'.'+ext, format=ext)
```


Ancestral PEO
brain
Ancestral PEO
heart
Ancestral PEO
kidney
Ancestral PEO
liver
Ancestral PEO
ovary
Ancestral PEO
testis
Derived PEO
brain
Derived PEO
heart
Derived PEO
kidney
Derived PEO
liver
Derived PEO
ovary
Derived PEO
testis
0
200
PEO shift count



[7]:
```
min_nshift = 0
num_category = b.branch_category.drop_duplicates().dropna().shape[0]

shift_col = 'l1ou_intersect_is_shift'

fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=num_category, figsize=(3.
 ↪5, 4.9), sharex=False)
any_col = 'orthogroup'
tmp0 = b.loc[b['branch_id']!='b0',:]
tmp = pandas.DataFrame(tmp0.
 ↪groupby(['branch_id',shift_col,'branch_category'])[any_col].count()).
 ↪unstack().fillna(0)
tmp.columns = tmp.columns.get_level_values(level=1)
tmp = tmp.unstack()
```

```
tmp = tmp.iloc[numpy.argsort([ int(s[1:]) for s in tmp.index ]),:]
placeholders = pandas.DataFrame([[numpy.nan,]*tmp.shape[1]], columns=tmp.
 ↪columns, index=['',])
totals = pandas.DataFrame([tmp.sum(axis=0).tolist()], columns=tmp.columns,␣
 ↪index=['Total',])
tmp = pandas.concat([tmp, placeholders, totals], axis=0)
for i in range(len(branch_categories)):
    tmp_my = tmp0.
 ↪loc[(tmp0['branch_category']==branch_categories[i]),'bl_dated']
    nbranch = (tmp0['branch_category']==branch_categories[i]).sum()
    nshift =␣
 ↪((tmp0[shift_col]==1)&(tmp0['branch_category']==branch_categories[i])).sum()
    total_my = tmp_my.sum()
    txt = '{}; Shift frequency = {} shift/My; # shifts = {:,}; # branches = {:
 ↪,}; Total branch MY = {:,}'
    print(txt.format(branch_categories[i], nshift/total_my, nshift, nbranch,␣
 ↪total_my))

    tmp2 = pandas.DataFrame(tmp.loc[:,tmp.columns.
 ↪get_level_values(0)==branch_categories[i]])
    tmp2.columns = ['no_shift', 'shift']
    tmp3 = tmp2.copy()
    sum_values = tmp2.sum(axis=1)
    tmp2.loc[(tmp2['shift']<min_nshift).tolist(),:] = numpy.nan
    for c in tmp2.columns:
        tmp2.loc[:,c] = tmp2.loc[:,c] / sum_values
    tmp2 = tmp2.reset_index(drop=False)
    #tmp2 = tmp2.iloc[numpy.argsort([ int(s[1:]) for s in tmp2['branch_id'] ]),:
 ↪]
    ax = kfplot.stacked_barplot(x=['shift', 'no_shift'], y='index', data=tmp2,␣
 ↪ax=axes[i],
                                ␣
 ↪colors=[category_colors[branch_categories[i]],(0.8,0.8,0.8)])
    ax.set_xlim(0, 1)
    ax.set_xlabel('')
    ax.set_ylabel('')
    ax.set_title(branch_categories[i], fontsize=font_size)
    ax.tick_params(axis='both', which='major', direction='out', length=2,␣
 ↪width=1, pad=1, top=False, left=False, right=False)
    xticks = [0, 0.5, 1]
    ax.set_xticks(xticks, minor=False)
    ax.set_xticklabels([ str(tick) for tick in xticks ], minor=False,␣
 ↪ha='center')
    ax.set_xticklabels(ax.get_xticklabels(), rotation=0, fontsize=font_size-1)
    ax.set_yticklabels(ax.get_yticklabels(), rotation=0, fontsize=font_size-1)
    for j in range(tmp3.shape[0]):
```

```
        nshift = tmp3['shift'].iloc[j]
        nbranch = tmp3.iloc[j,:].sum()
        if (nshift==nshift)&(nbranch==nbranch):
            percent = numpy.round(nshift/nbranch*100, decimals=1)
            #txt = str(percent)+'% ('+str(int(nshift))+'/'+str(int(nbranch))+')'
            txt = "{:,}/{:,}".format(int(nshift), int(nbranch))
            ax.text(x=0.5, y=j, s=txt, color='black', ha='center', va='center',␣
 ↪fontsize=5)
    if i%num_category!=0:
        ax.get_yaxis().set_visible(False)
    for part in ['top','bottom','left','right']:
        ax.spines[part].set_visible(False)

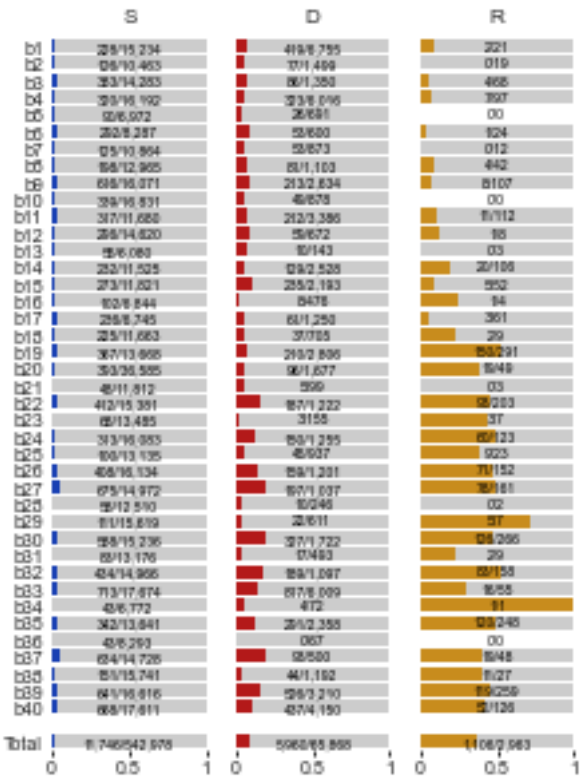
file_base = 'proportion_shift'
for ext in ['png','pdf','svg']:
    fig.savefig(file_base+'.'+ext, format=ext)

# Chisq test
contingency_table = numpy.array([
    [tmp.loc['Total',('S',True)].astype(int), tmp.loc['Total',('S',False)].
 ↪astype(int)],
    [tmp.loc['Total',('D',True)].astype(int), tmp.loc['Total',('D',False)].
 ↪astype(int)],
    [tmp.loc['Total',('R',True)].astype(int), tmp.loc['Total',('R',False)].
 ↪astype(int)],
])
out = scipy.stats.chi2_contingency(observed=contingency_table, correction=True,␣
 ↪lambda_=None)
chi,p,dof,expected = out
print('Chi-square test among 3 branch categories: chisq={:,}, P={}, dof={}'.
 ↪format(chi, p, dof))
```

```
S; Shift frequency = 0.00024804574942087113 shift/My; # shifts = 11,746; #
branches = 542,978; Total branch MY = 47,354,167.63812388
D; Shift frequency = 0.0016886637493336888 shift/My; # shifts = 5,960; #
branches = 65,868; Total branch MY = 3,529,417.8621123894
R; Shift frequency = 0.007029358246006006 shift/My; # shifts = 1,106; # branches
= 2,963; Total branch MY = 157,340.11004893875
```

```
/Users/kef74yk/anaconda3/lib/python3.6/site-packages/ipykernel_launcher.py:49:
RuntimeWarning: invalid value encountered in double_scalars
```

```
Chi-square test among 3 branch categories: chisq=21,064.636194292412, P=0.0,
dof=2
```



[8]:
```
criterion = 'iqtree_best_BIC'
alpha = 0.2
cols = ['model_df','model_rate','rooting_method','dating_method']
cmaps = ['cool','cool','cool','cool']
hist_xlabels = ['Degree of freedom in\n4x4 substitution matrix','Number of␣
 ↪categories\nfor rate heterogeneity','Rooting method', 'Dating method']

fig,axes = matplotlib.pyplot.subplots(nrows=2, ncols=len(cols), figsize=(7.
 ↪2,4), sharex=False)

model_df = {'JC':0,'JC69':0,'F81':3,'K80':1,'K2P':1,'HKY':4,'HKY85':4,'TN':
 ↪5,'TN93':5,'TNe':2,'K81':2,'K3P':2,
       'K3Pu':2,'K81u':5,'TPM2':2,'TPM2u':5,'TPM3':2,'TPM3u':5,'TIM':6,'TIMe':
 ↪3,'TIM2':6,'TIM2e':3,'TIM3':6,
       'TIM3e':3,'TVM':7,'TVMe':4,'SYM':5,'GTR':8,}

t['model_df'] = t[criterion]
t['model_df'] = t['model_df'].str.replace('\+.*','')
for key in model_df.keys():
    t.loc[t['model_df']==key,'model_df'] = model_df[key]
```

```
t['model_rate'] = t[criterion]
t.loc[t['model_rate'].str.contains('\+[GR]'),'model_rate'] = t.
 ↪loc[t['model_rate'].str.contains('\+[GR]'),'model_rate'].str.replace('.
 ↪*\+[GR]','').str.replace('\+.*','')
t.loc[~t['model_rate'].str.contains('^[0-9]'),'model_rate'] = 1
t.loc[:,'model_rate'] = t['model_rate'].astype(int)

print('The number of orthogroups analyzed for phylogeny:', (~t[criterion].
 ↪isnull()).sum())
#print('The number of orthogroups with nonzero parsimony-informative site:',␣
 ↪(t['prop_parsimony_informative_cleaned']!=0).sum())
print('The number of trees with +G models:', t[criterion].str.contains('\+G').
 ↪sum())
print('The number of trees with +R models:', t[criterion].str.contains('\+R').
 ↪sum())
print('The number of trees with *H models:', t[criterion].str.contains('\*H').
 ↪sum())
print('The number of trees with no rate heterogeneity:', (~t[criterion].str.
 ↪replace('\+I','').str.replace('\+F','').str.contains('\+')).sum())

for j in range(len(cols)):
    col = cols[j]
    print(col)
    if col=='rooting_method':
        t[col] = t[col].str.replace('NOTUNG','NTG').str.
 ↪replace('midpoint','MID')
    elif col=='dating_method':
        # some RDS trees were not annotated correctly.
        conditions = (t[col].isnull())&(~t['l1ou_fpkm_alpha_brain'].isnull())
        t.loc[conditions,col] = 'RDS'
    print(t.loc[:,[col,'orthogroup']].groupby(col).count().
 ↪to_dict()['orthogroup'])
    df_unique = t[col].dropna().drop_duplicates()
    df_unique = sorted(df_unique.tolist())
    num_df = len(df_unique)
    cmap = matplotlib.cm.get_cmap(cmaps[j])
    df_rgba = cmap(numpy.arange(0,1.001, 1/num_df))
    for i in range(len(df_rgba)):
        df_rgba[i][3] = alpha

    ax = axes[0,j]
    val = t[col]
    val = pandas.DataFrame(val.value_counts())
    ax = seaborn.barplot(x=val.index, y=val[col], ax=ax, palette=df_rgba)
    ax.set_yscale('log', basey=10)
    ax.set_ylim(1,13000)
```

```
    ax.set_xlabel(hist_xlabels[j])
    ax.set_ylabel('Orthogroup count')
    if col=='dating_method':
        ax.set_xticklabels(ax.get_xticklabels(), rotation=45)

    ax = axes[1,j]
    for i in numpy.arange(num_df):
        tmp = t.loc[t[col]==df_unique[i],:]
        if tmp.shape[0]==1:
            tmp = tmp.append(pandas.Series(), ignore_index=True)
        ax = seaborn.regplot(x='cleaned_num_seq', y='cleaned_num_site',␣
↪data=tmp, fit_reg=False,
                             color=df_rgba[i], scatter_kws={'alpha':
↪alpha,'rasterized':True,'s':5}, ax=ax)
    ax.set_xscale('log', basex=10)
    ax.set_yscale('log', basey=10)
    ax.set_xlabel('Number of genes')
    ax.set_ylabel('Number of codon sites')
    ax.set_xlim(3, 2**13*1.1)
    ax.set_ylim(10**1*3, 10**6/4)
    ax.set_xticks([10,100,1000])

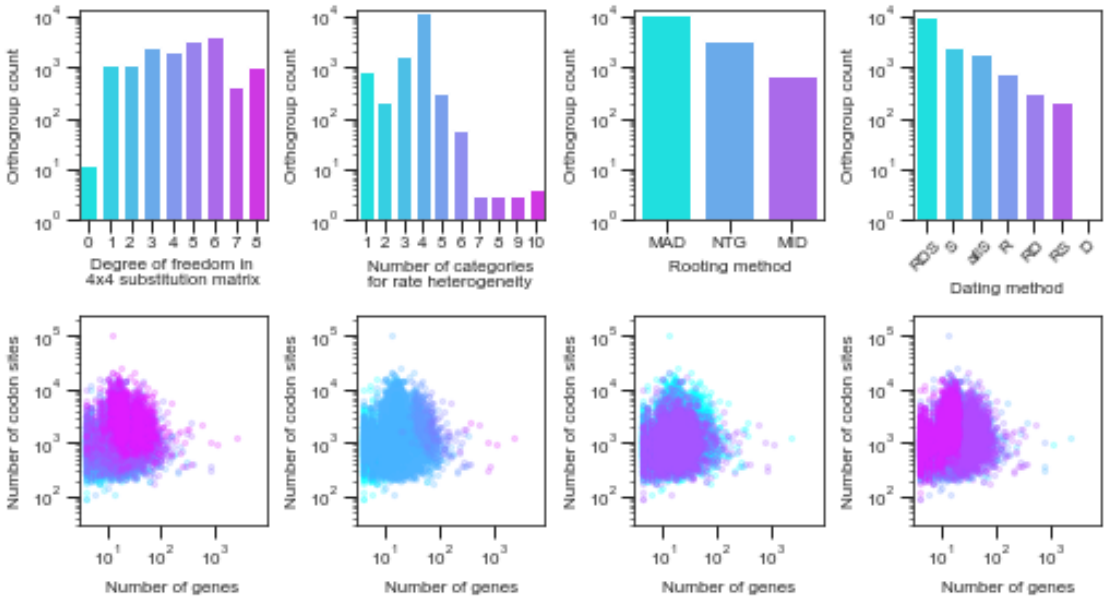
for ax in axes.flat:
    ax.tick_params(axis='both', which='major', direction='out', length=6,␣
↪width=1, pad=2, top=False, right=False, labelsize=font_size)
    ax.tick_params(axis='both', which='minor', top=False, right=False,␣
↪labelsize=font_size)

fig.tight_layout()
outbase = 'tree_inference'
fig.savefig(outbase+".pdf", format='pdf', transparent=True)
fig.savefig(outbase+".svg", format='svg', transparent=True)
```

```
The number of orthogroups analyzed for phylogeny: 15280
The number of trees with +G models: 10880
The number of trees with +R models: 3531
The number of trees with *H models: 0
The number of trees with no rate heterogeneity: 869
model_df
{0: 12, 1: 1107, 2: 1122, 3: 2371, 4: 1990, 5: 3304, 6: 3963, 7: 408, 8: 1003}
model_rate
{1: 869, 2: 201, 3: 1693, 4: 12135, 5: 312, 6: 57, 7: 3, 8: 3, 9: 3, 10: 4}
rooting_method
{'MAD': 11237, 'MID': 662, 'NTG': 3381}
dating_method
{'D': 1, 'R': 758, 'RD': 299, 'RDS': 9638, 'RS': 216, 'S': 2558, 'allS': 1810}
```

```
/Users/kef74yk/anaconda3/lib/python3.6/site-packages/ipykernel_launcher.py:63:
```

```
DeprecationWarning: The default dtype for empty Series will be 'object' instead
of 'float64' in a future version. Specify a dtype explicitly to silence this
warning.
```



[9]:
```
fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=3, figsize=(7.2,2.4),␣
↪sharex=False)
axes = axes.flat

num_leaves = numpy.arange(0,3000, 1)
halves = numpy.floor(num_leaves/2).astype(int)
halves[halves>100] = 100
sqroots = numpy.floor(num_leaves**0.5).astype(int)
max_nshifts = halves
max_nshifts[max_nshifts<sqroots] = sqroots[max_nshifts<sqroots]
df_max_nshift = pandas.DataFrame({'num_leaf':num_leaves,'max_nshift':
↪max_nshifts})
df_max_nshift.loc[(df_max_nshift['num_leaf']>=2000),'max_nshift'] = 10

color = 'black'
ymax = 105

for pp,ax in zip(pcm_prefixes,axes):
    tmp = t.loc[(~t[pp+'alpha_brain'].isnull()),:]
    tmp = pandas.merge(tmp, df_max_nshift, left_on='cleaned_num_seq',␣
↪right_on='num_leaf')
    num_tree = tmp.shape[0]
    num_max_shift = (tmp[pp+'num_shift']==tmp['max_nshift']).sum()
```

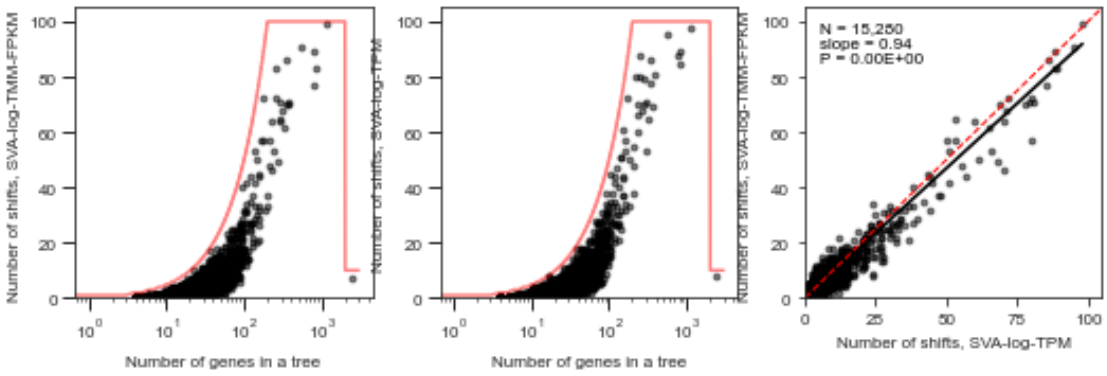
```
    label = '(N = '+str(num_tree)+', # of trees reaching the limit =␣
↪'+str(num_max_shift)+')'
    print(pp, label)
    ax = seaborn.regplot('cleaned_num_seq', pp+'num_shift', data=tmp,␣
↪fit_reg=False, ax=ax, color=color,
                         scatter_kws={'alpha':0.5,'rasterized':True,'s':8},␣
↪label=label)

    ax.plot('num_leaf', 'max_nshift', data=df_max_nshift, color='red', alpha=0.
↪5, label='Upper limit in regime shift inference')
    ax.set_ylim(0,ymax)
    ax.set_xscale('log', basex=10)
    #ax.set_yscale('log', basex=2)
    ax.tick_params(axis='both', which='major', direction='out', length=6,␣
↪width=1, pad=2, top=False, right=False, labelsize=font_size)
    ax.tick_params(axis='both', which='minor', top=False, right=False,␣
↪labelsize=font_size)
    ax.set_xlabel('Number of genes in a tree')
    ax.set_ylabel('Number of shifts, SVA-log-TMM-FPKM' if pp=='l1ou_fpkm_' else␣
↪'Number of shifts, SVA-log-TPM')

ax = axes[2]
seaborn.regplot('l1ou_tpm_num_shift', 'l1ou_fpkm_num_shift', t, fit_reg=False,␣
↪ax=ax, color=color,
                scatter_kws={'alpha':0.5,'rasterized':True,'s':8})
ols_annotations('l1ou_tpm_num_shift', 'l1ou_fpkm_num_shift', t, ax=ax)
ax.set_xlabel('Number of shifts, SVA-log-TPM')
ax.set_ylabel('Number of shifts, SVA-log-TMM-FPKM')
ax.plot([0,ymax],[0,ymax], color='red', lw=1, linestyle='--')
ax.set_xlim(0,ymax)
ax.set_ylim(0,ymax)

fig.tight_layout(pad=0)
outbase = 'ou_nshift'
fig.savefig(outbase+".pdf", format='pdf', transparent=True)
fig.savefig(outbase+".svg", format='svg', transparent=True)
```

```
l1ou_fpkm_ (N = 15280, # of trees reaching the limit = 0)
l1ou_tpm_ (N = 15280, # of trees reaching the limit = 3)
```



[10]:
```
import matplotlib_venn

fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=3, figsize=(7.2,2.4),␣
↪sharex=False)
axes = axes.flat

label_fpkm = 'FPKM'#'log TMM-SVA-FPKM'
label_tpm = 'TPM'#'log SVA-TPM'
colors = ['magenta','cyan']

tmp = b.copy()


shift_cols = ['l1ou_tpm_is_shift','l1ou_fpkm_is_shift']
window_search_col = shift_cols[0]
labels = ['TPM','FPKM']
window_sizes = [0,1,]
neighbors = ['parent','sister','child1','child2']

id_cols =␣
↪['orthogroup','numerical_label','parent','sister','child1','child2','branch_category']
tmp = b.loc[:,id_cols+shift_cols]
for sc in shift_cols:
    tmp.loc[:,sc] = tmp.loc[:,sc].astype(bool)
for neighbor in neighbors:
    tmp = attach_neighbor_stats(df=tmp, neighbor=neighbor,␣
↪columns=[window_search_col,])

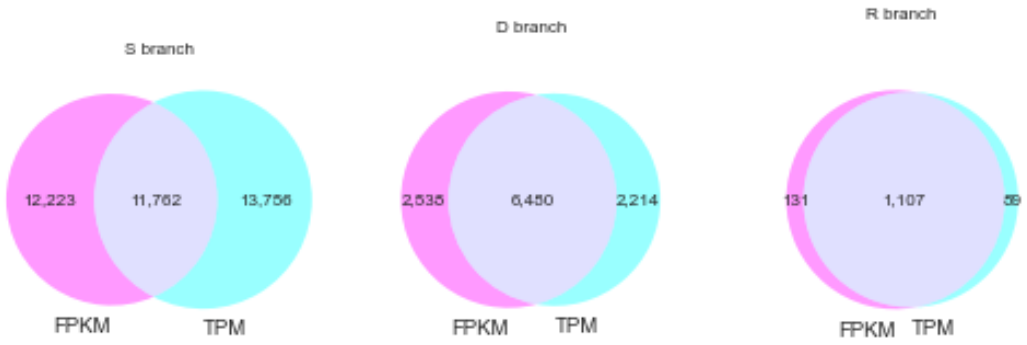

tmp.loc[:,'ogb_id'] = tmp['orthogroup'] + tmp['numerical_label'].astype(str)

def my_formatter(s):
    return "{:,}".format(s)
```

```
for event,ax,nt in zip(['S','D','R'],axes,[1,0.21,0.12]):
    tmp1 = tmp.loc[(tmp['branch_category']==event),:]
    set_fpkm = set(tmp1.loc[tmp1['l1ou_fpkm_is_shift']==1,'ogb_id'])
    set_tpm = set(tmp1.loc[tmp1['l1ou_tpm_is_shift']==1,'ogb_id'])

    v = matplotlib_venn.venn2(subsets=[set_fpkm,set_tpm],␣
 ↪set_labels=[label_fpkm,label_tpm], ax=ax,
                              set_colors=colors, normalize_to=nt,␣
 ↪subset_label_formatter=my_formatter)
    ax.set_title(event+' branch')

fig.tight_layout()
outbase = 'pcm_venn'
fig.savefig(outbase+".pdf", format='pdf', transparent=True)
fig.savefig(outbase+".svg", format='svg', transparent=True)
```



[11]:
```
force = False

#fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=1, figsize=(2.4,2.4),␣
 ↪sharex=False)
#ax = axes

tmp = b.loc[:,['orthogroup','hyphy_omega','mapdnds_omega']]
#tmp.loc[:,['hyphy_omega','mapdnds_omega']] = numpy.log(tmp.loc[:
 ↪,['hyphy_omega','mapdnds_omega']])
tmp.loc[:,['hyphy_omega','mapdnds_omega']] = tmp.loc[:
 ↪,['hyphy_omega','mapdnds_omega']].replace([numpy.inf,-numpy.inf],100)
tmp = tmp.dropna()
print('Number of branches with omega annotations:', tmp.shape[0])
orthogroups = tmp['orthogroup'].unique()
print('Number of orthogroups with omega annotations:', orthogroups.shape[0])
```

```
file_og_cor = 'orthogroup_correlation.tsv'
if (os.path.exists(file_og_cor))&(~force):
    print('Reading', file_og_cor)
    og_cor = pandas.read_csv(file_og_cor, sep='\t', header=0)
else:
    og_cor = pandas.DataFrame({'orthogroup':orthogroups,'pearson':numpy.
 ↪nan,'spearman':numpy.nan})
    for i in numpy.arange(len(orthogroups)):
        tmp_og = tmp.loc[(tmp['orthogroup']==orthogroups[i]),:]
        og_cor.loc[i,'pearson'] = scipy.stats.pearsonr(x=tmp_og['hyphy_omega'],␣
 ↪y=tmp_og['mapdnds_omega'])[0]
        og_cor.loc[i,'spearman'] = scipy.stats.
 ↪spearmanr(a=tmp_og['hyphy_omega'], b=tmp_og['mapdnds_omega']).correlation
        if i%1000==0:
            print("{0:%Y-%m-%d %H:%M:%S}".format(datetime.datetime.today()), ',␣
 ↪processing', i, 'th orthogroups')
    og_cor.to_csv(file_og_cor, sep='\t', index=False)

#kfplot.density_scatter(x='hyphy_omega', y='mapdnds_omega', df=tmp, ax=ax,␣
 ↪cor=True, diag=False, reg_family=None, hue_log=True)
#seaborn.regplot('hyphy_omega','mapdnds_omega', data=tmp, fit_reg=False)
```

```
Number of branches with omega annotations: 607873
Number of orthogroups with omega annotations: 15280
Reading orthogroup_correlation.tsv
```

[12]:
```
params = [pp+'alpha_',pp+'sigma2_',pp+'gamma_']
ymaxs = [0.08, 0.15, 5]
ylabels = ['$ $ (adaptation rate)', '$ ^2$ (expression drift variance)', '$ $␣
 ↪(stationary variance of expression level)']

for pp in pcm_prefixes:
    fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=3, figsize=(9,3),␣
 ↪sharex=False)
    for i in range(len(params)):
        ax = axes[i]
        df2 = t

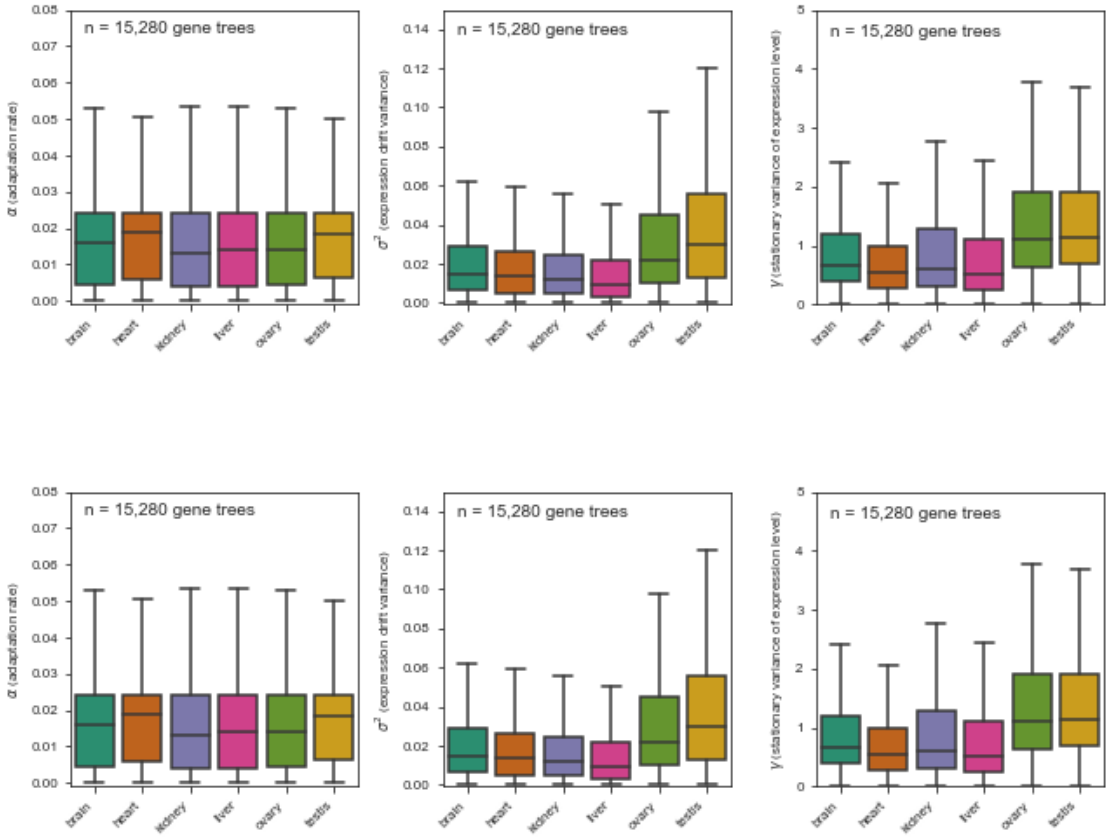
        df3 = df2.loc[:,df2.columns.str.startswith(params[i])].melt()
        df3['variable'] = df3['variable'].str.replace(params[i],'')

        ymin = -0.001
        lw = 2
        alpha = 0.95
        colors = ['#1B9E77','#D95F02','#7570B3','#E7298A','#66A61E','#E6AB02']
        texty = (ymaxs[i] - ymin) * 0.925
```

```
        seaborn.boxplot(x='variable', y='value', data=df3, ax=ax,␣
↪palette=colors, fliersize=0)

        ax.set_ylabel(ylabels[i])
        ax.set_xlabel('')
        ax.set_ylim(ymin, ymaxs[i])
        my_text='n = '+"{:,d}".format(df3.loc[df3.variable=='brain','variable'].
↪shape[0])+' gene trees'
        ax.text(x=-0.2, y=texty, s=my_text, fontsize=10, ha='left', va='center')
        ax.set_xticklabels(labels=ax.get_xticklabels(), rotation=45, ha='right')

    matplotlib.pyplot.tight_layout()
    outbase = 'sigma_boxplot_'+pp
    fig.savefig(outbase+".pdf", format='pdf')
    fig.savefig(outbase+".svg", format='svg')
```



[13]:
```
ys = ['log_mapdnds_omega','log_hyphy_omega']
#ylabs = ['Log $d_N/d_S$','Log $d_N/d_S$',]
ylabs = ['Log  ', 'Log  ']
#ys = ['log_mapdnds_omega', 'log_mapdnds_dn', 'log_mapdnds_ds']
```

```
#ylabs = ['Log $d_N/d_S$', 'Log $d_N$', 'Log $d_S$']
num_col=len(ys)
num_row=1
matplotlib.rcParams['font.size'] = 10

alpha_small=0.1
alpha_large=0.95
kernel='gau'
spnodes = b.spnode_coverage.unique()

is_parent_dup = b.so_event_parent=='D'
is_retrotransposition = (b.delta_intron_present<=max_delta_intron_present)
is_sister_retrotransposition = (b.
 ↪sister_delta_intron_present<=max_delta_intron_present)
is_lower_delta_intron_present = (b.delta_intron_present<=b.
 ↪sister_delta_intron_present)

if 'flat' in dir(axes):
    axes = axes.flat
else:
    axes = [axes,]

for sc in ['l1ou_intersect_is_shift']:
    print(sc)
    fig,axes = matplotlib.pyplot.subplots(nrows=num_row, ncols=num_col,␣
 ↪figsize=(3.4*num_col,3.6*num_row), sharex=False)
    for y,ylab,ax in zip(ys,ylabs,axes):
        print('\n', y)

        tmp = b.loc[:,['orthogroup',y]]
        #tmp[y] = tmp[y].replace([-numpy.inf,numpy.inf], numpy.nan)
        log_var_value = tmp.groupby('orthogroup')[y].median().var()
        var_value = numpy.exp(log_var_value)
        print('Variance of ortholog median (unlog):', var_value)

        df2 = b.loc[(b[sc+'_pair']),:]
        df2 = df2.loc[~(df2[y].isnull()|df2['sister_'+y].isnull()),:]
        df2.loc[(df2['sister_branch_category']=='R'),'branch_category'] = 'R'
        df2.loc[:,y] = df2.loc[:,y].clip(-10, 10)
        df2['dup_shift'] = ''
        for bc in branch_categories:
            df2.loc[(df2.branch_category==bc)&(df2[sc]==0),'dup_shift'] = bc+'-'
            df2.loc[(df2.branch_category==bc)&(df2[sc]==1),'dup_shift'] = bc+'+'
        df2 = df2.dropna(subset=[y,], axis=0)

        orders = []
        colors = []
```

```
        for bc in branch_categories:
            orders = orders + [bc+'-', bc+'+']
            colors = colors + [category_colors[bc], category_colors[bc]]
        seaborn.boxplot(x='dup_shift', y=y, data=df2, ax=ax, showfliers=False,␣
↪palette=colors, order=orders)

        #ax.set_xlim(-0.6, 3.6)
        #ax.set_xticks([0,1,2,3], minor=False)
        #ax.set_xticks([-0.6,-0.6,0.5,2.5], minor=True)
        #ax.set_xticklabels(['-','+','-','+',], minor=False, ha='center')
        #ax.set_xticklabels(['Exp. shift','\nPrec.␣
↪event','\nSpeciation','\nDuplication',], minor=True, ha='center')
        ax.tick_params(axis='x', which='major', direction='out', length=6,␣
↪width=1)
        ax.tick_params(axis='x', which='minor', direction='out', length=6,␣
↪width=0)
        ax.set_xlabel('')

        pos=0
        lowest = numpy.inf
        highest = -numpy.inf
        for ev in branch_categories:
            for sh in [0,1]:
                dat = df2.loc[(df2.branch_category==ev)&(df2[sc]==sh),y].values
                Q1, median, Q3 = numpy.percentile(numpy.asarray(dat), [25, 50,␣
↪75])
                IQR = Q3 - Q1
                loval = Q1 - 1.5 * IQR
                hival = Q3 + 1.5 * IQR
                wiskhi = numpy.compress(dat <= hival, dat)
                wisklo = numpy.compress(dat >= loval, dat)
                actual_hival = numpy.max(wiskhi)
                actual_loval = numpy.min(wisklo)
                if actual_hival > highest:
                    highest = actual_hival
                if actual_loval < lowest:
                    lowest = actual_loval
                #label_text = "{:,d}".format(len(dat))
                label_text = "{}".format(numpy.round(numpy.exp(numpy.
↪median(dat)), decimals=3))
                ax.text(x=pos, y=actual_hival+0.8, s=label_text,␣
↪fontsize=font_size, ha='center', va='center')
                pos+=1
                del dat
        #ax.set_ylim(lowest-0.1, highest+4)
        ax.set_ylim(-10.1, 10.1)
```

```
        ax.set_ylabel(ylab)
        ax.tick_params(axis='both', which='major', direction='out', length=6,␣
↪width=1, pad=1, top=False, right=False)

        for event in ['S','D','R']:
            xval = df2.loc[df2['dup_shift']==event+'-',y].values
            yval = df2.loc[df2['dup_shift']==event+'+',y].values
            #out = kfstat.brunner_munzel_test(xval, yval,␣
↪alternative="two-sided")
            (W, dof, p, Pest, Cl, Ch) = kfstat.bm_test(xval, yval, ttype=1,␣
↪alpha=0.05) #ttype, 1 = greater,-1 = lesser, 0 = two-sided
            print(event, 'Number of branch pairs =', len(xval))
            print(event, 'Brunner-Munzel stat =', W)
            print(event, 'P value =', p)
            print(event, 'Effect size and 95% CI =', Pest, Cl, Ch)
            print(event, 'Unlog median value of '+event+'- =', numpy.exp(numpy.
↪median(xval)))
            print(event, 'Unlog median value of '+event+'+ =', numpy.exp(numpy.
↪median(yval)))

    print(numpy.finfo(p))
    #del df2

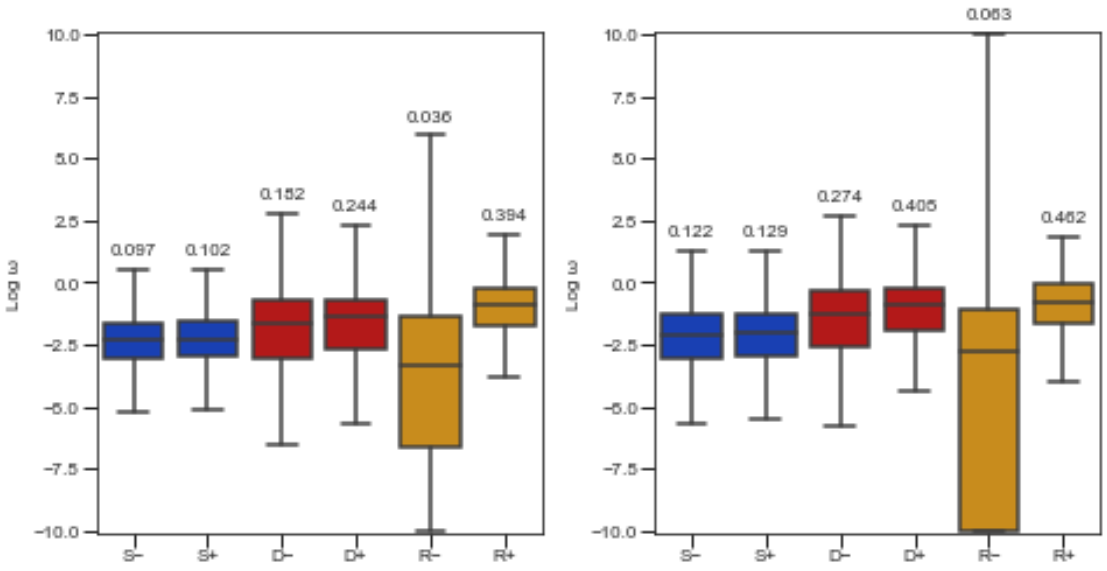
    fig.tight_layout()
    outbase = 'dNdS_dN_dS_boxplot_'+sc
    fig.savefig(outbase+".pdf", format='pdf')
    fig.savefig(outbase+".svg", format='svg')
```

```
l1ou_intersect_is_shift

 log_mapdnds_omega
Variance of ortholog median (unlog): 4.052727336760715
S Number of branch pairs = 11498
S Brunner-Munzel stat = 3.710725473681451
S P value = 0.0001035766799742932
S Effect size and 95% CI = 0.5141220684965032 0.5066625558204125
0.5215815811725939
S Unlog median value of S- = 0.09653370712268128
S Unlog median value of S+ = 0.10195232477385784
D Number of branch pairs = 5529
D Brunner-Munzel stat = 7.07301168594131
D P value = 8.040235144335384e-13
D Effect size and 95% CI = 0.5387574799620318 0.5280164239456809
0.5494985359783827
D Unlog median value of D- = 0.18236911096662003
D Unlog median value of D+ = 0.24378035689145436
R Number of branch pairs = 1075
```

```
R Brunner-Munzel stat = 25.299145968747506
R P value = 0.0
R Effect size and 95% CI = 0.7654909680908599 0.7449107814342645
0.7860711547474554
R Unlog median value of R- = 0.035579136470610964
R Unlog median value of R+ = 0.3942508012820513

 log_hyphy_omega
Variance of ortholog median (unlog): nan
S Number of branch pairs = 11290
S Brunner-Munzel stat = 3.342935721371553
S P value = 0.00041516114605388843
S Effect size and 95% CI = 0.5128365673158168 0.5053100801497592
0.5203630544818745
S Unlog median value of S- = 0.12181926686467885
S Unlog median value of S+ = 0.12919372346526056
D Number of branch pairs = 4119
D Brunner-Munzel stat = 9.9103346216216
D P value = 0.0
D Effect size and 95% CI = 0.5626106872379674 0.5502263445942862
0.5749950298816485
D Unlog median value of D- = 0.2737190043195873
D Unlog median value of D+ = 0.4051894631593254
R Number of branch pairs = 833
R Brunner-Munzel stat = 18.51086007403166
R P value = 0.0
R Effect size and 95% CI = 0.7296966805930055 0.705357239650684
0.7540361215353271
R Unlog median value of R- = 0.06323508882314291
R Unlog median value of R+ = 0.4619892444123987
Machine parameters for float64
---------------------------------------------------------------
precision =  15   resolution = 1.0000000000000001e-15
machep =    -52   eps =        2.2204460492503131e-16
negep =     -53   epsneg =     1.1102230246251565e-16
minexp =  -1022   tiny =       2.2250738585072014e-308
maxexp =   1024   max =        1.7976931348623157e+308
nexp =       11   min =        -max
---------------------------------------------------------------
```



[14]:
```
y = 'mapdnds_delta_omega'
ylabel = 'Δ Log $d_N/d_S$\n(shift br. - sister br.)'
ymin = -10
ymax = 10
alpha = 0.1
ps = 3
mk = 'o'
ols_method = 'ols' # ols or quantreg
show_xlab = False
no_colors = [(0.5,0.5,0.5),(0,0,0)]
negative_colors = matplotlib.cm.get_cmap('Paired').colors[0:2]
positive_colors = matplotlib.cm.get_cmap('Paired').colors[6:8]
stats = ['N','slope','slope_p']

textys = [0.3,0.95]

events = ['S+','D+','R+']
titles = ['S branches', 'D branches', 'R branches']

for sc in ['l1ou_intersect_is_shift',]:
    print(sc)
    for pp in pcm_prefixes:
        print(pp)
        fig,axes = matplotlib.pyplot.subplots(nrows=3, ncols=3, figsize=(4.8, 4.
↪8))
        df2 = b.loc[b[sc+'_pair'],:]
        df2.loc[(df2['sister_branch_category']=='R'),'branch_category'] = 'R'
        df2.loc[:,'dup_shift'] = ''
```

```
        for bc in branch_categories:
            df2.loc[(df2.branch_category==bc)&(df2[sc]==0),'dup_shift'] = bc+'-'
            df2.loc[(df2.branch_category==bc)&(df2[sc]==1),'dup_shift'] = bc+'+'

        for i,event in enumerate(events):
            dat = df2.loc[(df2[sc]==1)&(df2.dup_shift==event),:]
            dat.loc[:,'mapdnds_delta_omega'] =␣
↪dat['log_mapdnds_omega']-dat['sister_log_mapdnds_omega']

            j = 0
            ax = axes[j,i]
            x = pp+'delta_tau'
            ax.axhline(y=0, linestyle='--', color='black', lw=0.5)
            for colors,conditions,texty in␣
↪zip([negative_colors,positive_colors],[(dat[x]<0),(dat[x]>0)],textys):
                seaborn.regplot(x, y, data=dat.loc[conditions,:],␣
↪fit_reg=False, truncate=True, ax=ax, color=colors[0], marker=mk,
                                scatter_kws={'alpha':alpha,'rasterized':
↪True,'s':ps}, line_kws={'color':colors[1]})
                ols_annotations(x, y, dat.loc[conditions,:], ax, colors[1],␣
↪font_size, textxy=[0.05,texty], method=ols_method,
                                stats=stats)
            ax.set_xlim(-1,1)
            ax.set_ylim(ymin,ymax)
            if show_xlab:
                ax.set_xlabel('Shift in organ\nexp. specificity ( )' if i%3==1␣
↪else '')
            else:
                ax.set_xlabel('')
            ax.xaxis.set_ticks([-1,0,1])
            ax.set_ylabel(ylabel if (i==0)&(j==1) else '')
            if i!=0:
                ax.yaxis.set_ticklabels(['']*len(ax.get_yticklabels()))
            ax.set_title(titles[i], fontsize=font_size)

            j = 1
            ax = axes[j,i]
            x = pp+'delta_maxmu'
            ax.axhline(y=0, linestyle='--', color='black', lw=0.5)
            for colors,conditions,texty in␣
↪zip([negative_colors,positive_colors],[(dat[x]<0),(dat[x]>0)],textys):
                seaborn.regplot(x, y, data=dat.loc[conditions,:],␣
↪fit_reg=False, truncate=True, ax=ax, color=colors[0], marker=mk,
                                scatter_kws={'alpha':alpha,'rasterized':
↪True,'s':ps}, line_kws={'color':colors[1]})
```

```
                ols_annotations(x, y, dat.loc[conditions,:], ax, colors[1],␣
↪font_size, textxy=[0.05,texty], method=ols_method,
                                stats=stats)
            ax.set_xlim(-15,15)
            ax.set_ylim(ymin,ymax)
            expression_unit = 'FPKM' if pp=='l1ou_fpkm_' else 'TPM'
            if show_xlab:
                ax.set_xlabel('Shift in max expression\nlevel (Δ Log␣
↪'+expression_unit+')' if i%3==1 else '')
            else:
                ax.set_xlabel('')
            ax.xaxis.set_ticks([-10,0,10])
            ax.set_ylabel(ylabel if (i==0)&(j==1) else '')
            if i!=0:
                ax.yaxis.set_ticklabels(['']*len(ax.get_yticklabels()))

            j = 2
            ax = axes[j,i]
            x = pp+'mu_complementarity'
            ax.axhline(y=0, linestyle='--', color='black', lw=0.5)
            seaborn.regplot(x, y, data=dat, fit_reg=False, truncate=False,␣
↪ax=ax, color=no_colors[0], marker=mk,
                            scatter_kws={'alpha':alpha,'rasterized':True,'s':
↪ps}, line_kws={'color':no_colors[1]})
            ols_annotations(x, y, dat, ax, no_colors[1], font_size, textxy=[0.
↪05,0.95], method=ols_method, stats=stats)
            ax.set_xlim(0,1)
            ax.set_ylim(ymin,ymax)
            if show_xlab:
                ax.set_xlabel('Expression complementarity\nbetween sister␣
↪lineages' if i%3==1 else '')
            else:
                ax.set_xlabel('')
            ax.xaxis.set_ticks([0,0.5,1])
            ax.xaxis.set_ticklabels(['0','0.5','1'])
            ax.set_ylabel(ylabel if (i==0)&(j==1) else '')
            if i!=0:
                ax.yaxis.set_ticklabels(['']*len(ax.get_yticklabels()))

        fig.tight_layout()
        #fig.subplots_adjust(left=0, right=1, bottom=0, top=1)
        outbase = 'dNdS_vs_exp_properties_'+pp+sc
        fig.savefig(outbase+".pdf", format='pdf')
        fig.savefig(outbase+".svg", format='svg')
```

```
l1ou_intersect_is_shift
l1ou_fpkm_
```

```
/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/pandas/core/indexing.py:966: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
Try using .loc[row_indexer,col_indexer] = value instead

See the caveats in the documentation: https://pandas.pydata.org/pandas-
docs/stable/user_guide/indexing.html#returning-a-view-versus-a-copy
  self.obj[item] = s
/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/pandas/core/indexing.py:845: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
Try using .loc[row_indexer,col_indexer] = value instead

See the caveats in the documentation: https://pandas.pydata.org/pandas-
docs/stable/user_guide/indexing.html#returning-a-view-versus-a-copy
  self.obj[key] = _infer_fill_value(value)
/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/pandas/core/indexing.py:845: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
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A value is trying to be set on a copy of a slice from a DataFrame.
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See the caveats in the documentation: https://pandas.pydata.org/pandas-
docs/stable/user_guide/indexing.html#returning-a-view-versus-a-copy
  self.obj[item] = s
```

```
l1ou_tpm_

/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/pandas/core/indexing.py:966: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
Try using .loc[row_indexer,col_indexer] = value instead

See the caveats in the documentation: https://pandas.pydata.org/pandas-
docs/stable/user_guide/indexing.html#returning-a-view-versus-a-copy
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/Users/kef74yk/anaconda3/lib/python3.6/site-
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A value is trying to be set on a copy of a slice from a DataFrame.
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docs/stable/user_guide/indexing.html#returning-a-view-versus-a-copy
  self.obj[key] = _infer_fill_value(value)
/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/pandas/core/indexing.py:845: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
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See the caveats in the documentation: https://pandas.pydata.org/pandas-
docs/stable/user_guide/indexing.html#returning-a-view-versus-a-copy
  self.obj[key] = _infer_fill_value(value)
/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/pandas/core/indexing.py:966: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
Try using .loc[row_indexer,col_indexer] = value instead

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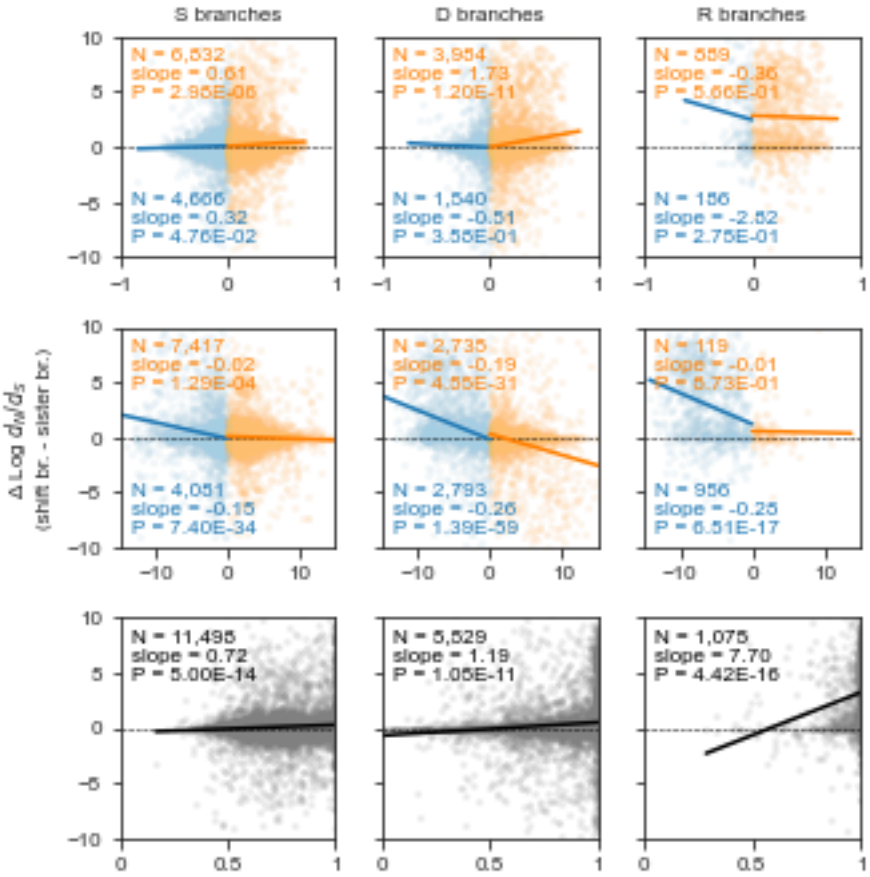
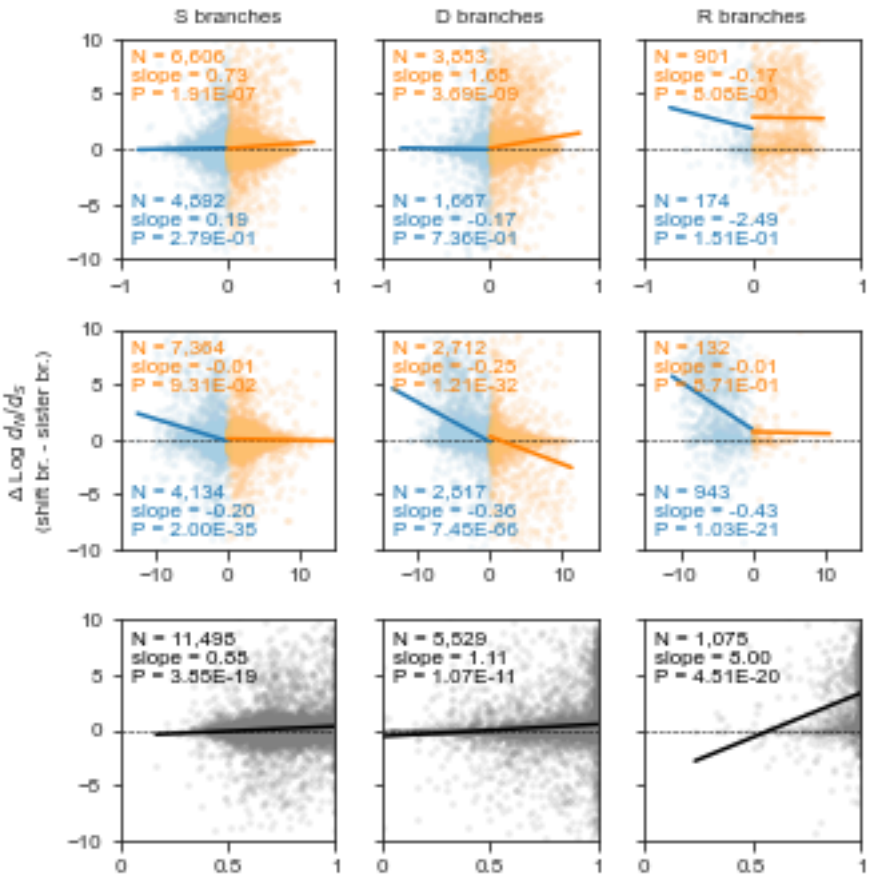
  self.obj[item] = s
/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/pandas/core/indexing.py:845: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
Try using .loc[row_indexer,col_indexer] = value instead

See the caveats in the documentation: https://pandas.pydata.org/pandas-
docs/stable/user_guide/indexing.html#returning-a-view-versus-a-copy
  self.obj[key] = _infer_fill_value(value)
/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/pandas/core/indexing.py:966: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
Try using .loc[row_indexer,col_indexer] = value instead

See the caveats in the documentation: https://pandas.pydata.org/pandas-
```

```
docs/stable/user_guide/indexing.html#returning-a-view-versus-a-copy
  self.obj[item] = s
```





[15]:
```
ylims=[8.7,4.5]
for pp,ymax in zip(pcm_prefixes,ylims):
    print(pp)
    fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=1, figsize=(2,2.3),␣
 ↪sharex=False)
    ax = axes

    x=pp+'gamma_'
    df3 = t.loc[:,t.columns.str.startswith(x)].melt()
    df3['variable'] = df3['variable'].str.replace(x,'')
    xmin=-0.6
    xmax=5.6
    ymin = -0.05
    lw=2
    alpha=0.95
    colors=['#1B9E77','#D95F02','#7570B3','#E7298A','#66A61E','#E6AB02']
    order = ['brain','heart','kidney','liver','ovary','testis']
    seaborn.boxplot(x='variable', y='value', data=df3, ax=ax, palette=colors,␣
 ↪showfliers=False, order=order)
```

```
    ax.set_ylabel('Stationary variance of\nexpression level ( )')
    ax.set_xlabel('')
    ax.set_xlim(xmin, xmax)
    ax.set_ylim(ymin, ymax)
    ax.set_xticklabels(order, rotation=45, ha='right')
    xloc = xmin+((xmax-xmin)/100*4)
    yloc = ymax-((ymax-ymin)/100*2)
    my_text='N = '+"{:,d}".format(df3.loc[(df3.variable=='brain')&(~df3.value.
↪isnull()),'variable'].shape[0])+' gene trees'
    fout = scipy.stats.friedmanchisquare(t[x+'brain'].values, t[x+'heart'].
↪values, t[x+'kidney'].values,
                                t[x+'liver'].values, t[x+'ovary'].values,␣
↪t[x+'testis'].values, )
    chistat = fout[0]
    chitext = ' ^2 = '+"{:.2e}".format(Decimal(str(chistat)))
    pval = fout[1]
    sign = '='
    if pval==0:
        pval = numpy.finfo(type(pval)).eps
        sign = '<'
    pval = "{:.2e}".format(Decimal(str(pval)))
    ptext = 'P '+sign+' '+pval
    my_text = my_text+'\n'+chitext
    my_text = my_text+'\n'+ptext
    #ax.text(x=xloc, y=yloc, s=my_text, fontsize=font_size, ha='left', va='top')
    ax.tick_params(axis='both', which='major', direction='out', length=6,␣
↪width=1, pad=2, top=False, right=False)

    matplotlib.pyplot.tight_layout()
    outbase = x+'organ_'+pp
    fig.savefig(outbase+".pdf", format='pdf', transparent=True)
    fig.savefig(outbase+".svg", format='svg', transparent=True)

    control = list()
    control = control + t[pp+'gamma_brain'].dropna().tolist()
    control = control + t[pp+'gamma_heart'].dropna().tolist()
    control = control + t[pp+'gamma_kidney'].dropna().tolist()
    control = control + t[pp+'gamma_liver'].dropna().tolist()

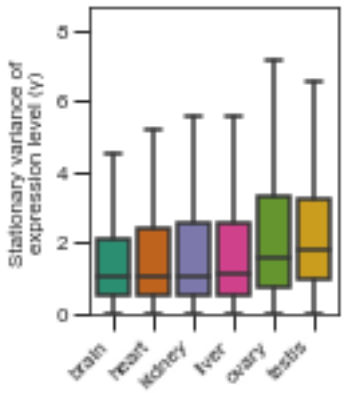
    target = list()
    target = target + t[pp+'gamma_ovary'].dropna().tolist()
    target = target + t[pp+'gamma_testis'].dropna().tolist()

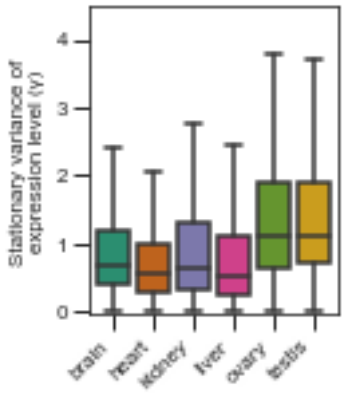
    (W, dof, p, Pest, Cl, Ch) = kfstat.bm_test(control, target)
    print(pp, 'Brunner-Munzel stat =', W)
    print(pp, 'P value =', p)
    print(pp, 'Effect size and 95% CI =', Pest, Cl, Ch)
```

```
    print(pp, 'Pest - Cl =', Pest - Cl)
    print(pp, 'Ch - Pest =', Ch - Pest)
    print()
```

```
l1ou_fpkm_
l1ou_fpkm_ Brunner-Munzel stat = 56.767067346862625
l1ou_fpkm_ P value = 0.0
l1ou_fpkm_ Effect size and 95% CI = 0.6081602634333626 0.60442581428692
0.6118947125798052
l1ou_fpkm_ Pest - Cl = 0.003734449146442609
l1ou_fpkm_ Ch - Pest = 0.003734449146442609

l1ou_tpm_
l1ou_tpm_ Brunner-Munzel stat = 94.8233631302835
l1ou_tpm_ P value = 0.0
l1ou_tpm_ Effect size and 95% CI = 0.6736075821146624 0.6700191196059939
0.6771960446233309
l1ou_tpm_ Pest - Cl = 0.0035884625086685107
l1ou_tpm_ Ch - Pest = 0.0035884625086685107
```





[16]:
```
#reg_family = statsmodels.genmod.families.family.NegativeBinomial()
reg_family = statsmodels.genmod.families.family.Poisson()
#reg_family = statsmodels.genmod.families.family.Gaussian()

num_row=2
num_col=2
alpha_small=0.1
alpha_large=0.9
kernel='gau'
# full figure size = 9.7 length x 7.2 width in inches
#fig,axes = matplotlib.pyplot.subplots(nrows=num_row, ncols=num_col, figsize=(2.
 ↪2*num_col,2.2*num_row), sharex=False)

xs = ['delta_tau','delta_maxmu','mu_complementarity']
xmins = {'delta_tau':-0.45,'delta_maxmu':-11,'mu_complementarity':0}
xmaxs = {'delta_tau':0.75,'delta_maxmu':11,'mu_complementarity':1}
#axis= {'delta_tau':axes.flat[1],'delta_maxmu':axes.
 ↪flat[2],'mu_complementarity':axes.flat[3]}
xlabels = {'delta_tau':'Shift in expression specificity',
           'delta_maxmu':'Shift in max expression level',
           'mu_complementarity':'Expression complementarity\nbetween sister␣
 ↪lineages'}
zero_vlines = {'delta_tau':False,'delta_maxmu':False,'mu_complementarity':False}

conditions = True
conditions = conditions&(b['spnode_coverage']!='root')

box_step = 0.15

for sc in shift_columns:
    #ax = axes[0,0]
    col1 = 'branch_category'
    col2 = 'spnode_coverage'
    df_branch = b.loc[(b[col1]!='No'),:].pivot_table(index=col2, columns=col1,␣
 ↪values='orthogroup', aggfunc='count').fillna(0)
    df_shift = b.loc[(b[col1]!='No')&(b[sc]==1),:].pivot_table(index=col2,␣
 ↪columns=col1, values='orthogroup', aggfunc='count').fillna(0)
    df_bl = b.loc[(b[col1]!='No'),:].pivot_table(index=col2, columns=col1,␣
 ↪values='bl_dated', aggfunc='sum').fillna(0)
    df_prop = df_shift / df_bl
    df_prop = df_prop.drop(sptree_root)
    df_prop = pandas.DataFrame(df_prop.stack())

    conf95_lowers = dict()
```

```
    conf95_uppers = dict()
    slopes = dict()
    for bc in branch_categories:
        dat = pandas.DataFrame(df_shift[bc])
        dat['bl'] = df_bl[bc]
        #formula = bc+'~1'
        formula = bc+'~bl-1'
        #mod = statsmodels.formula.api.glm(formula=formula, data=dat,␣
↪family=reg_family, freq_weights=dat['bl'])
        mod = statsmodels.formula.api.glm(formula=formula, data=dat,␣
↪family=reg_family)
        res = mod.fit()
        conf95_lowers[bc] = res.conf_int().loc['bl',0]
        conf95_uppers[bc] = res.conf_int().loc['bl',1]
        slopes[bc] = res.params['bl']
        print(sc, bc, 'num_shift =', dat[bc].sum(), 'total_bl =', dat['bl'].
↪sum(), 'shift/MY =', dat[bc].sum()/dat['bl'].sum())
    print(sc,'conf95_lower =', conf95_lowers)
    print(sc,'conf95_upper =', conf95_uppers)
    print(sc,'slope =', slopes)
```

```
l1ou_fpkm_is_shift S num_shift = 23985.0 total_bl = 47435809.20286555 shift/MY =
0.0005056306702268946
l1ou_fpkm_is_shift D num_shift = 9018.0 total_bl = 4739356.061232859 shift/MY =
0.001902790143531467
l1ou_fpkm_is_shift R num_shift = 1238.0 total_bl = 163542.86835132877 shift/MY =
0.007569880683152035
l1ou_fpkm_is_shift conf95_lower = {'S': 2.183119445576086e-06, 'D':
6.106426293159801e-06, 'R': 0.00028209263803218287}
l1ou_fpkm_is_shift conf95_upper = {'S': 2.1947428232433673e-06, 'D':
6.184910517345311e-06, 'R': 0.0002916342426424933}
l1ou_fpkm_is_shift slope = {'S': 2.1889311344097268e-06, 'D':
6.145668405252556e-06, 'R': 0.0002868634403373381}
l1ou_tpm_is_shift S num_shift = 25518.0 total_bl = 47435809.20286555 shift/MY =
0.0005379480276360182
l1ou_tpm_is_shift D num_shift = 8694.0 total_bl = 4739356.061232859 shift/MY =
0.0018344264257997974
l1ou_tpm_is_shift R num_shift = 1196.0 total_bl = 163542.86835132877 shift/MY =
0.007313067283562063
l1ou_tpm_is_shift conf95_lower = {'S': 2.1774986916571217e-06, 'D':
6.029995119022642e-06, 'R': 0.0002810877949159398}
l1ou_tpm_is_shift conf95_upper = {'S': 2.189240661272377e-06, 'D':
6.112092914266233e-06, 'R': 0.00029071850272207754}
l1ou_tpm_is_shift slope = {'S': 2.1833696764647494e-06, 'D':
6.0710440166444375e-06, 'R': 0.0002859031488190086 6}
l1ou_intersect_is_shift S num_shift = 11762.0 total_bl = 47435809.20286555
shift/MY = 0.0002479561368859176
```

```
l1ou_intersect_is_shift D num_shift = 6480.0 total_bl = 4739356.061232859
shift/MY = 0.0013672743546333894
l1ou_intersect_is_shift R num_shift = 1107.0 total_bl = 163542.86835132877
shift/MY = 0.006768867460621408
l1ou_intersect_is_shift conf95_lower = {'S': 1.9712411712291976e-06, 'D':
5.7516899231161895e-06, 'R': 0.0002766506739228304}
l1ou_intersect_is_shift conf95_upper = {'S': 1.98823158605984e-06, 'D':
5.848362005042187e-06, 'R': 0.00028668393881475}
l1ou_intersect_is_shift slope = {'S': 1.9797363786445187e-06, 'D':
5.800025964079188e-06, 'R': 0.0002816673063687902}
```

[17]:
```
num_row=1
num_col=4
alpha_small=0.1
alpha_large=0.9
kernel='gau'
box_step = 0.15
# full figure size = 9.7 length x 7.2 width in inches

for sc in ['l1ou_intersect_is_shift',]:
    for pp in pcm_prefixes:
        print(sc, pp)
        fig,axes = matplotlib.pyplot.subplots(nrows=num_row, ncols=num_col,␣
↪figsize=(7.2+2.4,2.6*num_row), sharex=False)

        if pp=='l1ou_fpkm_':
            expression_unit = 'SVA-log-TMM-FPKM'
        elif pp=='l1ou_tpm_':
            expression_unit = 'SVA-log-TPM'

        xs = [pp+'delta_tau',pp+'delta_maxmu',pp+'mu_complementarity']
        xmins = {pp+'delta_tau':-0.3,pp+'delta_maxmu':
↪-10,pp+'mu_complementarity':0}
        xmaxs = {pp+'delta_tau':0.6,pp+'delta_maxmu':10,pp+'mu_complementarity':
↪1}
        axis= {pp+'delta_tau':axes.flat[1],pp+'delta_maxmu':axes.
↪flat[2],pp+'mu_complementarity':axes.flat[3]}
        xlabels = {pp+'delta_tau':'Change in expression\nspecificity ($Δ $)',
                   pp+'delta_maxmu':'Change in max␣
↪expressionlevel\n($Δ _{max}$, w/ '+expression_unit+')',
                   pp+'mu_complementarity':'Expression complementarity\nbetween␣
↪sister branches (TEC)'}
        zero_vlines = {pp+'delta_tau':False,pp+'delta_maxmu':
↪False,pp+'mu_complementarity':False}

        conditions = True
        conditions = conditions&(b['spnode_coverage']!='root')
```

```
        for x in xs:
            box_position = 1 + (box_step*len(branch_categories))
            yticks = [0.0,0.2,0.4,0.6,0.8,1.0]
            bins=numpy.arange(xmins[x]-((xmaxs[x]-xmins[x])/50),␣
↪xmaxs[x]+((xmaxs[x]-xmins[x])/50), (xmaxs[x]-xmins[x])/100)
            ax = axis[x]
            if 'delta_' in x:
                 ax.axvline(x=0, lw=0.5, linestyle='--', color='black')
            df_tmp=b.loc[(b[sc]==1)&(conditions),:]
            ax = kfplot.hist_boxplot(x=x, category='branch_category',␣
↪df=df_tmp, colors=category_colors, xlim=[xmins[x],xmaxs[x]], bins=bins,␣
↪alpha=0.9, box_step=0.15, ax=ax)
            ax.set_xlabel(xlabels[x])
            for bc1,bc2 in itertools.combinations(branch_categories, 2):
                v1 = df_tmp.loc[(df_tmp['branch_category']==bc1),x].values
                v2 = df_tmp.loc[(df_tmp['branch_category']==bc2),x].values
                statistic,pvalue = scipy.stats.ks_2samp(v1, v2,␣
↪alternative='two-sided', mode='auto')
                print('{}; {}-{}: D = {:.2}, P = {:.2}'.format(x, bc1, bc2,␣
↪statistic, pvalue))

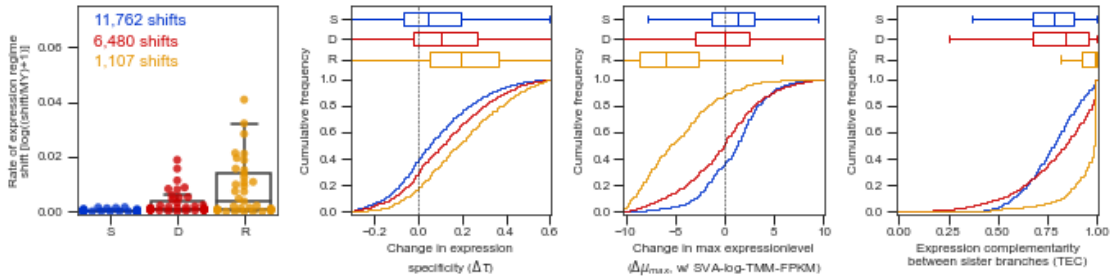
        ax = axes.flat[0]
        col1 = 'branch_category'
        col2 = 'spnode_coverage'
        df_branch = b.loc[(b[col1]!='No'),:].pivot_table(index=col2,␣
↪columns=col1, values='orthogroup', aggfunc='count').fillna(0)
        df_shift = b.loc[(b[col1]!='No')&(b[sc]==1),:].pivot_table(index=col2,␣
↪columns=col1, values='orthogroup', aggfunc='count').fillna(0)
        df_bl = b.loc[(b[col1]!='No'),:].pivot_table(index=col2, columns=col1,␣
↪values='bl_dated', aggfunc='sum').fillna(0)
        df_prop = df_shift / df_bl
        df_prop = df_prop.drop(sptree_root)
        df_prop = pandas.DataFrame(df_prop.stack())
        df_prop = numpy.log(df_prop+1)
        colors = [ category_colors[bc] for bc in branch_categories ]
        seaborn.boxplot(x=df_prop.index.get_level_values(1), y=0, data=df_prop,␣
↪order=branch_categories, palette=colors, ax=ax, boxprops={'facecolor':
↪'None'}, showfliers=False)
        seaborn.swarmplot(x=df_prop.index.get_level_values(1), y=0,␣
↪data=df_prop, order=branch_categories, palette=colors, ax=ax, alpha=0.8)
        ax.set_ylim(-0.001,0.075)
        ax.set_ylabel('Rate of expression regime\nshift [log((shift/MY)+1)]')
        ax.set_xlabel('')
        ymin,ymax = ax.get_ylim()
        label_y = ymax - ((ymax-ymin)*0.035)
```

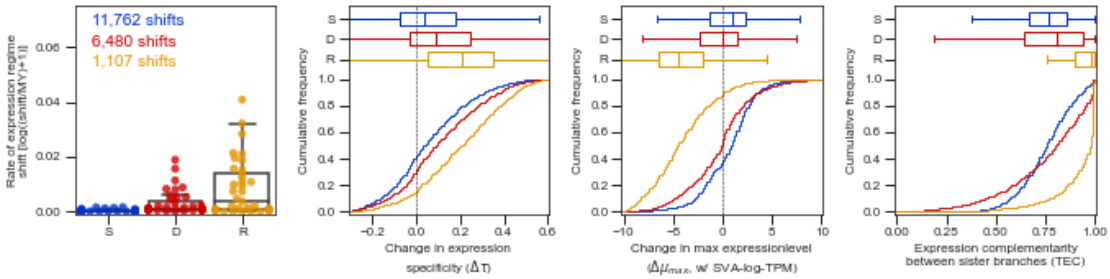
```
        for ev in branch_categories:
            num_shift = b.loc[(b.branch_category==ev)&(b[sc]==1)&(conditions),:
↪].shape[0]
            num_text = "{:,d}".format(num_shift)+' shifts'
            color = category_colors[ev]
            ax.text(-0.25, label_y, num_text, va='top', ha='left', color=color)
            label_y = label_y - ((ymax-ymin)*0.1)

        for ax in axes.flat:
            ax.tick_params(axis='both', which='major', direction='out',␣
↪length=6, width=1, pad=2, top=False, right=False)

        fig.tight_layout()
        outbase = 'shiftStats2_'+pp+sc
        fig.savefig(outbase+".pdf", format='pdf', transparent=True)
        fig.savefig(outbase+".svg", format='svg', transparent=True)
```

```
l1ou_intersect_is_shift l1ou_fpkm_
l1ou_fpkm_delta_tau; S-D: D = 0.12, P = 7.1e-49
l1ou_fpkm_delta_tau; S-R: D = 0.26, P = 6.4e-62
l1ou_fpkm_delta_tau; D-R: D = 0.16, P = 2.7e-21
l1ou_fpkm_delta_maxmu; S-D: D = 0.17, P = 3.9e-101
l1ou_fpkm_delta_maxmu; S-R: D = 0.64, P = 0.0
l1ou_fpkm_delta_maxmu; D-R: D = 0.48, P = 8.6e-186
l1ou_fpkm_mu_complementarity; S-D: D = 0.17, P = 1.8e-107
l1ou_fpkm_mu_complementarity; S-R: D = 0.59, P = 8.4e-305
l1ou_fpkm_mu_complementarity; D-R: D = 0.42, P = 1.5e-146
l1ou_intersect_is_shift l1ou_tpm_
l1ou_tpm_delta_tau; S-D: D = 0.1, P = 1.4e-39
l1ou_tpm_delta_tau; S-R: D = 0.31, P = 7.3e-84
l1ou_tpm_delta_tau; D-R: D = 0.21, P = 2.1e-37
l1ou_tpm_delta_maxmu; S-D: D = 0.19, P = 3.2e-131
l1ou_tpm_delta_maxmu; S-R: D = 0.61, P = 4.9e-323
l1ou_tpm_delta_maxmu; D-R: D = 0.48, P = 1.5e-191
l1ou_tpm_mu_complementarity; S-D: D = 0.17, P = 9e-104
l1ou_tpm_mu_complementarity; S-R: D = 0.59, P = 1.2e-305
l1ou_tpm_mu_complementarity; D-R: D = 0.43, P = 1.1e-151
```





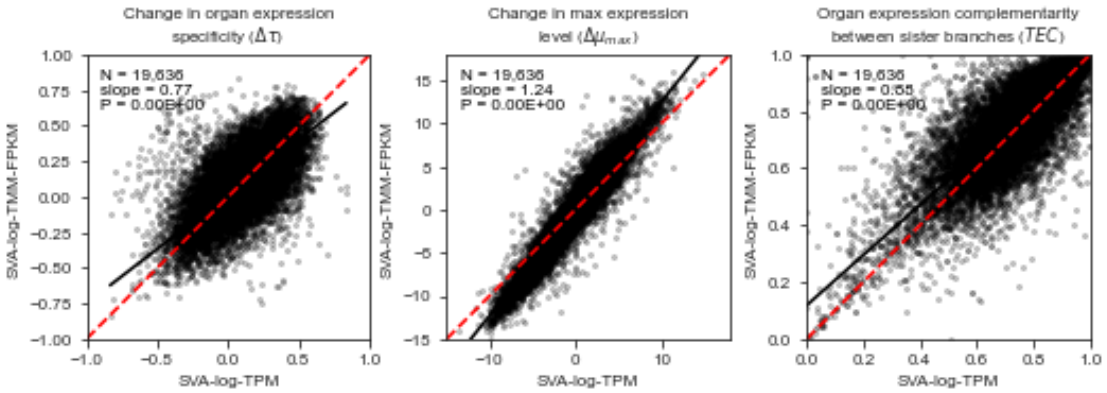
[18]:
```
fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=3, figsize=(7.2,2.5),␣
↪sharex=False)
axes = axes.flat

alpha = 0.2
size = 4

conditions = True
conditions = conditions&(b['spnode_coverage']!='root')
conditions = conditions&(b['l1ou_intersect_is_shift']==1)
tmp = b.loc[conditions,:]

xs = ['delta_tau','delta_maxmu','mu_complementarity']
labels = ['Change in organ expression\nspecificity ($Δ $)',
          'Change in max expression\nlevel ($Δ _{max}$)',
          'Organ expression complementarity\nbetween sister branches ($TEC$)'
         ]
xyranges = [[-1,1],[-15,18],[0,1]]
for i,x in enumerate(xs):
    ax = axes[i]
    seaborn.regplot('l1ou_tpm_'+x, 'l1ou_fpkm_'+x, data=tmp, ax=ax,␣
↪color='black', fit_reg=False,
                    scatter_kws={'alpha':alpha,'s':size,'rasterized':True})
    #pearson_r = numpy.round(scipy.stats.pearsonr(x=tmp['l1ou_tpm_'+x],␣
↪y=tmp['l1ou_fpkm_'+x])[0], decimals=2)
    #cor_text = "Pearson's r = {}".format(pearson_r)
    #ax.set_title(labels[i]+'\n'+cor_text)
    ols_annotations('l1ou_tpm_'+x, 'l1ou_fpkm_'+x, data=tmp, ax=ax)
    ax.set_title(labels[i])
    ax.set_xlabel('SVA-log-TPM')
    ax.set_ylabel('SVA-log-TMM-FPKM')
    ax.set_xlim(xyranges[i])
    ax.set_ylim(xyranges[i])
    ax.plot(xyranges[i], xyranges[i], linestyle='--', color='red')
```

```
fig.tight_layout(pad=0)
outbase = 'shiftStats_correlation'
fig.savefig(outbase+".pdf", format='pdf', transparent=True)
fig.savefig(outbase+".svg", format='svg', transparent=True)
```



[19]:
```
fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=1, figsize=(4,4),␣
↪sharex=False)

shift_col = 'l1ou_intersect_is_shift'
var1 = 'parent_chromosome'
var2 = 'chromosome'
var_ph = 'orthogroup'

excluded_spp =␣
↪'Astyanax_mexicanus|Danio_rerio|Gadus_morhua|Oryzias_latipes|Oreochromis_niloticus|Xenopus_
excluded_spp = [ sp.replace('_','_') for sp in excluded_spp.split('|') ]

coordinates = {
    'A':[0, -1],
    'X':[-0.866025403784386467637, 0.5],
    'Y':[0.866025403784386467637, 0.5],
}

excluded_spnodes = list()
for n in sptree.traverse():
    contain_excluded_spp = all([ node_sp in excluded_spp for node_sp in n.
↪get_leaf_names() ])
    if contain_excluded_spp:
        excluded_spnodes.append(n.name)
print('excluded spnodes in chromosome analysis:', excluded_spnodes)
is_excluded_node = b['spnode_coverage'].isin(excluded_spnodes)
```

```
b2 = b.loc[~is_excluded_node,:]

is_chr_shift = (b2['parent_chromosome']!=b2['chromosome'])
is_exp_shift = b2[shift_col].fillna(0).astype(bool)
is_all = True


# show pivot table
pivot_all = pandas.DataFrame(b2.groupby([var1,var2])[var_ph].count()).
 ↪reset_index().pivot(var1, var2).fillna(0)
pivot_chr_shift = pandas.DataFrame(b2.loc[is_chr_shift,:].
 ↪groupby([var1,var2])[var_ph].count()).reset_index().pivot(var1, var2).
 ↪fillna(0)
pivot_exp_shift = pandas.DataFrame(b2.loc[is_exp_shift,:].
 ↪groupby([var1,var2])[var_ph].count()).reset_index().pivot(var1, var2).
 ↪fillna(0)
pivot_exp_all_ratio = pivot_exp_shift/pivot_all
pivot_exp_all_ratio.columns = pivot_exp_all_ratio.columns.get_level_values(1)
#IPython.display.display(pivot_exp_all_ratio)

pivot_out = pandas.DataFrame(numpy.zeros(pivot_exp_all_ratio.shape))
for i in numpy.arange(pivot_out.shape[0]):
    for j in numpy.arange(pivot_out.shape[1]):
        percent = str(int(numpy.round(pivot_exp_all_ratio.values[i,j]*100,␣
 ↪decimals=0)))
        numerator = str(int(pivot_exp_shift.values[i,j]))
        denominator = str(int(pivot_all.values[i,j]))
        pivot_out.loc[i,j] = percent+'%\n('+numerator+'/'+denominator+')'
pivot_out.index = pivot_all.index
pivot_out.columns = pivot_all.columns

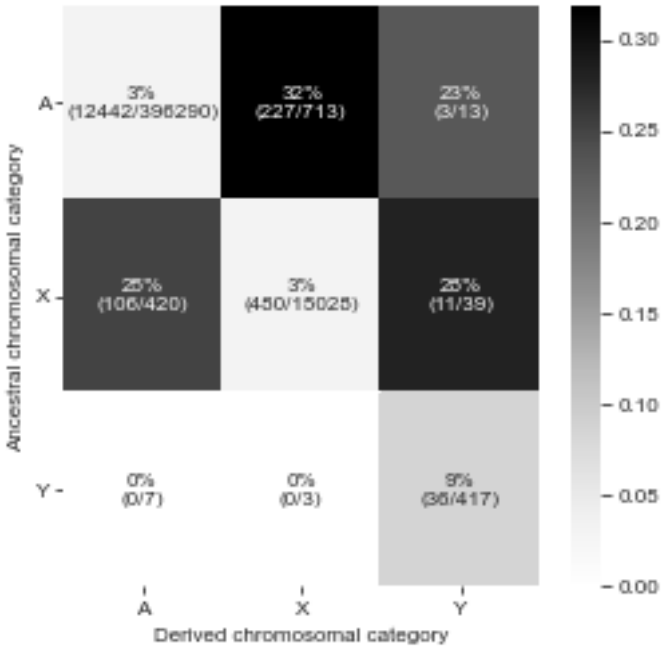
rows = pivot_all.index
cols = pivot_all.columns.get_level_values(1)
#ax.axis('tight')
#ax.axis('off')
#the_table = ax.table(cellText=pivot_out.values, colLabels=cols,␣
 ↪rowLabels=rows, loc='center')

ax = axes
seaborn.heatmap(pivot_exp_all_ratio, annot=pivot_out.values, fmt='',␣
 ↪cmap='Greys', ax=ax, annot_kws={'fontsize':font_size})
ax.set_xlabel('Derived chromosomal category')
ax.set_ylabel('Ancestral chromosomal category')
ax.tick_params(pad=2, length=3, rotation=0, labelsize=font_size)

del b2
```

```
outbase = 'chromosome_heatmap'
fig.savefig(outbase+".pdf", format='pdf', transparent=True)
fig.savefig(outbase+".svg", format='svg', transparent=True)
```

```
excluded spnodes in chromosome analysis: ['10', '11', '13',
'Xenopus_tropicalis', 'Astyanax_mexicanus', 'Danio_rerio', 'Gadus_morhua', '14',
'19', 'Oryzias_latipes', 'Oreochromis_niloticus', 'Anolis_carolinensis',
'Gallus_gallus', 'Ornithorhynchus_anatinus', 'Chinchilla_lanigera']
```



[20]:
```
# tissue network
min_taus = [0,0.5]
min_max_second_mu_ratios = [0,] # test 0 and 1
min_bss = [0,99]
min_delta_tau = -numpy.inf
nboot = 10000
nsubsample=numpy.inf#174#sum_R
shift_col = 'l1ou_intersect_is_shift'
pcm_prefixes = ['l1ou_fpkm_', 'l1ou_tpm_']
edge_width_weight=0.4
hide_nonsig=True
ancestral_max_unif_tau = None # 0.3
derived_max_unif_tau = None #0.3
bbox_length = 150
margin_size = 15
```

```
fdr_threshold = 0.05
calc_fdr = False

coordinates = {
    'brain':[0, -1],
    'heart':[0.866025403784386467637, -0.5],
    'kidney':[0.866025403784386467637, 0.5],
    'liver':[0,1],
    'ovary':[-0.866025403784386467637, 0.5],
    'testis':[-0.866025403784386467637, -0.5],
}

for pp,min_tau,min_max_second_mu_ratio,min_bs in itertools.
 ↪product(pcm_prefixes[::-1], min_taus, min_max_second_mu_ratios, min_bss):
    corrected = dict()
    observed = dict()
    expected = dict()
    bs = dict()
    Ns = dict()
    fdrs = dict()
    fdr_flag = True
    var1 = 'parent_'+pp+'max_organ'
    var2 = pp+'max_organ'
    specificity_term =␣
 ↪pp+'muRatio'+str(min_max_second_mu_ratio)+'_minTau'+str(min_tau)+'_minBS'+str(min_bs)
    print('\n', specificity_term)
    for event in branch_categories+['All',]:
        print('event =', event)
        conditions = True
        conditions = conditions&(b[shift_col]==1)
        if event is not 'All':
            conditions = conditions&(b.branch_category==event)
        conditions = conditions&(b.spnode_coverage!=sptree_root)
        conditions = (conditions)&(b['parent_'+pp+'tau']>=min_tau)
        conditions = (conditions)&(b[pp+'tau']>=min_tau)
        conditions = (conditions)&(b[pp+'delta_tau']>=min_delta_tau)
        conditions =␣
 ↪(conditions)&(b[pp+'max_second_mu_ratio']>=min_max_second_mu_ratio)
        conditions =␣
 ↪(conditions)&(b['parent_'+pp+'max_second_mu_ratio']>=min_max_second_mu_ratio)
        if min_bs!=0:
            conditions = (conditions)&(b['parent_support_iqtree']>=min_bs)
        #conditions = conditions&(b.parent_reconcil_support>=0.9)
        #conditions = conditions&(b.max_mu>=0.1)
        #conditions = conditions&(b.parent_max_mu>=0.1)
        #conditions = conditions&(b.max_mu/b.second_max_mu>=1.5)
        #conditions = conditions&(b.parent_max_mu/b.parent_second_max_mu>=1.5)
```

```
        df2 = b.loc[conditions,:]
        print('n before filterings =', df2.shape[0])
        out = shift_freq_bootstrap(df1=df2, var1=var1, var2=var2,␣
↪down_reg=False,
                                   exclude_self=True, nboot=nboot,␣
↪nsubsample=nsubsample)
        corrected[event],observed[event],expected[event],bs[event],Ns[event] =␣
↪out
        print('sample standard deviation =', numpy.sqrt(((corrected[event] -␣
↪expected[event])**2).sum(axis=0).sum(axis=0) / ((corrected[event].
↪shape[0]*corrected[event].shape[1])-1-corrected[event].shape[1])))
        IPython.display.display(observed[event])

        observed[event].
↪to_csv('shift_count_observed_'+specificity_term+'_'+event+'.tsv', sep='\t',␣
↪index=True)
        expected[event].
↪to_csv('shift_count_expected_'+specificity_term+'_'+event+'.tsv', sep='\t',␣
↪index=True)
        corrected[event].
↪to_csv('shift_count_corrected_'+specificity_term+'_'+event+'.tsv', sep='\t',␣
↪index=True)

        observed[event].stack().
↪to_csv('stack_shift_count_observed_'+specificity_term+'_'+event+'.tsv',␣
↪sep='\t', index=True)
        expected[event].stack().
↪to_csv('stack_shift_count_expected_'+specificity_term+'_'+event+'.tsv',␣
↪sep='\t', index=True)
        corrected[event].stack().
↪to_csv('stack_shift_count_corrected_'+specificity_term+'_'+event+'.tsv',␣
↪sep='\t', index=True)

        test_method = 'random'
        out = draw_network(corrected[event], observed[event], expected[event],␣
↪bs[event], self_arrow=False, self_vertex_size=False,
                           show_vertex_stat=False, edge_width=1,␣
↪hide_nonsig=hide_nonsig,
                          coordinates=coordinates, test=test_method)
        g,layout,visual_style = out
        outbase = wd+'shift_network_'+specificity_term+'_'+test_method+'_'+event
        igraph.plot(g, target=outbase+'.svg', layout=layout, bbox=(bbox_length,␣
↪bbox_length), background=None, margin=margin_size, **visual_style)
        texts = []
        texts.append(event)
        texts.append('N = '+"{:,d}".format(Ns[event]))
```

```
        add_igraph_legends(svg_file=outbase+'.svg', height=bbox_length,␣
↪width=bbox_length, texts=texts)
        command = inkscape+' --export-pdf='+wd+outbase+'.pdf'+' '+wd+outbase+'.
↪svg'
        os.system(command)
        #IPython.display.SVG(outbase+'.svg')

        if calc_fdr:
            vertex_dict = {'vertex':organs, 'color':organ_colors}
            quantile = get_quantile(observed[event], bs[event])
            try:
                fdrs[event] = get_quantile_fdr(quantile,␣
↪fdr_threshold=fdr_threshold)
            except AssertionError:
                print('FDR cannot be calculated. Skipped.')
                fdr_flag = False
            except ValueError:
                print('FDR cannot be calculated. Skipped.')
                fdr_flag = False
            else:
                out = draw_network2(observed[event], quantile, fdrs[event],␣
↪no_fp=True,
                                    self_arrow=False, self_vertex_size=False,␣
↪show_vertex_stat=False, no_obs=False,
                                    edge_width=2, edge_width_weight=5,␣
↪hide_nonsig=False, vertex_dict=vertex_dict, coordinates=coordinates,
                                    show_edge_color=True,␣
↪scaled_edge_curve=True, relative_freq_edge_width=False, sig_color='greenpink'
                                    )
                g,layout,visual_style = out
                outbase = wd+'fdr_shift_network_'+specificity_term+'_'+event
                igraph.plot(g, target=outbase+'.svg', layout=layout,␣
↪bbox=(bbox_length, bbox_length), background=None, margin=margin_size,␣
↪**visual_style)
                texts = []
                texts.append(event)
                texts.append('N = '+"{:,d}".format(Ns[event]))
                add_igraph_legends(svg_file=outbase+'.svg', height=bbox_length,␣
↪width=bbox_length, texts=texts)
                command = inkscape+' --export-pdf='+wd+outbase+'.pdf'+'␣
↪'+wd+outbase+'.svg'
                os.system(command)

    if fdr_flag&calc_fdr:
        # Unidirectional table
        tmp2 = pandas.DataFrame()
```

```
        for event in branch_categories:
            df_pvalue = observed[event].copy()
            df_pvalue.loc[:,:] = (observed[event].values > bs[event]).
↪sum(axis=0) / bs[event].shape[0]
            for ind,col in itertools.product(df_pvalue.index, df_pvalue.
↪columns):
                if ind==col:
                    df_pvalue.at[ind,col] = numpy.nan
            obs = pandas.DataFrame(observed[event].stack())
            exp = pandas.DataFrame(expected[event].stack())
            pval = pandas.DataFrame(df_pvalue.stack()) * 100
            fdr = pandas.DataFrame(fdrs[event].stack()).iloc[:,0]
            tmp = pandas.concat([obs, exp, pval, fdr], axis=1)
            tmp.columns = ['Observed','Expected','Permutation-based percentile␣
↪rank','FDR<0.05']
            tmp = tmp.reset_index()
            tmp.columns = tmp.columns.str.replace('parent_'+pp+'max_organ',␣
↪'Ancestral PEO')
            tmp.columns = tmp.columns.str.replace(pp+'max_organ', 'Derived PEO')
            tmp = tmp.dropna()
            tmp.loc[:,'Branch'] = event
            col_order = ['Branch','Ancestral PEO','Derived␣
↪PEO','Observed','Expected','Permutation-based percentile rank','FDR<0.05']
            tmp = tmp.loc[:,col_order]
            is_sig = tmp.loc[:,'FDR<0.05'].values
            tmp.loc[is_sig,'FDR<0.05'] = 'yes'
            tmp.loc[~is_sig,'FDR<0.05'] = 'no'
            tmp2 = pandas.concat([tmp2,tmp], ignore_index=True, axis=0)
        outfile = 'shift_summary_'+specificity_term+'.tsv'
        tmp2.to_csv(outfile, sep='\t', index=True)

del corrected,expected,observed,bs,Ns

# Chi-square test
pp = 'l1ou_fpkm_'
mu_ratio = 0
min_tau = 0
min_bs = 0
contingency_list = list()
for bc in branch_categories:
    tsv_file = 'shift_count_observed_{}muRatio{}_minTau{}_minBS{}_{}.tsv'
    tsv_file = tsv_file.format(pp, mu_ratio, min_tau, min_bs, bc)
    tmp = pandas.read_table(tsv_file, index_col=0)
    contingency_list.append(tmp.astype(int).values.flatten())
contingency_table = numpy.array(contingency_list)
is_observed = (contingency_table.sum(axis=0)>0)
contingency_table = contingency_table[:,is_observed]
```

```
out = scipy.stats.chi2_contingency(observed=contingency_table, correction=True,␣
↪lambda_=None)
chi,p,dof,expected = out
print('Chi-square test among 3 branch categories: chisq={:,}, P={}, dof={}'.
↪format(chi, p, dof))
```

```
 l1ou_tpm_muRatio0_minTau0_minBS0
event = S
n before filterings = 11746
N after filtering = 6617
sample standard deviation = 267.3594426707461
```

l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_tpm_max_organ						
brain	0.0	193.0	214.0	139.0	492.0	513.0
heart	91.0	0.0	68.0	39.0	107.0	121.0
kidney	103.0	70.0	0.0	118.0	186.0	182.0
liver	60.0	34.0	110.0	0.0	101.0	102.0
ovary	517.0	166.0	232.0	182.0	0.0	706.0
testis	489.0	177.0	249.0	200.0	656.0	0.0

```
event = D
n before filterings = 5960
N after filtering = 3495
sample standard deviation = 135.37208846222526
```

l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_tpm_max_organ						
brain	0.0	54.0	61.0	54.0	149.0	198.0
heart	63.0	0.0	23.0	25.0	60.0	89.0
kidney	56.0	52.0	0.0	82.0	130.0	119.0
liver	52.0	32.0	75.0	0.0	117.0	96.0
ovary	215.0	84.0	129.0	121.0	0.0	427.0
testis	264.0	103.0	137.0	124.0	304.0	0.0

```
event = R
n before filterings = 1106
N after filtering = 713
sample standard deviation = 34.049246167874735
```

l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_tpm_max_organ						
brain	0.0	16.0	7.0	5.0	28.0	48.0
heart	15.0	0.0	10.0	6.0	21.0	46.0
kidney	14.0	24.0	0.0	18.0	13.0	51.0
liver	2.0	1.0	5.0	0.0	4.0	20.0
ovary	33.0	17.0	30.0	20.0	0.0	146.0

```
testis                       26.0   15.0    15.0    8.0   49.0     0.0


event = All
n before filterings = 19096
N after filtering = 11007
sample standard deviation = 436.0393924880891
```

l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_tpm_max_organ						
brain	0.0	267.0	282.0	198.0	680.0	765.0
heart	170.0	0.0	104.0	73.0	192.0	257.0
kidney	173.0	153.0	0.0	219.0	348.0	357.0
liver	120.0	67.0	194.0	0.0	227.0	221.0
ovary	777.0	271.0	398.0	327.0	0.0	1291.0
testis	789.0	305.0	411.0	338.0	1033.0	0.0

```
 l1ou_tpm_muRatio0_minTau0_minBS99
event = S
n before filterings = 5717
N after filtering = 3122
sample standard deviation = 125.71332017109673
```

l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_tpm_max_organ						
brain	0.0	100.0	87.0	73.0	233.0	234.0
heart	38.0	0.0	23.0	21.0	46.0	51.0
kidney	55.0	37.0	0.0	51.0	76.0	75.0
liver	27.0	15.0	70.0	0.0	47.0	49.0
ovary	246.0	77.0	101.0	79.0	0.0	298.0
testis	273.0	99.0	136.0	95.0	310.0	0.0

```
event = D
n before filterings = 3061
N after filtering = 1799
sample standard deviation = 70.89962646450866
```

l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_tpm_max_organ						
brain	0.0	32.0	34.0	35.0	86.0	101.0
heart	35.0	0.0	11.0	9.0	28.0	42.0
kidney	28.0	27.0	0.0	37.0	52.0	76.0
liver	32.0	20.0	35.0	0.0	58.0	48.0
ovary	119.0	45.0	63.0	62.0	0.0	250.0
testis	134.0	50.0	63.0	47.0	140.0	0.0

```
event = R
```

```
n before filterings = 628
N after filtering = 395
sample standard deviation = 17.742557163867247
```

l1ou_tpm_max_organ / parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	12.0	3.0	3.0	17.0	18.0
heart	7.0	0.0	4.0	4.0	12.0	22.0
kidney	6.0	17.0	0.0	10.0	7.0	28.0
liver	1.0	0.0	4.0	0.0	3.0	12.0
ovary	16.0	8.0	19.0	10.0	0.0	82.0
testis	17.0	10.0	11.0	5.0	27.0	0.0

```
event = All
n before filterings = 9529
N after filtering = 5386
sample standard deviation = 213.2151605464185
```

l1ou_tpm_max_organ / parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	145.0	124.0	111.0	339.0	355.0
heart	80.0	0.0	38.0	34.0	87.0	116.0
kidney	89.0	82.0	0.0	99.0	143.0	181.0
liver	63.0	35.0	111.0	0.0	111.0	111.0
ovary	386.0	133.0	186.0	151.0	0.0	636.0
testis	428.0	162.0	215.0	149.0	486.0	0.0

```
 l1ou_tpm_muRatio0_minTau0.5_minBS0
event = S
n before filterings = 5407
N after filtering = 2440
sample standard deviation = 104.02846536341698
```

l1ou_tpm_max_organ / parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	105.0	117.0	88.0	228.0	247.0
heart	30.0	0.0	19.0	14.0	36.0	47.0
kidney	40.0	20.0	0.0	51.0	66.0	59.0
liver	30.0	13.0	57.0	0.0	44.0	55.0
ovary	74.0	25.0	31.0	37.0	0.0	162.0
testis	167.0	75.0	125.0	96.0	282.0	0.0

```
event = D
n before filterings = 2508
N after filtering = 1142
sample standard deviation = 45.90762558051996
```

l1ou_tpm_max_organ parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	22.0	23.0	23.0	43.0	84.0
heart	22.0	0.0	3.0	10.0	19.0	23.0
kidney	10.0	5.0	0.0	18.0	24.0	27.0
liver	20.0	12.0	36.0	0.0	48.0	45.0
ovary	35.0	9.0	27.0	24.0	0.0	109.0
testis	117.0	41.0	68.0	61.0	134.0	0.0

event = R
n before filterings = 290
N after filtering = 147
sample standard deviation = 6.262471039887569

l1ou_tpm_max_organ parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	2.0	1.0	3.0	4.0	17.0
heart	5.0	0.0	2.0	2.0	5.0	20.0
kidney	1.0	1.0	0.0	0.0	0.0	4.0
liver	1.0	0.0	4.0	0.0	2.0	5.0
ovary	4.0	3.0	1.0	2.0	0.0	21.0
testis	9.0	6.0	3.0	3.0	16.0	0.0

event = All
n before filterings = 8284
N after filtering = 3762
sample standard deviation = 154.65131013359417

l1ou_tpm_max_organ parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	130.0	141.0	114.0	279.0	349.0
heart	57.0	0.0	24.0	26.0	60.0	90.0
kidney	51.0	26.0	0.0	69.0	91.0	90.0
liver	51.0	25.0	98.0	0.0	95.0	106.0
ovary	113.0	37.0	60.0	63.0	0.0	295.0
testis	297.0	126.0	198.0	163.0	438.0	0.0

l1ou_tpm_muRatio0_minTau0.5_minBS99
event = S
n before filterings = 2797
N after filtering = 1217
sample standard deviation = 51.15382501689103

l1ou_tpm_max_organ parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	60.0	52.0	44.0	111.0	119.0
heart	12.0	0.0	8.0	8.0	16.0	14.0

kidney	24.0	11.0	0.0	27.0	26.0	27.0
liver	11.0	6.0	37.0	0.0	23.0	26.0
ovary	36.0	12.0	12.0	21.0	0.0	79.0
testis	107.0	43.0	68.0	45.0	132.0	0.0

event = D
n before filterings = 1282
N after filtering = 567
sample standard deviation = 21.755287970514175

l1ou_tpm_max_organ parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	11.0	11.0	16.0	24.0	43.0
heart	15.0	0.0	3.0	6.0	9.0	11.0
kidney	6.0	4.0	0.0	5.0	9.0	17.0
liver	12.0	9.0	16.0	0.0	24.0	24.0
ovary	19.0	4.0	18.0	11.0	0.0	50.0
testis	55.0	18.0	33.0	20.0	64.0	0.0

event = R
n before filterings = 174
N after filtering = 80
sample standard deviation = 3.1484517998403234

l1ou_tpm_max_organ parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	1.0	0.0	2.0	1.0	5.0
heart	1.0	0.0	0.0	1.0	4.0	9.0
kidney	1.0	1.0	0.0	0.0	0.0	1.0
liver	1.0	0.0	3.0	0.0	2.0	3.0
ovary	2.0	2.0	1.0	0.0	0.0	16.0
testis	6.0	4.0	1.0	2.0	10.0	0.0

event = All
n before filterings = 4294
N after filtering = 1880
sample standard deviation = 76.13306751530278

l1ou_tpm_max_organ parent_l1ou_tpm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	72.0	63.0	62.0	137.0	167.0
heart	28.0	0.0	11.0	15.0	29.0	34.0
kidney	31.0	16.0	0.0	32.0	36.0	45.0
liver	24.0	15.0	57.0	0.0	50.0	54.0
ovary	57.0	18.0	32.0	32.0	0.0	147.0
testis	171.0	65.0	104.0	68.0	208.0	0.0

```
 l1ou_fpkm_muRatio0_minTau0_minBS0
event = S
n before filterings = 11746
N after filtering = 6886
sample standard deviation = 245.19105957603753
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	377.0	238.0	295.0	308.0	459.0
heart	230.0	0.0	137.0	225.0	185.0	268.0
kidney	133.0	93.0	0.0	186.0	129.0	162.0
liver	190.0	188.0	184.0	0.0	180.0	236.0
ovary	169.0	143.0	106.0	175.0	0.0	305.0
testis	361.0	246.0	239.0	313.0	426.0	0.0

```
event = D
n before filterings = 5960
N after filtering = 3586
sample standard deviation = 125.45799930283056
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	76.0	71.0	102.0	101.0	154.0
heart	125.0	0.0	72.0	94.0	94.0	165.0
kidney	73.0	62.0	0.0	78.0	89.0	106.0
liver	128.0	133.0	128.0	0.0	155.0	194.0
ovary	104.0	65.0	72.0	126.0	0.0	191.0
testis	196.0	117.0	135.0	173.0	207.0	0.0

```
event = R
n before filterings = 1106
N after filtering = 746
sample standard deviation = 31.595094351223743
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	14.0	8.0	11.0	12.0	40.0
heart	40.0	0.0	25.0	35.0	37.0	87.0
kidney	9.0	5.0	0.0	9.0	2.0	26.0
liver	36.0	29.0	42.0	0.0	27.0	70.0
ovary	16.0	14.0	11.0	18.0	0.0	35.0
testis	17.0	21.0	10.0	10.0	30.0	0.0

```
event = All
n before filterings = 19096
N after filtering = 11395
sample standard deviation = 399.2952002397656
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	470.0	320.0	411.0	431.0	656.0
heart	398.0	0.0	235.0	361.0	319.0	523.0
kidney	216.0	167.0	0.0	276.0	229.0	297.0
liver	357.0	359.0	361.0	0.0	370.0	503.0
ovary	295.0	228.0	192.0	326.0	0.0	535.0
testis	588.0	397.0	390.0	504.0	681.0	0.0

l1ou_fpkm_muRatio0_minTau0_minBS99
event = S
n before filterings = 5717
N after filtering = 3307
sample standard deviation = 118.45128065945984

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	195.0	112.0	141.0	152.0	225.0
heart	98.0	0.0	62.0	85.0	77.0	90.0
kidney	65.0	51.0	0.0	102.0	61.0	87.0
liver	96.0	75.0	85.0	0.0	70.0	96.0
ovary	80.0	76.0	53.0	90.0	0.0	147.0
testis	209.0	134.0	128.0	162.0	203.0	0.0

event = D
n before filterings = 3061
N after filtering = 1826
sample standard deviation = 63.53810496821362

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	44.0	36.0	55.0	56.0	86.0
heart	70.0	0.0	36.0	44.0	53.0	87.0
kidney	40.0	32.0	0.0	37.0	44.0	65.0
liver	72.0	57.0	72.0	0.0	80.0	100.0
ovary	52.0	28.0	37.0	56.0	0.0	91.0
testis	101.0	58.0	67.0	74.0	96.0	0.0

event = R
n before filterings = 628
N after filtering = 408
sample standard deviation = 15.80211741497752

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	7.0	2.0	4.0	10.0	19.0
heart	16.0	0.0	12.0	23.0	17.0	39.0

kidney	5.0	4.0	0.0	6.0	1.0	13.0
liver	23.0	16.0	22.0	0.0	14.0	37.0
ovary	8.0	8.0	9.0	10.0	0.0	21.0
testis	14.0	16.0	7.0	7.0	18.0	0.0

event = All
n before filterings = 9529
N after filtering = 5618
sample standard deviation = 196.28866925653753

l1ou_fpkm_max_organ parent_l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	247.0	151.0	200.0	223.0	332.0
heart	185.0	0.0	110.0	153.0	148.0	218.0
kidney	111.0	91.0	0.0	147.0	110.0	166.0
liver	192.0	153.0	183.0	0.0	170.0	236.0
ovary	141.0	115.0	100.0	158.0	0.0	262.0
testis	331.0	210.0	205.0	245.0	325.0	0.0

l1ou_fpkm_muRatio0_minTau0.5_minBS0
event = S
n before filterings = 4959
N after filtering = 2299
sample standard deviation = 92.23749573568381

l1ou_fpkm_max_organ parent_l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	187.0	113.0	126.0	151.0	208.0
heart	48.0	0.0	32.0	54.0	39.0	60.0
kidney	28.0	26.0	0.0	68.0	48.0	47.0
liver	45.0	46.0	82.0	0.0	51.0	79.0
ovary	34.0	19.0	17.0	34.0	0.0	55.0
testis	104.0	87.0	107.0	114.0	190.0	0.0

event = D
n before filterings = 2262
N after filtering = 1058
sample standard deviation = 38.8931588183576

l1ou_fpkm_max_organ parent_l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
brain	0.0	34.0	17.0	34.0	38.0	61.0
heart	33.0	0.0	18.0	22.0	21.0	36.0
kidney	17.0	14.0	0.0	25.0	22.0	24.0
liver	36.0	34.0	40.0	0.0	57.0	68.0
ovary	15.0	10.0	16.0	19.0	0.0	35.0
testis	67.0	33.0	57.0	62.0	93.0	0.0

```
event = R
n before filterings = 264
N after filtering = 149
sample standard deviation = 6.845836834841906
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	4.0	1.0	0.0	1.0	9.0
heart	10.0	0.0	4.0	9.0	9.0	24.0
kidney	1.0	0.0	0.0	1.0	0.0	2.0
liver	5.0	3.0	6.0	0.0	1.0	23.0
ovary	1.0	5.0	2.0	2.0	0.0	0.0
testis	6.0	5.0	1.0	2.0	12.0	0.0

```
event = All
n before filterings = 7568
N after filtering = 3544
sample standard deviation = 135.0823187369566
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	225.0	132.0	160.0	192.0	279.0
heart	92.0	0.0	54.0	87.0	69.0	120.0
kidney	46.0	41.0	0.0	94.0	72.0	73.0
liver	86.0	83.0	129.0	0.0	110.0	172.0
ovary	51.0	34.0	35.0	55.0	0.0	90.0
testis	181.0	130.0	167.0	184.0	301.0	0.0

```
 l1ou_fpkm_muRatio0_minTau0.5_minBS99
event = S
n before filterings = 2568
N after filtering = 1168
sample standard deviation = 47.04147442583773
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	99.0	53.0	65.0	71.0	112.0
heart	22.0	0.0	13.0	26.0	17.0	20.0
kidney	10.0	18.0	0.0	36.0	22.0	22.0
liver	24.0	22.0	42.0	0.0	22.0	33.0
ovary	13.0	12.0	10.0	17.0	0.0	33.0
testis	66.0	54.0	61.0	61.0	92.0	0.0

```
event = D
n before filterings = 1179
```

```
N after filtering = 530
sample standard deviation = 19.094916912802102
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	20.0	5.0	17.0	18.0	33.0
heart	19.0	0.0	9.0	9.0	10.0	22.0
kidney	10.0	7.0	0.0	9.0	7.0	13.0
liver	23.0	15.0	21.0	0.0	33.0	35.0
ovary	9.0	5.0	13.0	6.0	0.0	13.0
testis	32.0	19.0	28.0	27.0	43.0	0.0

```
event = R
n before filterings = 149
N after filtering = 75
sample standard deviation = 3.2516885764346233
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	1.0	0.0	0.0	1.0	4.0
heart	2.0	0.0	2.0	6.0	4.0	13.0
kidney	1.0	0.0	0.0	0.0	0.0	1.0
liver	3.0	2.0	3.0	0.0	1.0	11.0
ovary	1.0	2.0	2.0	0.0	0.0	0.0
testis	4.0	3.0	0.0	2.0	6.0	0.0

```
event = All
n before filterings = 3939
N after filtering = 1791
sample standard deviation = 67.98354220222437
```

l1ou_fpkm_max_organ	brain	heart	kidney	liver	ovary	testis
parent_l1ou_fpkm_max_organ						
brain	0.0	120.0	58.0	82.0	90.0	150.0
heart	44.0	0.0	24.0	42.0	31.0	55.0
kidney	21.0	25.0	0.0	45.0	31.0	36.0
liver	50.0	39.0	67.0	0.0	56.0	81.0
ovary	23.0	19.0	25.0	23.0	0.0	46.0
testis	104.0	77.0	91.0	92.0	144.0	0.0

```
Chi-square test among 3 branch categories: chisq=530.740393856863,
P=1.5244714357425737e-77, dof=58
```

[21]:
```
pp = 'l1ou_fpkm_'
mu_ratio = 0
min_tau = 0
min_bs = 0
```

```
# Unidirectional
tmp_list = list()
for bc in branch_categories:
    for stat in ['observed','expected']:
        tsv_file = 'shift_count_{}_{}muRatio{}_minTau{}_minBS{}_{}.tsv'
        tsv_file = tsv_file.format(stat, pp, mu_ratio, min_tau, min_bs, bc)
        tmp = pandas.read_table(tsv_file, index_col=0)
        tmp.index.name = None
        tmp = pandas.DataFrame(tmp.stack())
        tmp.columns = [bc+'_'+stat,]
        tmp_list.append(tmp)
tmp2 = pandas.concat(tmp_list, axis=1)
for col in tmp2.columns[tmp2.columns.str.endswith('_observed')]:
    tmp2.loc[:,col] = tmp2.loc[:,col].astype(int)
tmp2 = tmp2.reset_index()
tmp2.columns = tmp2.columns.str.replace('level_0', 'ancestral_PEO')
tmp2.columns = tmp2.columns.str.replace('level_1', 'derived_PEO')
for bc in branch_categories:
    tmp2.loc[:,bc+'_pvalue'] = numpy.nan
    tmp2.loc[:,bc+'_chi2'] = numpy.nan
    total_obs = tmp2.loc[:,bc+'_observed'].sum()
    total_exp = tmp2.loc[:,bc+'_expected'].sum()
    assert total_obs==total_exp, 'Total counts should match.'

outfile = 'shift_chisq_test_unidirectional.tsv'
tmp2.to_csv(outfile, sep='\t', index=True)

# Bidirectional
organ_combinations = itertools.combinations(organs, 2)
df_bi = pandas.DataFrame(organ_combinations)
df_bi.columns = ['PEO1','PEO2']
cols = [ bc+'_'+stat for bc,stat in itertools.product(branch_categories,␣
 ↪['observed','expected']) ]
for col in cols:
    df_bi.loc[:,col] = 0
for i in df_bi.index:
    o1 = df_bi.loc[i,'PEO1']
    o2 = df_bi.loc[i,'PEO2']
    is_target1 = ((tmp2.loc[:,'ancestral_PEO']==o1)&(tmp2.loc[:
 ↪,'derived_PEO']==o2))
    is_target2 = ((tmp2.loc[:,'ancestral_PEO']==o2)&(tmp2.loc[:
 ↪,'derived_PEO']==o1))
    is_target = is_target1 | is_target2
    tmp = tmp2.loc[is_target,cols].sum(axis=0)
    df_bi.loc[i,cols] = tmp.values
```

```
for bc in branch_categories:
    total_obs = df_bi.loc[:,bc+'_observed'].sum()
    total_exp = df_bi.loc[:,bc+'_expected'].sum()
    for i in df_bi.index:
        obs = df_bi.loc[i,bc+'_observed']
        exp = df_bi.loc[i,bc+'_expected']

outfile = 'shift_chisq_test_bidirectional.tsv'
df_bi.to_csv(outfile, sep='\t', index=True)
df_bi.head()
```

[21]:

	PEO1	PEO2	S_observed	S_expected	D_observed	D_expected	R_observed	R_expected
0	brain	heart	607.0	505.507195	201.0	192.884207	54.0	52.791154
1	brain	kidney	371.0	398.683574	144.0	167.185266	17.0	22.351151
2	brain	liver	485.0	535.961005	230.0	252.900053	47.0	49.070692
3	brain	ovary	477.0	530.775255	205.0	227.337199	28.0	31.958141
4	brain	testis	820.0	720.330343	350.0	312.114196	57.0	50.941958

[22]:
```
for pp,min_tau,min_max_second_mu_ratio,min_bs in itertools.
↪product(pcm_prefixes, min_taus, min_max_second_mu_ratios, min_bss):
    specificity_term =␣
↪pp+'muRatio'+str(min_max_second_mu_ratio)+'_minTau'+str(min_tau)+'_minBS'+str(min_bs)
    print(specificity_term)

    edat = dict()
    erank = dict()
    for event in ['S','D','R']:
        infile = 'stack_shift_count_observed_'+specificity_term+'_'+event+'.tsv'
        tmp = pandas.read_csv(infile, sep='\t', header=None, index_col=[0,1])
        edat[event] = tmp.astype(int).values.flatten()
    is_nonzero = (edat['S']+edat['D']+edat['R']!=0)
    for event in ['S','D','R']:
        edat[event] = edat[event][is_nonzero]
        #erank[event] = edat[event].argsort()

    for event1,event2 in itertools.combinations(['S','D','R'], 2):
        edat_ct = numpy.array([edat[event1],edat[event2]])
        #erank_ct = numpy.array([erank[event1],erank[event2]])
        try:
            chisq_dat = scipy.stats.chi2_contingency(edat_ct, correction=True)
```

```
            #chisq_rank = scipy.stats.chi2_contingency(erank_ct,␣
↪correction=True)
            print(event1, event2, 'raw count. P-value =', chisq_dat[1], 'chisq␣
↪stat =', chisq_dat[0])
            #print(event1, event2, 'rank. P-value =', chisq_rank[1], 'chisq␣
↪stat =', chisq_rank[0])
        except:
            print(event1, event2, 'raw count. Error in chisq test')

    #all
    edat_ct = numpy.array([edat['S'],edat['D'],edat['R']])
    #erank_ct = numpy.array([erank['S'],erank['D'],erank['R']])
    chisq_dat = scipy.stats.chi2_contingency(edat_ct, correction=True)
    #chisq_rank = scipy.stats.chi2_contingency(erank_ct, correction=True)
    print('ALL raw count. P-value =', chisq_dat[1], 'chisq stat =',␣
↪chisq_dat[0])
    #print('ALL rank. P-value =', chisq_rank[1], 'chisq stat =', chisq_rank[0])
    print()
```

```
l1ou_fpkm_muRatio0_minTau0_minBS0
S D raw count. P-value = 1.1645425725499324e-33 chisq stat = 232.6015555526961
S R raw count. P-value = 3.15741388058073e-54 chisq stat = 337.26871370739775
D R raw count. P-value = 7.322841049325359e-27 chisq stat = 196.83199619773367
ALL raw count. P-value = 1.5244714357425737e-77 chisq stat = 530.740393856863

l1ou_fpkm_muRatio0_minTau0_minBS99
S D raw count. P-value = 1.1656647990706282e-19 chisq stat = 157.77142932826834
S R raw count. P-value = 4.92143783390324e-28 chisq stat = 203.0640970783855
D R raw count. P-value = 3.0619835981501303e-06 chisq stat = 77.09101926176949
ALL raw count. P-value = 4.6986592404860774e-36 chisq stat = 309.68191950099987

l1ou_fpkm_muRatio0_minTau0.5_minBS0
S D raw count. P-value = 8.887362232292662e-18 chisq stat = 147.27294260834327
S R raw count. P-value = 2.941578886654832e-31 chisq stat = 220.05562051022451
D R raw count. P-value = 3.816019765323653e-14 chisq stat = 126.51240092175345
ALL raw count. P-value = 5.811232248715891e-43 chisq stat = 347.9745963183017

l1ou_fpkm_muRatio0_minTau0.5_minBS99
S D raw count. P-value = 5.566817868652583e-12 chisq stat = 113.72968199442163
S R raw count. P-value = 2.377658640736338e-17 chisq stat = 144.86730756686904
D R raw count. P-value = 0.0004896507293822123 chisq stat = 60.807030670771894
ALL raw count. P-value = 4.223659765548238e-22 chisq stat = 228.57604722134585

l1ou_tpm_muRatio0_minTau0_minBS0
S D raw count. P-value = 1.2803596852689708e-29 chisq stat = 211.44194549979858
S R raw count. P-value = 3.2765565191475903e-44 chisq stat = 286.7964343857895
D R raw count. P-value = 1.189506679469606e-24 chisq stat = 184.99699829145175
```

```
ALL raw count. P-value = 1.1858636662178189e-66 chisq stat = 474.31996529441284

l1ou_tpm_muRatio0_minTau0_minBS99
S D raw count. P-value = 1.0523789030835427e-14 chisq stat = 129.760188956094
S R raw count. P-value = 2.2029154641494666e-24 chisq stat = 183.55598383597146
D R raw count. P-value = 5.481109524503753e-08 chisq stat = 88.8422765150004
ALL raw count. P-value = 9.238148961661861e-31 chisq stat = 279.6357445931875

l1ou_tpm_muRatio0_minTau0.5_minBS0
S D raw count. P-value = 1.3961237112388258e-18 chisq stat = 151.7750466106425
S R raw count. P-value = 3.0760106664249445e-14 chisq stat = 127.05739423406402
D R raw count. P-value = 1.6272885044004317e-08 chisq stat = 92.26093633030023
ALL raw count. P-value = 8.693352683566968e-31 chisq stat = 279.7874088371217

l1ou_tpm_muRatio0_minTau0.5_minBS99
S D raw count. P-value = 1.3431121459082411e-07 chisq stat = 86.28509322451443
S R raw count. P-value = 8.085657493226364e-09 chisq stat = 94.20781351567337
D R raw count. P-value = 0.006416527451683615 chisq stat = 51.36161390751743
ALL raw count. P-value = 2.3979096921829816e-13 chisq stat = 172.81407742787528
```

[23]:
```
reverse=True

for pp,min_tau,min_max_second_mu_ratio,min_bs in itertools.
 ↪product(pcm_prefixes, min_taus, min_max_second_mu_ratios, min_bss):
    specificity_term =␣
 ↪pp+'muRatio'+str(min_max_second_mu_ratio)+'_minTau'+str(min_tau)+'_minBS'+str(min_bs)
    print(specificity_term)
    observed = dict()
    for event in ['S','D','R']:
        infile = 'shift_count_observed_'+specificity_term+'_'+event+'.tsv'
        observed[event] = pandas.read_csv(infile, sep='\t', header=0,␣
 ↪index_col=0)
    num_data = len(observed['S'].index) * len(observed['S'].columns) *␣
 ↪len(observed.keys())
    df1 = pandas.DataFrame(index=numpy.arange(num_data),␣
 ↪columns=['event','state','organ','shift_value'])
    i=0
    for k in observed.keys():
        for state in ['ancestral','derived']:
            if state=='ancestral':
                axis=1
            elif state=='derived':
                axis=0
            values = observed[k].sum(axis=axis)
            values = values / values.sum()
            next_i = i+len(values)
```

```
            #tmp = pandas.DataFrame({'organ':values.index.tolist(),␣
↪'shift_value':values.tolist()})
            #tmp['event'] = k
            #tmp['stete'] = state
            df1.loc[i:(next_i-1),'event'] = k
            df1.loc[i:(next_i-1),'state'] = state
            df1.loc[i:(next_i-1),'organ'] = values.index.tolist()
            df1.loc[i:(next_i-1),'shift_value'] = values.tolist()
            df1 = pandas.concat([df1,tmp], ignore_index=True, sort=False)
            i = next_i
    #df1.loc[:,'organ'] = df1['organ'].str.replace('unif.\n<0.3', 'unif.')

    #colors = {'brain':'#1B9E77','heart':'#D95F02','kidney':'#7570B3','liver':
↪'#E7298A','ovary':'#66A61E','testis':'#E6AB02'}
    #colors =␣
↪['#1B9E77','#D95F02','#7570B3','#E7298A','#66A61E','#E6AB02','darkgray']
    colors = ['#1B9E77','#D95F02','#7570B3','#E7298A','#66A61E','#E6AB02',]
    fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=1, figsize=(2,2),␣
↪sharex=False)
    ax=axes
    df1 = df1.pivot_table(index=['state','event'], columns='organ',␣
↪values='shift_value', aggfunc='first').fillna(0)
    df1 = df1.loc[[ (l1,l2) for l1 in ['ancestral', 'derived'] for l2 in␣
↪branch_categories ],:]
    if reverse:
        df1 = df1.iloc[:,::-1]
        colors.reverse()
    df1.plot.bar(stacked=True, ax=ax, color=colors, legend=False,␣
↪fontsize=font_size)
    ax.set_xlabel('', fontsize=font_size)
    ax.set_ylabel('Frequency', fontsize=font_size)
    ax.set_xticks(numpy.arange(len(branch_categories)*2), minor=False)
    ax.set_xticks([(len(branch_categories)-1)/2,␣
↪len(branch_categories)+((len(branch_categories)-1)/2)], minor=True)
    ax.set_xticklabels(branch_categories*2, minor=False, ha='center',␣
↪rotation=0, fontsize=font_size)
    ax.set_xticklabels(['\nAncestral','\nDerived'], minor=True, ha='center',␣
↪rotation=0, fontsize=font_size)
    ax.tick_params(axis='x', which='major', direction='out', length=6, width=1)
    ax.tick_params(axis='x', which='minor', direction='out', length=6, width=0)
    ax.tick_params(axis='both', which='major', direction='out', length=6,␣
↪width=1, pad=2, top=False, right=False)
    ax.set_ylim(0, 1)

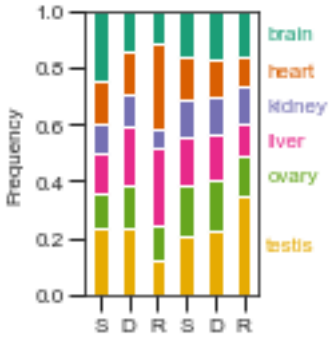
    handles, labels = ax.get_legend_handles_labels()
```

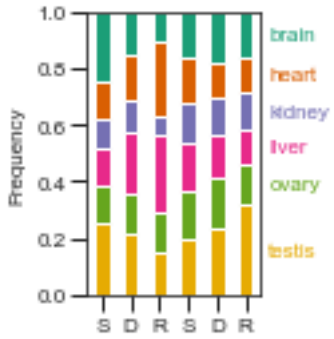
```
    #ax.legend(handles[::-1], labels[::-1], bbox_to_anchor=(1,1), loc=2,␣
↪fontsize=font_size)

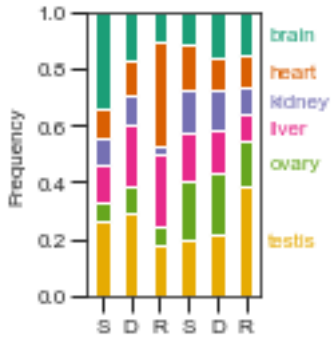
    xmax = 0
    for p in ax.patches:
        xmax = max(xmax, p.get_x())
    rightmost_y_coordinates = list()
    for p in ax.patches:
        if p.get_x()==xmax:
            rightmost_y_coordinates.append(p.get_y())
    rightmost_y_coordinates.append(1)
    rightmost_y_coordinates = numpy.array(rightmost_y_coordinates)[::-1]
    rightmost_y_coordinates = (rightmost_y_coordinates[1:] +␣
↪rightmost_y_coordinates[:-1]) / 2
    colors.reverse()
    for tis,c,y in zip(labels[::-1], colors, rightmost_y_coordinates):
        ax.text(x=(len(branch_categories)*2)-0.2, y=y, s=tis,␣
↪fontsize=font_size, color=c, va='center', ha='left')

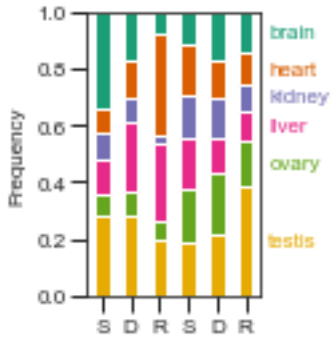
    fig.tight_layout()
    outbase = 'shift_freq_ancestral_derived_'+specificity_term
    fig.savefig(outbase+".pdf", format='pdf', transparent=True)
    fig.savefig(outbase+".svg", format='svg', transparent=True)
```

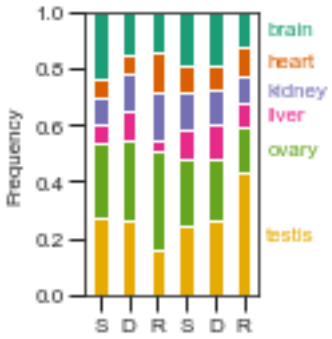
```
l1ou_fpkm_muRatio0_minTau0_minBS0
l1ou_fpkm_muRatio0_minTau0_minBS99
l1ou_fpkm_muRatio0_minTau0.5_minBS0
l1ou_fpkm_muRatio0_minTau0.5_minBS99
l1ou_tpm_muRatio0_minTau0_minBS0
l1ou_tpm_muRatio0_minTau0_minBS99
l1ou_tpm_muRatio0_minTau0.5_minBS0
l1ou_tpm_muRatio0_minTau0.5_minBS99
```

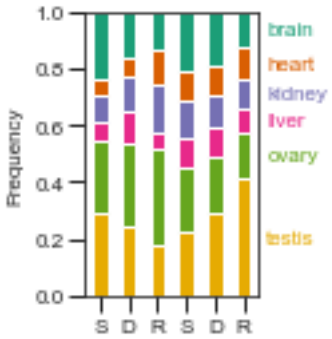


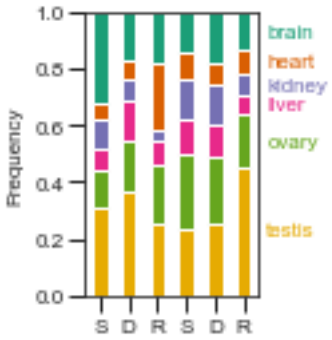

1.0
0.5
0.6
0.4
0.2
0.0
Frequency
S D R S D R
brain
heart
kidney
liver
ovary
testis

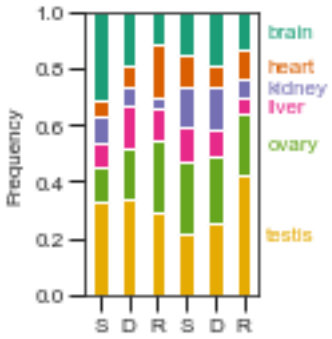

1.0
0.5
0.6
0.4
0.2
0.0
Frequency
S D R S D R
brain
heart
kidney
liver
ovary
testis


1.0
0.5
0.6
0.4
0.2
0.0
Frequency
S D R S D R
brain
heart
kidney
liver
ovary
testis


1.0
0.5
0.6
0.4
0.2
0.0
Frequency
S D R S D R
brain
heart
kidney
liver
ovary
testis


1.0
0.5
0.6
0.4
0.2
0.0
Frequency
S D R S D R
brain
heart
kidney
liver
ovary
testis


1.0
0.5
0.6
0.4
0.2
0.0
Frequency
S D R S D R
brain
heart
kidney
liver
ovary
testis



[24]:
```
ylab = 'PEO shift symmetry'
nrep = 1000
orders = branch_categories

def get_bootstrap(df):
    num_category = numpy.prod(df.shape)
    fill_series = pandas.Series([0,]*num_category)
    shape = df.shape
    x = df.values.flatten()
    size = x.sum().astype(int)
    ind = numpy.arange(0,x.shape[0])
    p = x/size
    rand = numpy.random.choice(a=ind, size=size, p=p)
    count = pandas.Series(rand).value_counts().add(fill_series).fillna(0).values
    table = numpy.reshape(a=count, newshape=shape)
    return table

for pp,min_tau,min_max_second_mu_ratio,min_bs in itertools.
↪product(pcm_prefixes, min_taus, min_max_second_mu_ratios, min_bss):
    specificity_term =␣
↪pp+'muRatio'+str(min_max_second_mu_ratio)+'_minTau'+str(min_tau)+'_minBS'+str(min_bs)
    print(specificity_term)
    observed = dict()
    for event in ['S','D','R']:
        infile = 'shift_count_observed_'+specificity_term+'_'+event+'.tsv'
        observed[event] = pandas.read_csv(infile, sep='\t', header=0,␣
↪index_col=0)

    fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=1, figsize=(1.7,2.2),␣
↪sharex=False)
    ax = axes
    #axes = axes.flat
    dat = observed
```

```
    resampled_symmetry = dict()

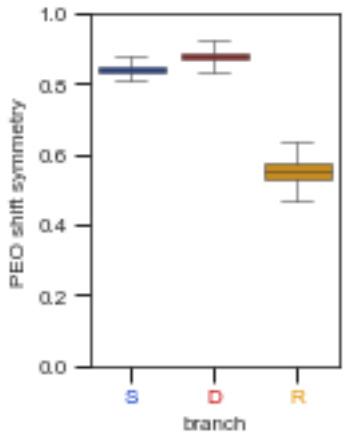
    for event in branch_categories:
        resampled_symmetry[event] = pandas.DataFrame(index=numpy.arange(nrep),␣
↪columns=['event','value'])
        resampled_symmetry[event]['event'] = event
        for i in numpy.arange(nrep):
            bs_table = get_bootstrap(df=observed[event])
            resampled_symmetry[event].loc[i,'value'] =␣
↪calc_symmetry(pivot_table=bs_table)
    df_bp = pandas.concat(resampled_symmetry)
    df_bp = df_bp.reset_index()
    df_bp['x'] = 0
    x = 0
    for ev in branch_categories:
        df_bp.loc[(df_bp.event==ev),'x'] = x
        x += 1
    df_bp['value'] = df_bp['value'].astype(float)
    seaborn.boxplot(x='event', y='value', data=df_bp, fliersize=0,␣
↪palette=category_colors.values(),
                    order=category_colors.keys(), linewidth=0.5)
    ax.set_xlim(-0.5, len(branch_categories)-0.5)
    ax.set_ylim(0, 1)
    ax.set_xlabel('branch')
    ax.set_ylabel(ylab, fontsize=font_size)
    ax.tick_params(axis='both', which='major', direction='out', length=6,␣
↪width=1, pad=2, top=False, right=False, labelsize=font_size)
    ax.set_xticks(numpy.arange(len(branch_categories)))
    ax.set_xticklabels(labels=branch_categories, fontsize=font_size)
    [t.set_color(category_colors[t.get_text()]) for t in ax.
↪get_xticklabels(minor=False) ]

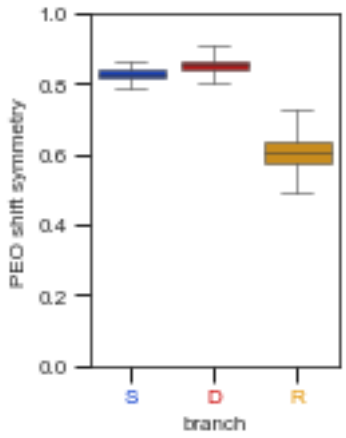
    for bc1,bc2 in itertools.combinations(branch_categories, 2):
        v1 = df_bp.loc[(df_bp['event']==bc1),'value'].values
        v2 = df_bp.loc[(df_bp['event']==bc2),'value'].values
        statistic,pvalue = scipy.stats.ks_2samp(v1, v2,␣
↪alternative='two-sided', mode='auto')
        print('{}; {}-{}: D = {:.2}, P = {:.2}'.format(x, bc1, bc2, statistic,␣
↪pvalue))

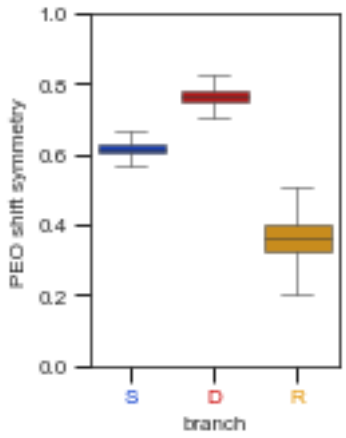
    fig.tight_layout(pad=0)
    outbase = 'shift_symmetry2_'+specificity_term
    fig.savefig(outbase+".pdf", format='pdf', transparent=True)
    fig.savefig(outbase+".svg", format='svg', transparent=True)
```

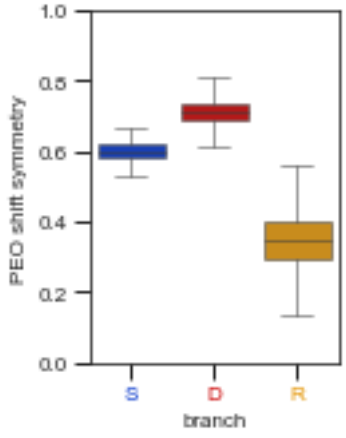
```
l1ou_fpkm_muRatio0_minTau0_minBS0
3; S-D: D = 0.82, P = 0.0
```

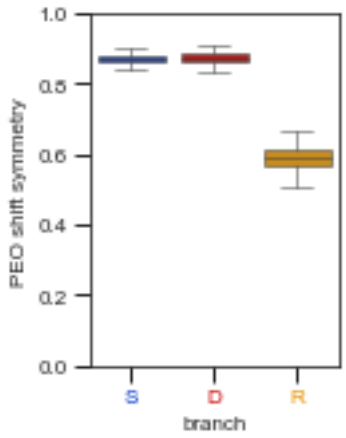
```
3; S-R: D = 1.0, P = 0.0
3; D-R: D = 1.0, P = 0.0
l1ou_fpkm_muRatio0_minTau0_minBS99
3; S-D: D = 0.58, P = 2.7e-158
3; S-R: D = 1.0, P = 0.0
3; D-R: D = 1.0, P = 0.0
l1ou_fpkm_muRatio0_minTau0.5_minBS0
3; S-D: D = 1.0, P = 0.0
3; S-R: D = 1.0, P = 0.0
3; D-R: D = 1.0, P = 0.0
l1ou_fpkm_muRatio0_minTau0.5_minBS99
3; S-D: D = 0.94, P = 0.0
3; S-R: D = 0.99, P = 0.0
3; D-R: D = 1.0, P = 0.0
l1ou_tpm_muRatio0_minTau0_minBS0
3; S-D: D = 0.11, P = 2.6e-05
3; S-R: D = 1.0, P = 0.0
3; D-R: D = 1.0, P = 0.0
l1ou_tpm_muRatio0_minTau0_minBS99
3; S-D: D = 0.24, P = 3e-25
3; S-R: D = 1.0, P = 0.0
3; D-R: D = 1.0, P = 0.0
l1ou_tpm_muRatio0_minTau0.5_minBS0
3; S-D: D = 0.99, P = 0.0
3; S-R: D = 0.65, P = 6.6e-199
3; D-R: D = 0.95, P = 0.0
l1ou_tpm_muRatio0_minTau0.5_minBS99
3; S-D: D = 0.9, P = 0.0
3; S-R: D = 0.74, P = 2.3e-268
3; D-R: D = 0.93, P = 0.0
```

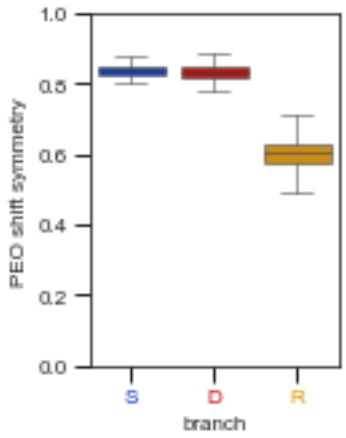


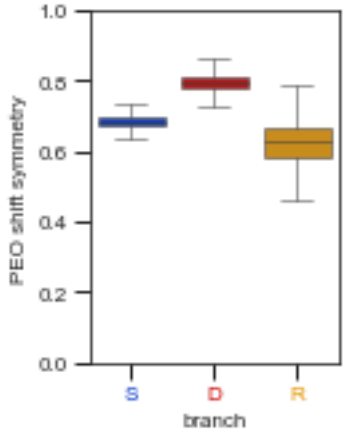

1.0
0.8
0.6
0.4
0.2
0.0
PEO shift symmetry
S
D
R
branch

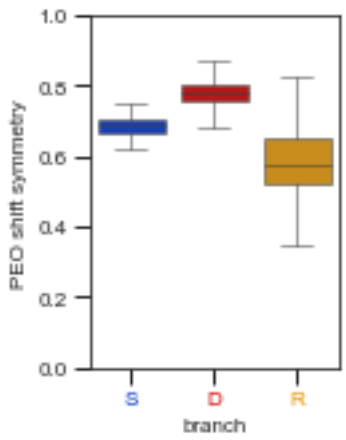

1.0
0.8
0.6
0.4
0.2
0.0
PEO shift symmetry
S
D
R
branch


1.0
0.8
0.6
0.4
0.2
0.0
PEO shift symmetry
S
D
R
branch


1.0
0.8
0.6
0.4
0.2
0.0
PEO shift symmetry
S
D
R
branch


1.0
0.8
0.6
0.4
0.2
0.0
PEO shift symmetry
S
D
R
branch


1.0
0.8
0.6
0.4
0.2
0.0
PEO shift symmetry
S
D
R
branch



[25]:
```
dfs = dict()
for min_tau,pp,min_bs in itertools.product(min_taus,pcm_prefixes,min_bss):
    specificity_term =␣
↪pp+'muRatio'+str(min_max_second_mu_ratio)+'_minTau'+str(min_tau)+'_minBS'+str(min_bs)
    print(specificity_term)
    for event in ['All','S','D','R']:
        tmp = pandas.
↪read_csv('stack_shift_count_observed_'+specificity_term+'_'+event+'.tsv',␣
↪sep='\t', header=0, index_col=[0,1])
        dfs[specificity_term+'_'+event] = tmp['0']
    fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=3, figsize=(7.2,3.6),␣
↪sharex=False)
    axes = axes.flat
    df_plot = dict()
    for i,event in enumerate(['S','D','R']):
        tmp = dfs[specificity_term+'_'+event]
        tmp = tmp.reset_index()
        tmp.columns = ['from','to','count']
        tmp['y'] = tmp['from'] + '→' + tmp['to']
        tmp = tmp.loc[(tmp['from']!=tmp['to']),:]
        if i==0:
            tmp = tmp.sort_values(by='count', ascending=False)
            sorted_y = tmp.loc[:,'y']
            sorted_y = pandas.DataFrame({'y':sorted_y})
        else:
            tmp = pandas.merge(sorted_y, tmp, sort=False)
        df_plot[event] = tmp
    for i,event in enumerate(['S','D','R']):
        ax = axes[i]
        color = category_colors[event]
```

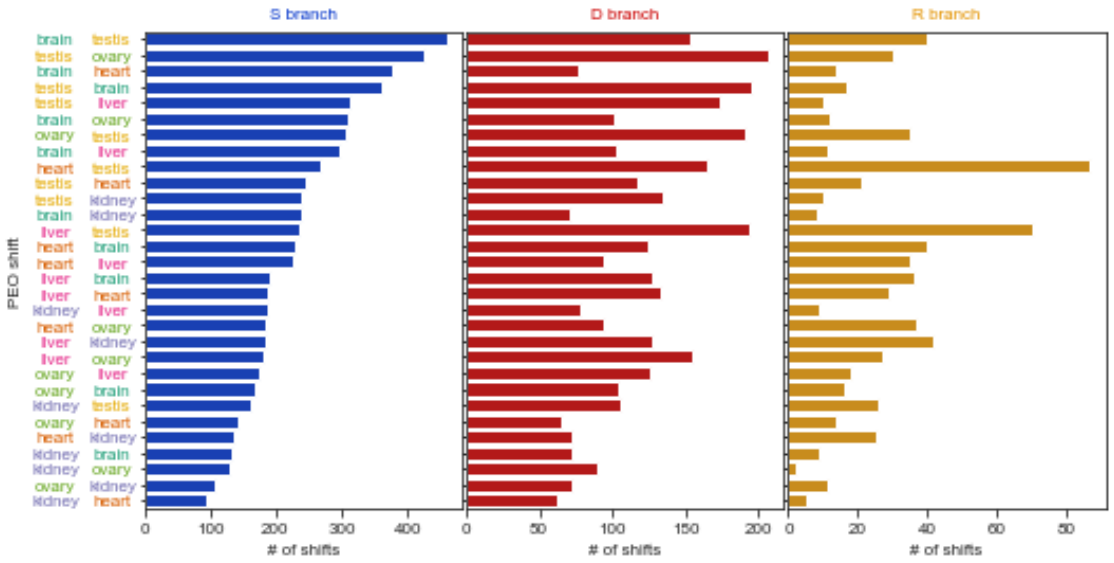
```
        seaborn.barplot(x='count', y='y', data=df_plot[event], orient='h',␣
↪color=color, ax=ax)
        ax.set_xlabel('# of shifts')
        if event=='S':
            ax.set_ylabel('PEO shift')
            yticks = numpy.arange(0, df_plot[event].shape[0])
            ax.set_yticks(yticks, minor=False)
            ax.set_yticks(yticks+1e-3, minor=True)
            ax.set_yticklabels(df_plot[event]['from'], minor=False, ha='center')
            ax.set_yticklabels(df_plot[event]['to'], minor=True, ha='center')
            ax.tick_params(axis='y', which='major', direction='out', length=2,␣
↪width=1, pad=40)
            ax.tick_params(axis='y', which='minor', direction='out', length=0,␣
↪width=1, pad=15)
            [t.set_color(organ_colors_dict[t.get_text()]) for t in ax.
↪get_yticklabels(minor=False) ]
            [t.set_color(organ_colors_dict[t.get_text()]) for t in ax.
↪get_yticklabels(minor=True) ]
        else:
            ax.set_ylabel('')
            ax.tick_params(axis='y', which='major', direction='out', length=2,␣
↪width=1, pad=0)
            ax.set_yticklabels([''] * len(ax.get_yticklabels()))
        ax.set_title(event+' branch', fontsize=font_size, color=color)

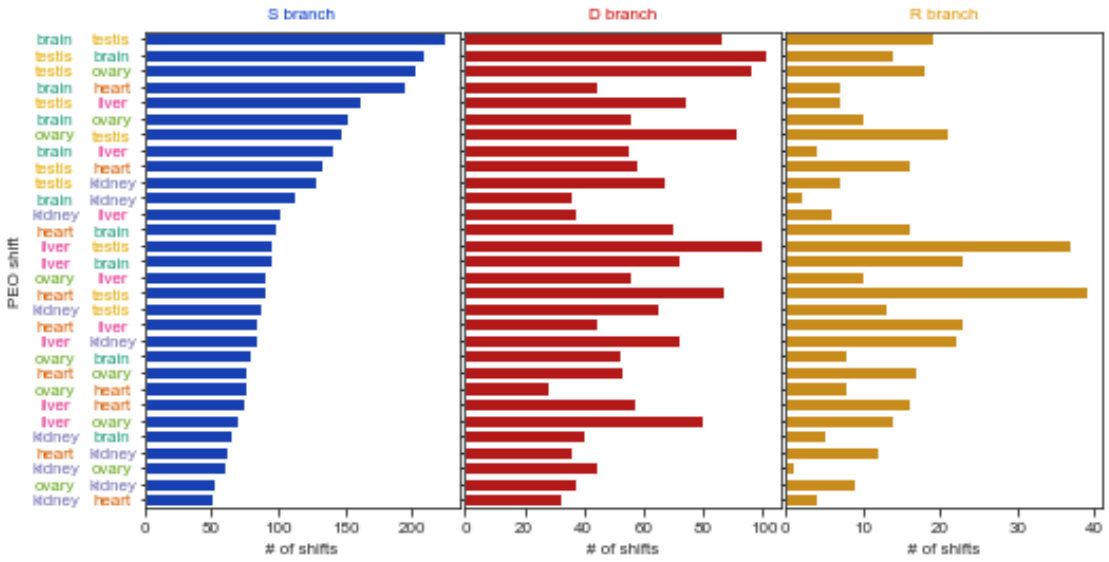
    fig.tight_layout(pad=0)
    outbase = 'PEO_shift_hist_'+specificity_term
    fig.savefig(outbase+".pdf", format='pdf', transparent=True)
    fig.savefig(outbase+".svg", format='svg', transparent=True)

    for pair in itertools.combinations(['S','D','R'], 2):
        pout = scipy.stats.pearsonr(df_plot[pair[0]]['count'],␣
↪df_plot[pair[1]]['count'])
        sout = scipy.stats.spearmanr(df_plot[pair[0]]['count'],␣
↪df_plot[pair[1]]['count'])
        print('{}-{}: pearsonr = {}, spearmanr = {}'.format(pair[0], pair[1],␣
↪pout[0], sout.correlation))
```

```
l1ou_fpkm_muRatio0_minTau0_minBS0
S-D: pearsonr = 0.601615621885016, spearmanr = 0.5981974295684188
S-R: pearsonr = 0.20616978664149052, spearmanr = 0.2769368382524662
D-R: pearsonr = 0.5270126462152529, spearmanr = 0.5649705247837534
l1ou_fpkm_muRatio0_minTau0_minBS99
S-D: pearsonr = 0.5309322972593387, spearmanr = 0.5482794034168859
S-R: pearsonr = 0.05154543361868519, spearmanr = 0.16124369271160363
D-R: pearsonr = 0.6556653003532937, spearmanr = 0.6545881271370931
l1ou_tpm_muRatio0_minTau0_minBS0
```

```
S-D: pearsonr = 0.9219567897634421, spearmanr = 0.8541226268521085
S-R: pearsonr = 0.7038241612457165, spearmanr = 0.6221753162382043
D-R: pearsonr = 0.8076823113985413, spearmanr = 0.6353819378663778
l1ou_tpm_muRatio0_minTau0_minBS99
S-D: pearsonr = 0.8809955210373743, spearmanr = 0.8283234981036648
S-R: pearsonr = 0.6230748608544636, spearmanr = 0.5867543583327695
D-R: pearsonr = 0.8597693023670354, spearmanr = 0.6422681347070208
l1ou_fpkm_muRatio0_minTau0.5_minBS0
S-D: pearsonr = 0.651728380289062, spearmanr = 0.7372760899569756
S-R: pearsonr = 0.12666101012379385, spearmanr = 0.14087349265134982
D-R: pearsonr = 0.3890561843953191, spearmanr = 0.34661220012149385
l1ou_fpkm_muRatio0_minTau0.5_minBS99
S-D: pearsonr = 0.5951344734684358, spearmanr = 0.5794769914989731
S-R: pearsonr = 0.026809299816154538, spearmanr = 0.07749191500501597
D-R: pearsonr = 0.46103806104175044, spearmanr = 0.5117623117247345
l1ou_tpm_muRatio0_minTau0.5_minBS0
S-D: pearsonr = 0.8155750539105285, spearmanr = 0.7975728956423863
S-R: pearsonr = 0.5843572432840924, spearmanr = 0.49480153486299155
D-R: pearsonr = 0.6719878172691942, spearmanr = 0.5931253949854308
l1ou_tpm_muRatio0_minTau0.5_minBS99
S-D: pearsonr = 0.8420239814752041, spearmanr = 0.7209830229639094
S-R: pearsonr = 0.48568618847029565, spearmanr = 0.4311789084897865
D-R: pearsonr = 0.695267938002528, spearmanr = 0.5991733757920211
```




S branch
D branch
R branch
PEO shift
brain testis
testis brain
testis ovary
brain heart
testis liver
brain ovary
ovary testis
brain liver
testis heart
testis kidney
brain kidney
kidney liver
heart brain
liver testis
liver brain
ovary liver
heart testis
kidney testis
heart liver
liver kidney
ovary brain
heart ovary
ovary heart
liver heart
liver ovary
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ovary kidney
kidney heart
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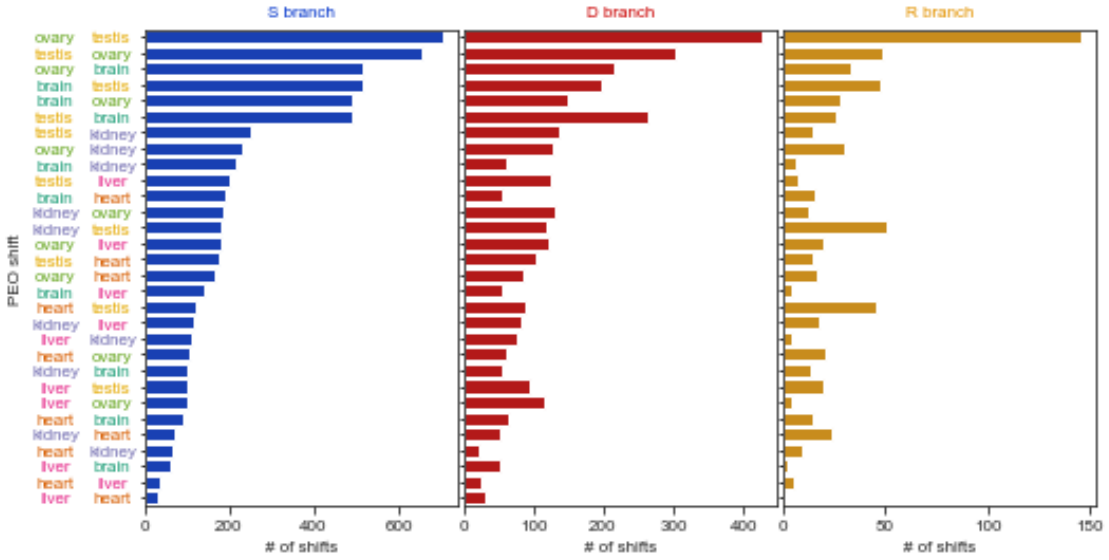
# of shifts
0 20 40 60 80 100
# of shifts
0 10 20 30 40
# of shifts


S branch
D branch
R branch
PEO shift
ovary testis
testis ovary
ovary brain
brain testis
brain ovary
testis brain
testis kidney
ovary kidney
brain kidney
testis liver
brain heart
kidney ovary
kidney testis
ovary liver
testis heart
ovary heart
brain liver
heart testis
kidney liver
liver kidney
heart ovary
kidney brain
liver testis
liver ovary
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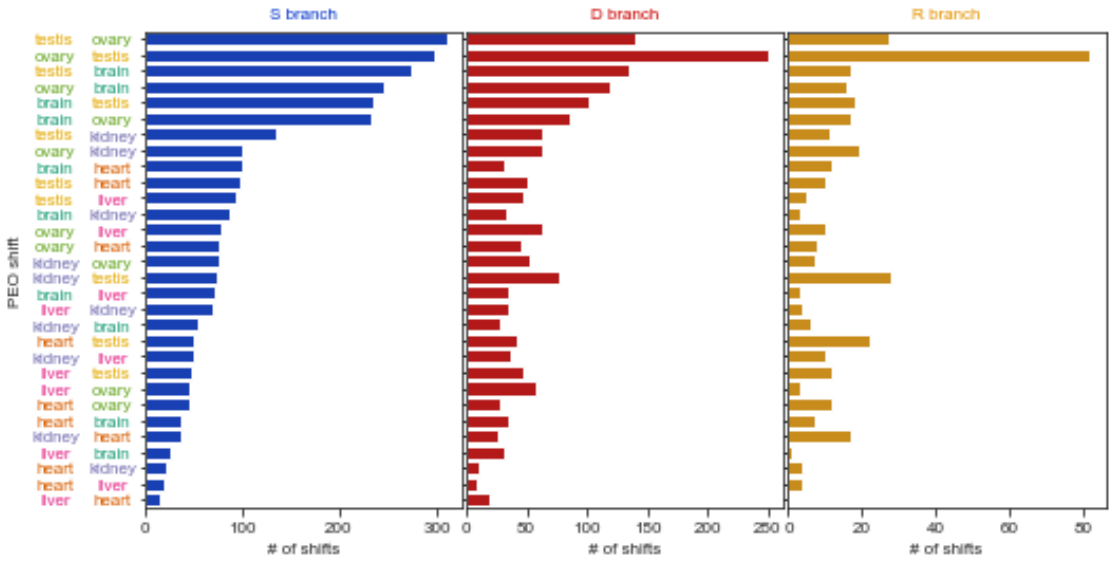
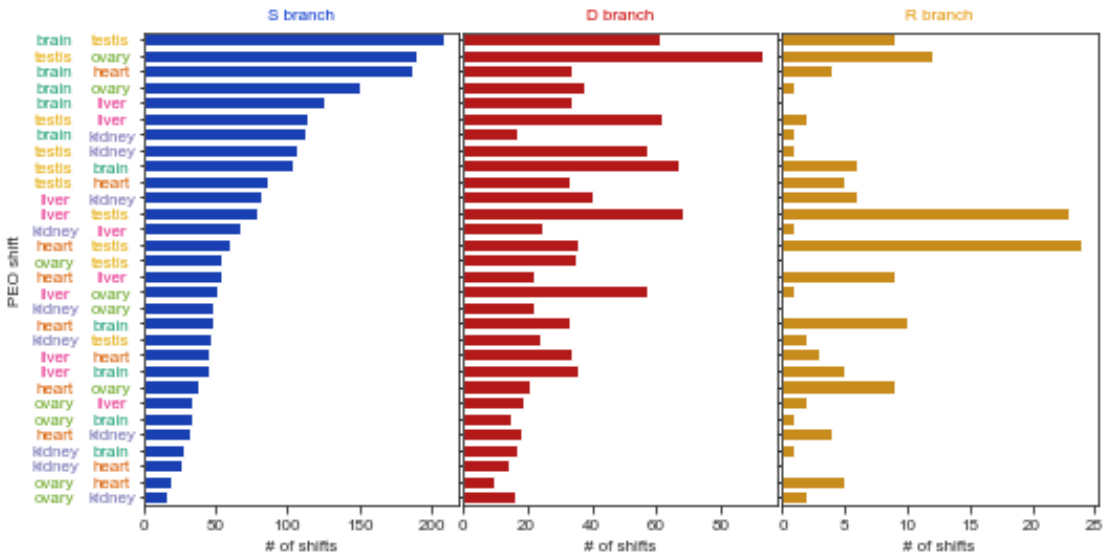
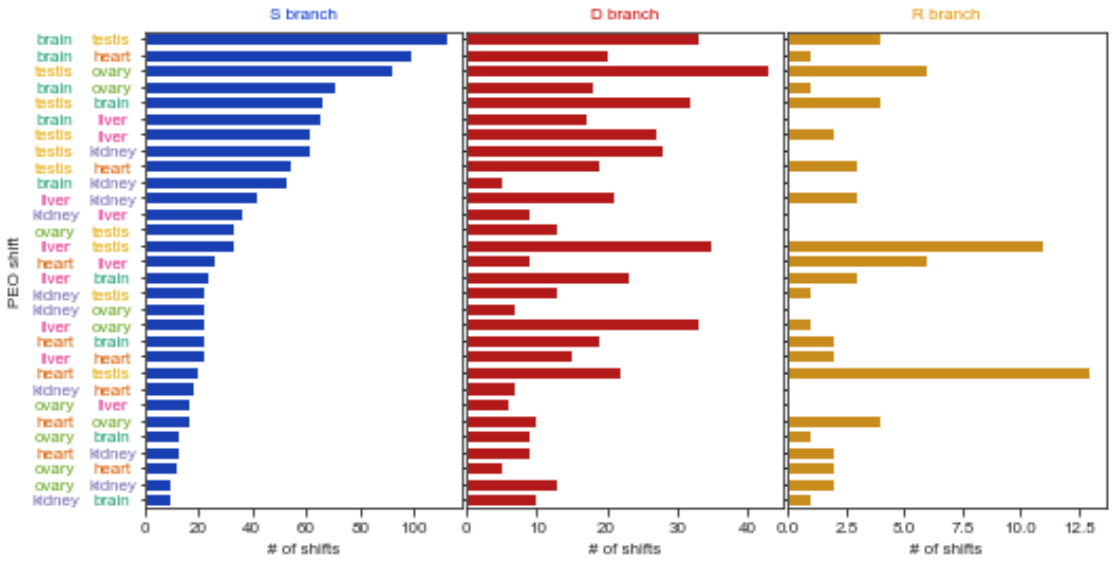
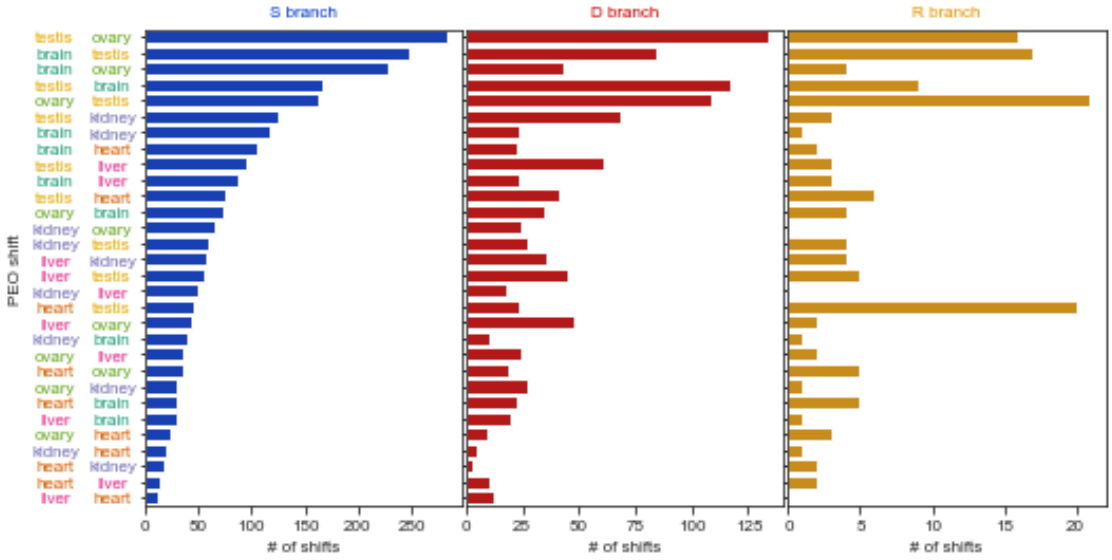
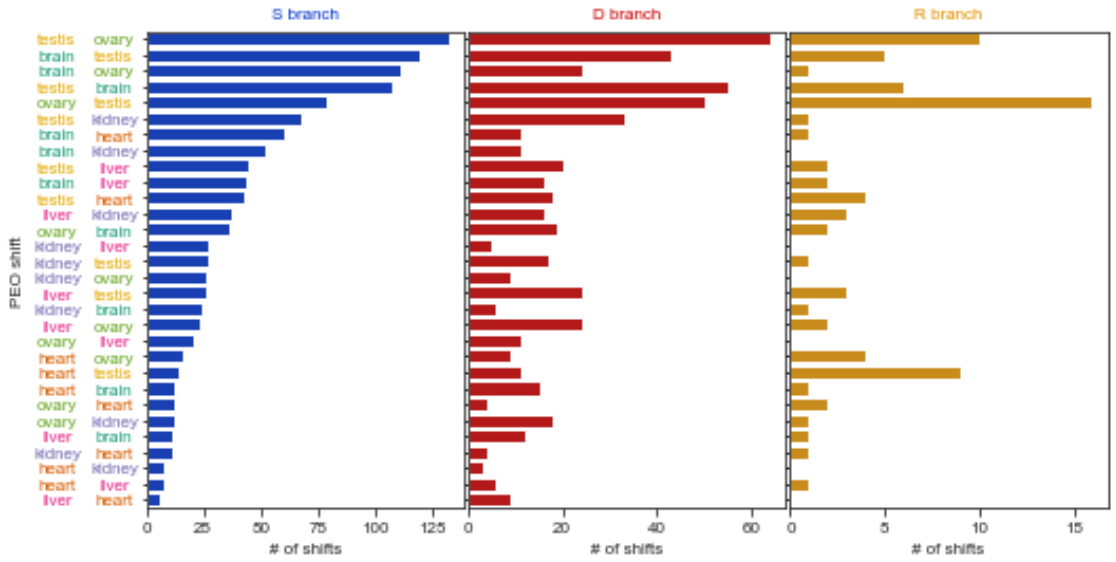
liver brain
heart liver
liver heart
0 200 400 600
# of shifts
0 100 200 300 400
# of shifts
0 50 100 150
# of shifts


S branch
D branch
R branch
PEO shift
testis ovary
ovary testis
testis brain
ovary brain
brain testis
brain ovary
testis kidney
ovary kidney
brain heart
testis heart
testis liver
brain kidney
ovary liver
ovary heart
kidney ovary
kidney testis
brain liver
liver kidney
kidney brain
heart testis
kidney liver
liver testis
liver ovary
heart ovary
heart brain
kidney heart
liver brain
heart kidney
heart liver
liver heart
0 100 200 300
0 50 100 150 200 250
0 20 40 60 80
# of shifts
# of shifts
# of shifts


S branch
D branch
R branch
PEO shift
brain testis
testis ovary
brain heart
brain ovary
brain liver
testis liver
brain kidney
testis kidney
testis brain
testis heart
liver kidney
liver testis
kidney liver
heart testis
ovary testis
heart liver
liver ovary
kidney ovary
heart brain
kidney testis
liver heart
liver brain
heart ovary
ovary liver
ovary brain
heart kidney
kidney brain
kidney heart
ovary heart
ovary kidney
0 50 100 150 200
0 20 40 60 80
0 5 10 15 20 25
# of shifts
# of shifts
# of shifts


S branch
D branch
R branch
PEO shift
brain testis
brain heart
testis ovary
brain ovary
testis brain
brain liver
testis liver
testis kidney
testis heart
brain kidney
liver kidney
kidney liver
ovary testis
liver testis
heart liver
liver brain
kidney testis
kidney ovary
liver ovary
heart brain
liver heart
heart testis
kidney heart
ovary liver
heart ovary
ovary brain
heart kidney
ovary heart
ovary kidney
kidney brain
0 20 40 60 80 100
0 10 20 30 40
0.0 2.5 5.0 7.5 10.0 12.5
# of shifts
# of shifts
# of shifts


S branch
D branch
R branch
PEO shift
testis ovary
brain testis
brain ovary
testis brain
ovary testis
testis kidney
brain kidney
brain heart
testis liver
brain liver
testis heart
ovary brain
kidney ovary
kidney testis
liver kidney
liver testis
kidney liver
heart testis
liver ovary
kidney brain
ovary liver
heart ovary
ovary kidney
heart brain
liver brain
ovary heart
kidney heart
heart kidney
heart liver
liver heart
0 50 100 150 200 250
0 25 50 75 100 125
0 5 10 15 20
# of shifts
# of shifts
# of shifts



[26]:
```
thresholds = [0.1,1,3,5]

# read transcriptomes
dir_tissue_mean = '/Users/kef74yk/Dropbox_p/db/Ensembl/release-91/
 ↪curated_transcriptome/2018_5_1/tpm/tissue_mean'
tcs = dict()
for sp in spp:
    file = os.path.join(dir_tissue_mean, sp.replace(' ','_')+'.tissue.mean.tsv')
    tcs[sp] = pandas.read_csv(file, sep='\t', header=0, index_col=0)

# calc expression ratio
expressed_ratio = pandas.DataFrame()
for sp,threshold in itertools.product(spp, thresholds):
    num_gene = tcs[sp].shape[0]
    tmp = (tcs[sp]>threshold).sum()/num_gene
    tmp['species'] = sp
    tmp['threshold'] = threshold
    tmp['num_gene'] = num_gene
    tmp = tmp.to_frame().T
    expressed_ratio = pandas.concat([expressed_ratio,tmp], ignore_index=True)

# plot
dfs = dict()
for min_tau,pp,min_bs,threshold in itertools.
 ↪product(min_taus,['l1ou_fpkm_'],min_bss,thresholds):
    specificity_term =␣
 ↪pp+'muRatio'+str(min_max_second_mu_ratio)+'_minTau'+str(min_tau)+'_minBS'+str(min_bs)
    print(specificity_term)
```

```
   for event in ['All','S','D','R']:
       tmp = pandas.
↪read_csv('stack_shift_count_observed_'+specificity_term+'_'+event+'.tsv',␣
↪sep='\t', header=0, index_col=[0,1])
       dfs[specificity_term+'_'+event] = tmp['0']
   fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=3, figsize=(7.2,3.6),␣
↪sharex=False)
   axes = axes.flat
   df_plot = dict()
   for i,event in enumerate(['S','D','R']):
       tmp = dfs[specificity_term+'_'+event]
       tmp = tmp.reset_index()
       tmp.columns = ['from','to','count']
       tmp['y'] = tmp['from'] + '→' + tmp['to']
       tmp = tmp.loc[(tmp['from']!=tmp['to']),:]
       # Normalization by expressed gene ratio
       er = expressed_ratio.
↪loc[(expressed_ratio['threshold']==threshold),organs].median()
       er = er/er.mean()
       tmp.loc[:,'count_normalized'] = tmp.loc[:,'count']
       tmp.loc[:,'count_normalized'] /= er[tmp['from']].values
       tmp.loc[:,'count_normalized'] /= er[tmp['to']].values
       if i==0:
           tmp = tmp.sort_values(by='count_normalized', ascending=False)
           sorted_y = tmp.loc[:,'y']
           sorted_y = pandas.DataFrame({'y':sorted_y})
       else:
           tmp = pandas.merge(sorted_y, tmp, sort=False)
       df_plot[event] = tmp
   for i,event in enumerate(['S','D','R']):
       ax = axes[i]
       color = category_colors[event]
       seaborn.barplot(x='count_normalized', y='y', data=df_plot[event],␣
↪orient='h', color=color, ax=ax)
       #ax.set_xlim(0,xymax)
       #ax.set_ylim(0,xymax)
       ax.set_xlabel('# of normalized shifts')
       if event=='S':
           ax.set_ylabel('PEO shift')
           yticks = numpy.arange(0, df_plot[event].shape[0])
           ax.set_yticks(yticks, minor=False)
           ax.set_yticks(yticks+1e-3, minor=True)
           ax.set_yticklabels(df_plot[event]['from'], minor=False, ha='center')
           ax.set_yticklabels(df_plot[event]['to'], minor=True, ha='center')
           ax.tick_params(axis='y', which='major', direction='out', length=2,␣
↪width=1, pad=40)
```

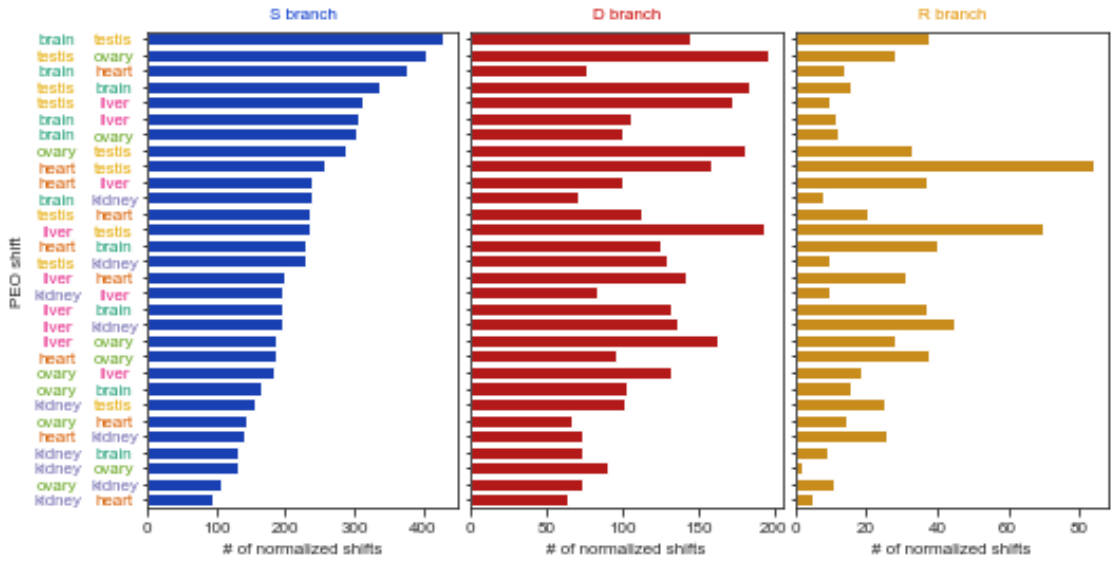
```
            ax.tick_params(axis='y', which='minor', direction='out', length=0,␣
↪width=1, pad=15)
            [t.set_color(organ_colors_dict[t.get_text()]) for t in ax.
↪get_yticklabels(minor=False) ]
            [t.set_color(organ_colors_dict[t.get_text()]) for t in ax.
↪get_yticklabels(minor=True) ]
        else:
            ax.set_ylabel('')
            ax.tick_params(axis='y', which='major', direction='out', length=2,␣
↪width=1, pad=0)
            ax.set_yticklabels([''] * len(ax.get_yticklabels()))
        ax.set_title(event+' branch', fontsize=font_size, color=color)

    fig.tight_layout(pad=0)
    outbase =␣
↪'PEO_shift_numExpressedGeneNormalized_'+specificity_term+'_expThreshold'+str(threshold)
    fig.savefig(outbase+".pdf", format='pdf', transparent=True)
    fig.savefig(outbase+".svg", format='svg', transparent=True)

    for pair in itertools.combinations(['S','D','R'], 2):
        pout = scipy.stats.pearsonr(df_plot[pair[0]]['count_normalized'],␣
↪df_plot[pair[1]]['count_normalized'])
        sout = scipy.stats.spearmanr(df_plot[pair[0]]['count_normalized'],␣
↪df_plot[pair[1]]['count_normalized'])
        print('{}-{}: pearsonr = {}, spearmanr = {}'.format(pair[0], pair[1],␣
↪pout[0], sout.correlation))
```

```
l1ou_fpkm_muRatio0_minTau0_minBS0
S-D: pearsonr = 0.5410168526762561, spearmanr = 0.5715239154616241
S-R: pearsonr = 0.1753212146871715, spearmanr = 0.27252502780867627
D-R: pearsonr = 0.5286843487244848, spearmanr = 0.5813125695216907
l1ou_fpkm_muRatio0_minTau0_minBS0
S-D: pearsonr = 0.5022875522939251, spearmanr = 0.5483870967741935
S-R: pearsonr = 0.20135883538135968, spearmanr = 0.24404894327030033
D-R: pearsonr = 0.5729216714132666, spearmanr = 0.585761957730812
l1ou_fpkm_muRatio0_minTau0_minBS0
S-D: pearsonr = 0.5656209274037655, spearmanr = 0.6080088987764182
S-R: pearsonr = 0.35329095449106834, spearmanr = 0.42869855394883205
D-R: pearsonr = 0.670835879217093, spearmanr = 0.6809788654060066
l1ou_fpkm_muRatio0_minTau0_minBS0
S-D: pearsonr = 0.6614350376280237, spearmanr = 0.7139043381535038
S-R: pearsonr = 0.5010578221385856, spearmanr = 0.5546162402669632
D-R: pearsonr = 0.743101018784715, spearmanr = 0.7228031145717464
l1ou_fpkm_muRatio0_minTau0_minBS99
S-D: pearsonr = 0.4532188119619963, spearmanr = 0.48209121245828696
S-R: pearsonr = -0.0016112755556108027, spearmanr = 0.14438264738598441
```

```
D-R: pearsonr = 0.6537649009676451, spearmanr = 0.6542825361512792
l1ou_fpkm_muRatio0_minTau0_minBS99
S-D: pearsonr = 0.3612728360219229, spearmanr = 0.3730812013348164
S-R: pearsonr = -0.015099113643584485, spearmanr = 0.10166852057842046
D-R: pearsonr = 0.6905369778044107, spearmanr = 0.6694104560622914
l1ou_fpkm_muRatio0_minTau0_minBS99
S-D: pearsonr = 0.3559158040735669, spearmanr = 0.47986651835372635
S-R: pearsonr = 0.10456058871705029, spearmanr = 0.19199110122358176
D-R: pearsonr = 0.7720463772788436, spearmanr = 0.7530589543937708
l1ou_fpkm_muRatio0_minTau0_minBS99
S-D: pearsonr = 0.45670334552227737, spearmanr = 0.5652947719688542
S-R: pearsonr = 0.28640037372446764, spearmanr = 0.3348164627363737
D-R: pearsonr = 0.824547007618165, spearmanr = 0.7486095661846496
l1ou_fpkm_muRatio0_minTau0.5_minBS0
S-D: pearsonr = 0.62020788290504, spearmanr = 0.742018026618497
S-R: pearsonr = 0.09579146077980835, spearmanr = 0.12183993996558765
D-R: pearsonr = 0.3698530358910138, spearmanr = 0.3198932703876434
l1ou_fpkm_muRatio0_minTau0.5_minBS0
S-D: pearsonr = 0.5850270137481305, spearmanr = 0.7174638487208009
S-R: pearsonr = 0.07901001398799448, spearmanr = 0.12138092158580513
D-R: pearsonr = 0.36790460398377367, spearmanr = 0.3534523349663721
l1ou_fpkm_muRatio0_minTau0.5_minBS0
S-D: pearsonr = 0.5600344607496623, spearmanr = 0.6886194280012738
S-R: pearsonr = 0.10086776393164132, spearmanr = 0.16594287984344205
D-R: pearsonr = 0.40351876644490386, spearmanr = 0.4283807513617259
l1ou_fpkm_muRatio0_minTau0.5_minBS0
S-D: pearsonr = 0.5640964201494536, spearmanr = 0.7205784204671858
S-R: pearsonr = 0.13964779249554532, spearmanr = 0.2652858656289121
D-R: pearsonr = 0.42688354514991617, spearmanr = 0.47978652776211306
l1ou_fpkm_muRatio0_minTau0.5_minBS99
S-D: pearsonr = 0.5536278956679052, spearmanr = 0.5719688542825361
S-R: pearsonr = -0.005889481541357603, spearmanr = 0.05009218381837329
D-R: pearsonr = 0.4410980794502596, spearmanr = 0.5096823546362735
l1ou_fpkm_muRatio0_minTau0.5_minBS99
S-D: pearsonr = 0.5014184826152503, spearmanr = 0.5701890989988877
S-R: pearsonr = -0.027285643398619695, spearmanr = 0.0386273638092479
D-R: pearsonr = 0.43633577919571626, spearmanr = 0.5216939891214121
l1ou_fpkm_muRatio0_minTau0.5_minBS99
S-D: pearsonr = 0.45828864334425834, spearmanr = 0.6022246941045606
S-R: pearsonr = -0.01143196530746761 6, spearmanr = 0.09209773706517062
D-R: pearsonr = 0.4630890763654339, spearmanr = 0.5701074552961051
l1ou_fpkm_muRatio0_minTau0.5_minBS99
S-D: pearsonr = 0.4517691426632375, spearmanr = 0.5701890989988877
S-R: pearsonr = 0.030580834048735288, spearmanr = 0.11950242955773359
D-R: pearsonr = 0.4730841762014321, spearmanr = 0.5849329446773276
```


S branch
D branch
R branch
PEO shift
brain testis
testis ovary
brain heart
testis brain
testis liver
brain liver
brain ovary
ovary testis
heart testis
heart liver
brain kidney
testis heart
liver testis
heart brain
testis kidney
liver heart
kidney liver
liver brain
liver kidney
liver ovary
heart ovary
ovary liver
ovary brain
kidney testis
ovary heart
heart kidney
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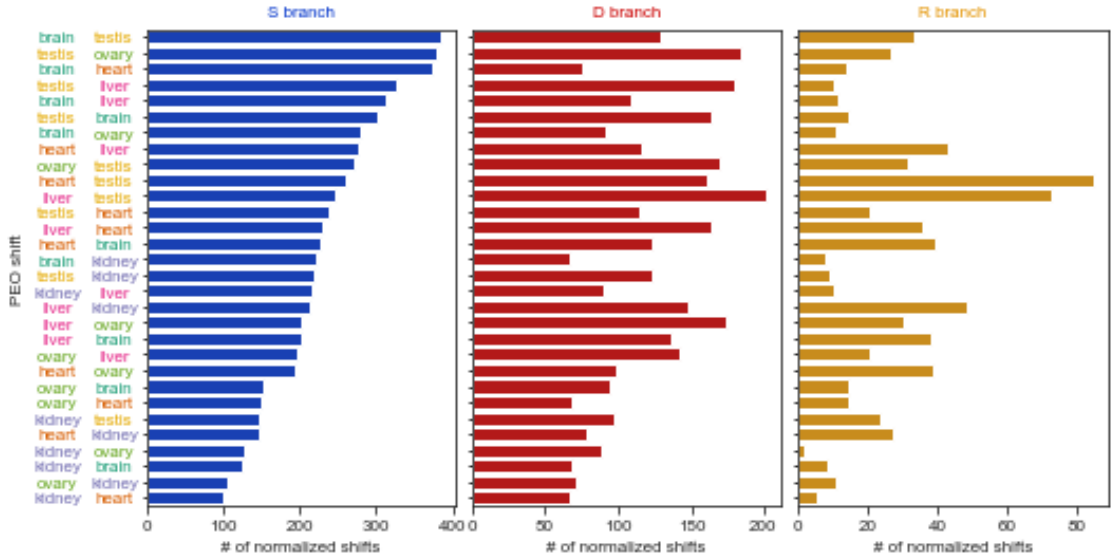
ovary kidney
kidney heart
0 100 200 300 400
# of normalized shifts
0 50 100 150 200
# of normalized shifts
0 20 40 60 80
# of normalized shifts


S branch
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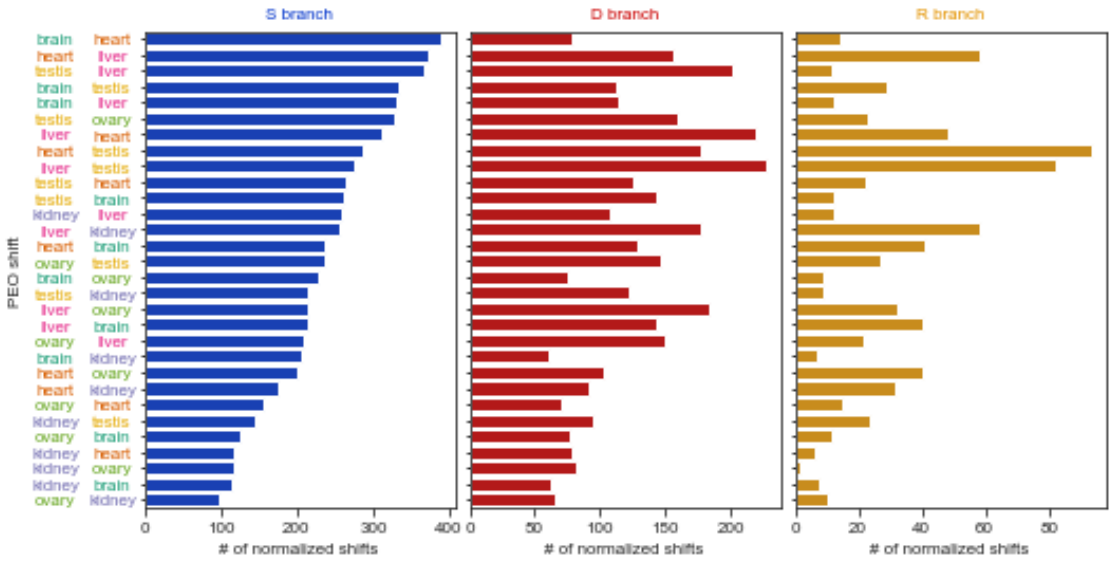
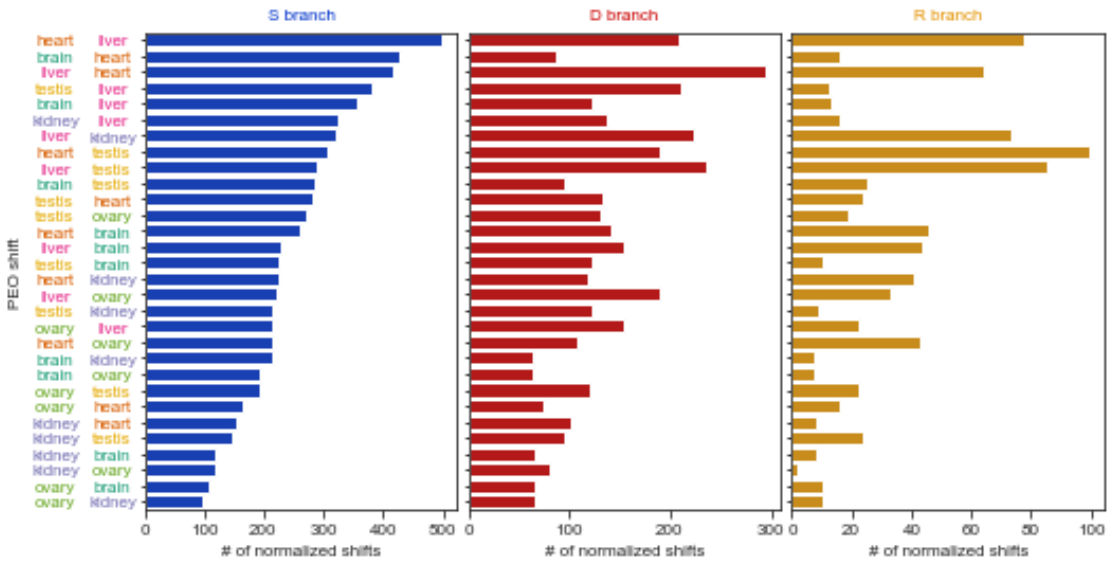
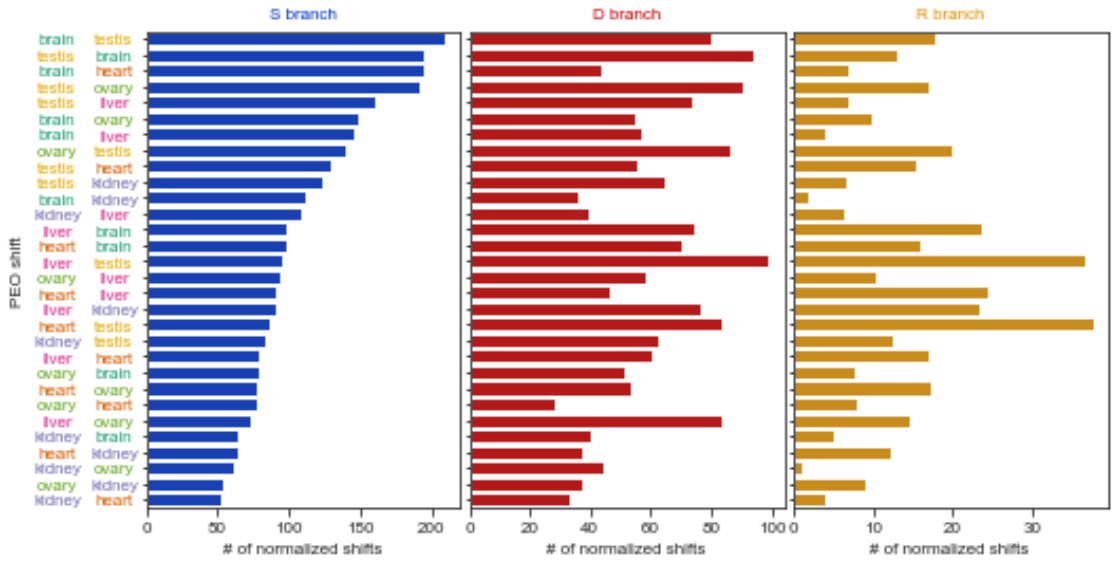
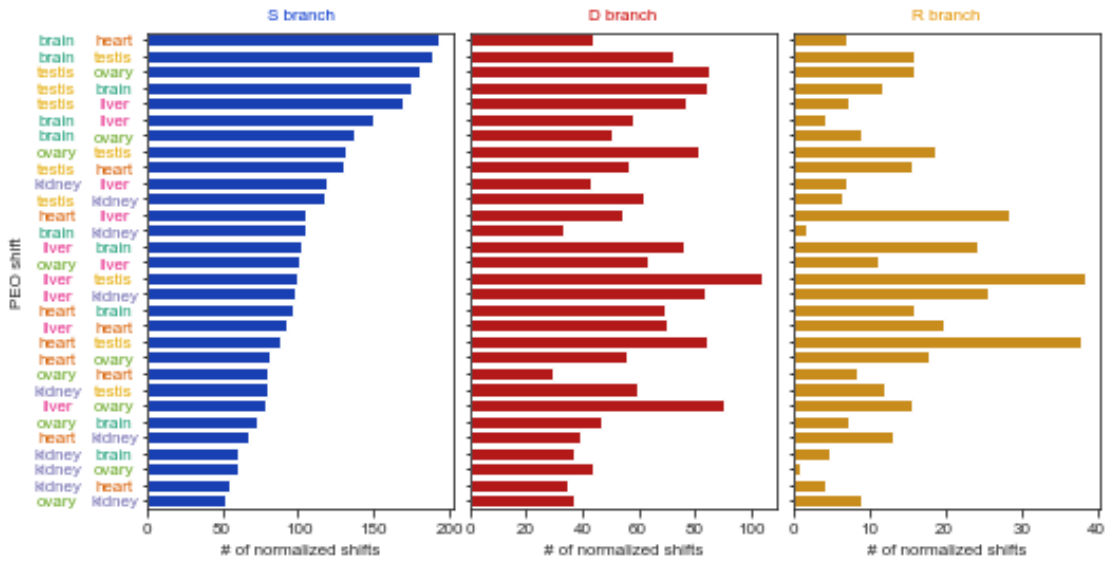
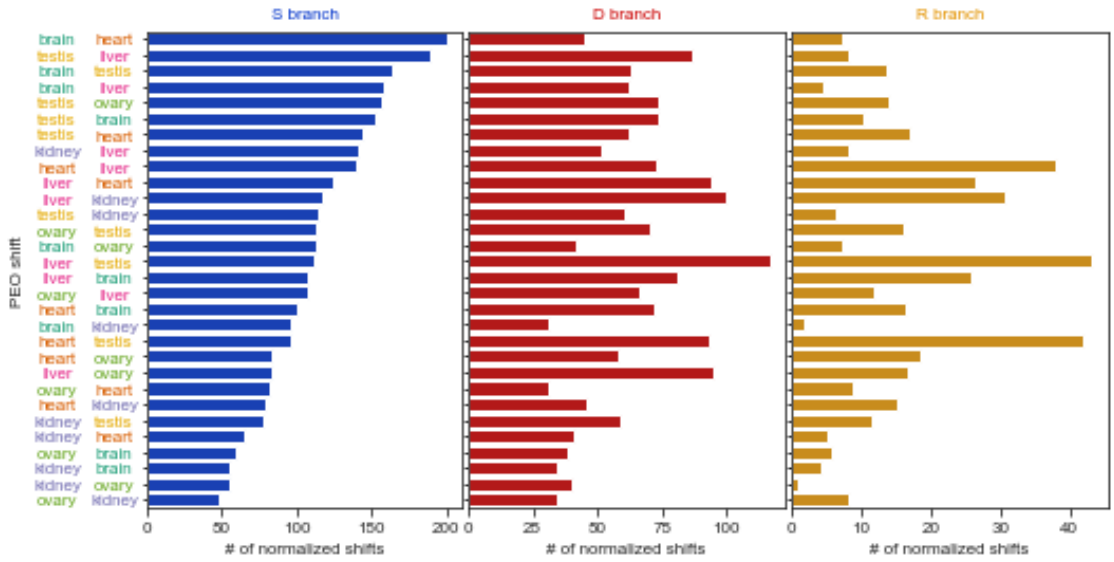
PEO shift
brain testis
testis ovary
brain heart
testis liver
brain liver
testis brain
brain ovary
heart liver
ovary testis
heart testis
liver testis
testis heart
liver heart
heart brain
brain kidney
testis kidney
kidney liver
liver kidney
liver ovary
liver brain
ovary liver
heart ovary
ovary brain
ovary heart
kidney testis
heart kidney
kidney ovary
kidney brain
ovary kidney
kidney heart
0 100 200 300 400
# of normalized shifts
0 50 100 150 200
# of normalized shifts
0 20 40 60 80
# of normalized shifts

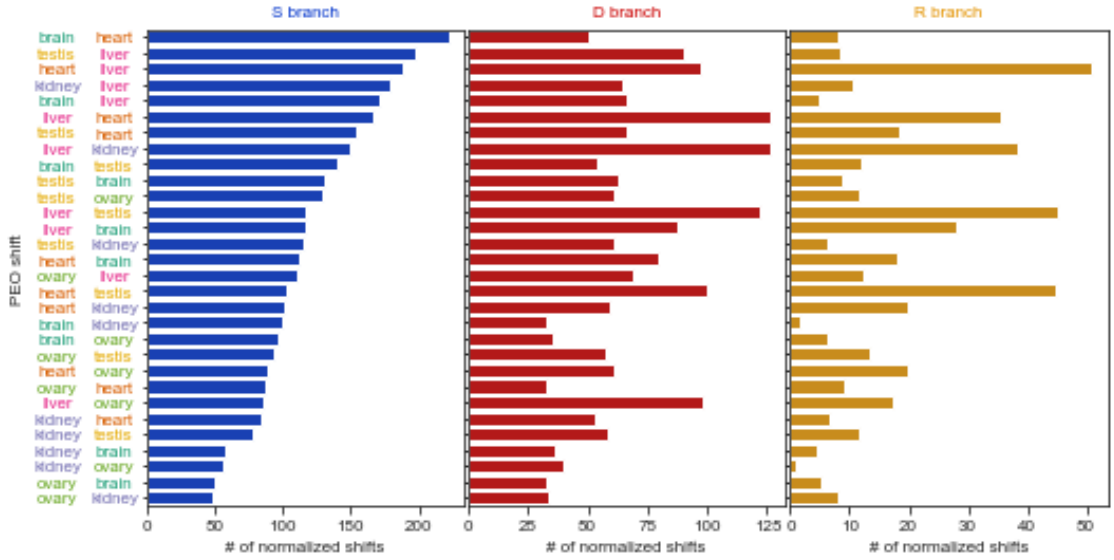

S branch
D branch
R branch
PEO shift
brain heart
heart liver
testis liver
brain testis
brain liver
testis ovary
liver heart
heart testis
liver testis
testis heart
testis brain
kidney liver
liver kidney
heart brain
ovary testis
brain ovary
testis kidney
liver ovary
liver brain
ovary liver
brain kidney
heart ovary
heart kidney
ovary heart
kidney testis
ovary brain
kidney heart
kidney ovary
kidney brain
ovary kidney
0 100 200 300 400
# of normalized shifts
0 50 100 150 200
# of normalized shifts
0 20 40 60 80
# of normalized shifts

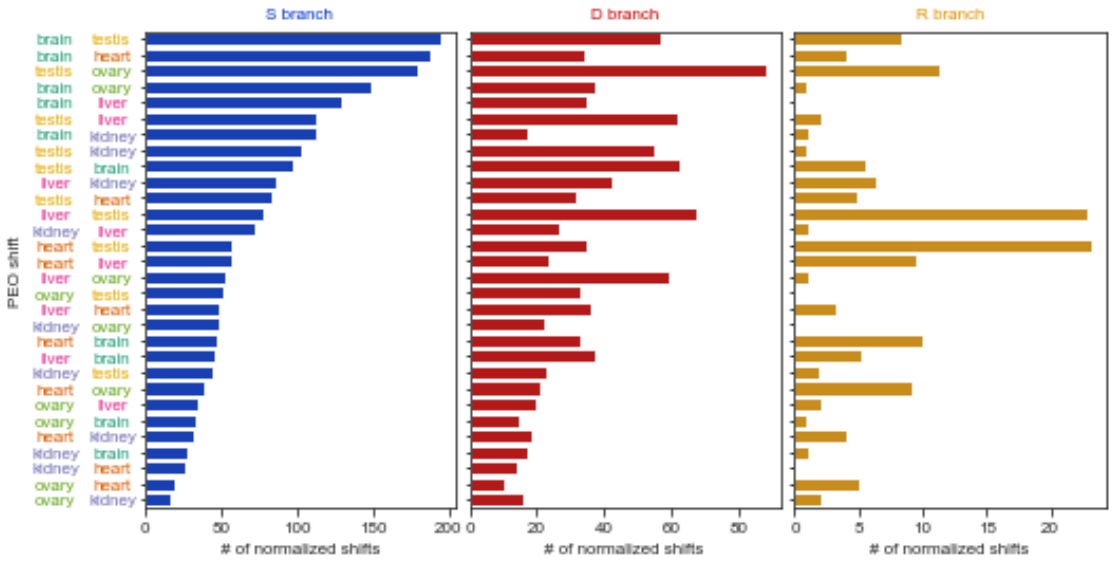

S branch
D branch
R branch
PEO shift
heart liver
brain heart
liver heart
testis liver
brain liver
kidney liver
liver kidney
heart testis
liver testis
brain testis
testis heart
testis ovary
heart brain
liver brain
testis brain
heart kidney
liver ovary
testis kidney
ovary liver
heart ovary
brain kidney
brain ovary
ovary testis
ovary heart
kidney heart
kidney testis
kidney brain
kidney ovary
ovary brain
ovary kidney
0 100 200 300 400 500
# of normalized shifts
0 100 200 300
# of normalized shifts
0 20 40 60 80 100
# of normalized shifts

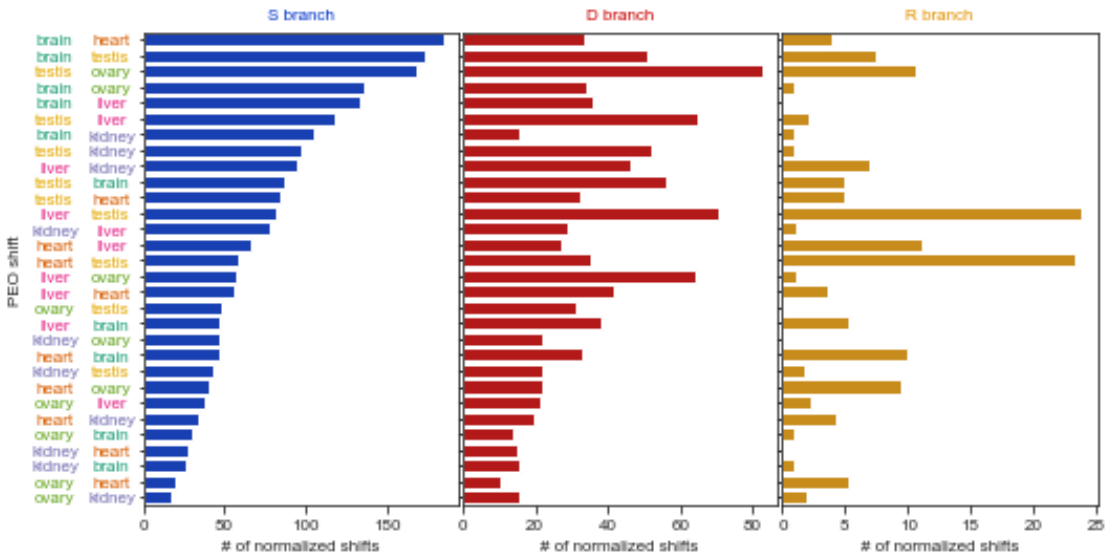

S branch
D branch
R branch
PEO shift
brain testis
testis brain
brain heart
testis ovary
testis liver
brain ovary
brain liver
ovary testis
testis heart
testis kidney
brain kidney
kidney liver
liver brain
heart brain
liver testis
ovary liver
heart liver
liver kidney
heart testis
kidney testis
liver heart
ovary brain
heart ovary
ovary heart
liver ovary
kidney brain
heart kidney
kidney ovary
ovary kidney
kidney heart
0 50 100 150 200
# of normalized shifts
0 20 40 60 80 100
# of normalized shifts
0 10 20 30
# of normalized shifts

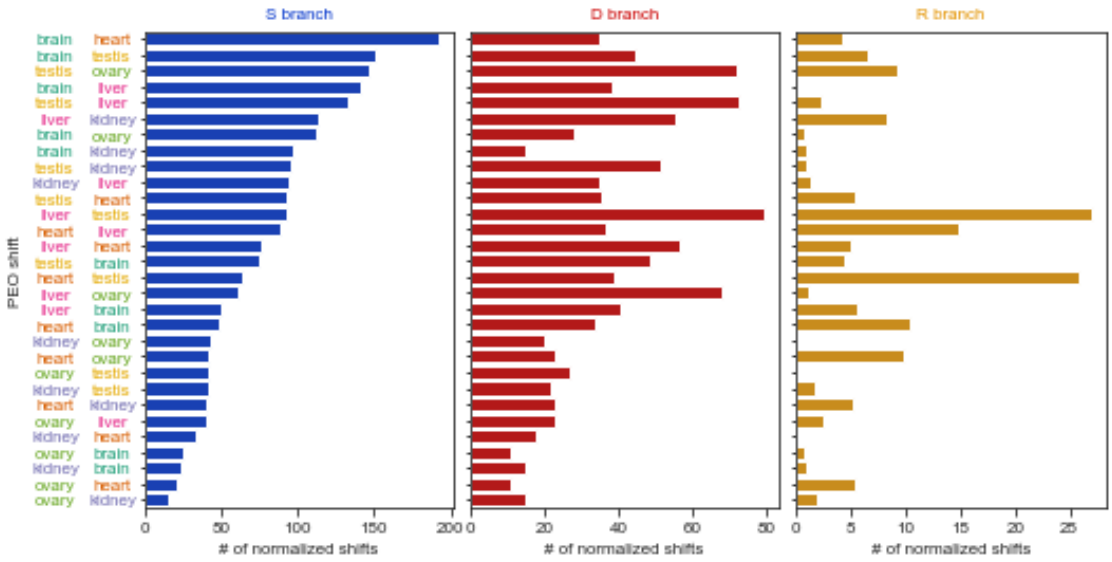

S branch
D branch
R branch
PEO shift
brain heart
brain testis
testis ovary
testis brain
testis liver
brain liver
brain ovary
ovary testis
testis heart
kidney liver
testis kidney
heart liver
brain kidney
liver brain
ovary liver
liver testis
liver kidney
heart brain
liver heart
heart testis
heart ovary
ovary heart
kidney testis
liver ovary
ovary brain
heart kidney
kidney brain
kidney ovary
kidney heart
ovary kidney
0 50 100 150 200
# of normalized shifts
0 20 40 60 80 100
# of normalized shifts
0 10 20 30 40
# of normalized shifts

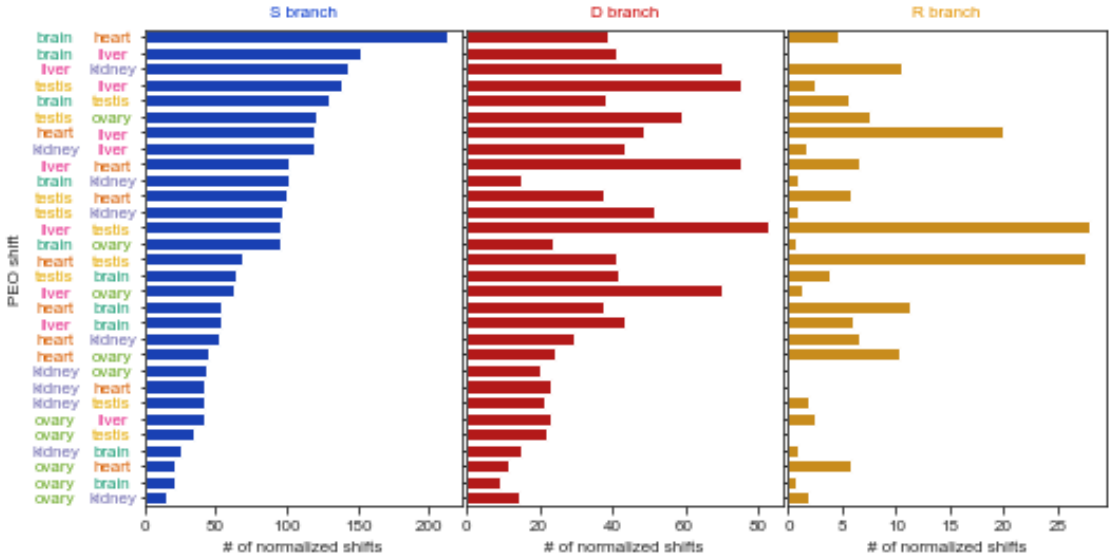

S branch
D branch
R branch
PEO shift
brain heart
testis liver
brain testis
brain liver
testis ovary
testis brain
testis heart
kidney liver
heart liver
liver heart
liver kidney
testis kidney
ovary testis
brain ovary
liver testis
liver brain
ovary liver
heart brain
brain kidney
heart testis
heart ovary
liver ovary
ovary heart
heart kidney
kidney testis
kidney heart
ovary brain
kidney brain
kidney ovary
ovary kidney
0 50 100 150 200
# of normalized shifts
0 25 50 75 100
# of normalized shifts
0 10 20 30 40
# of normalized shifts

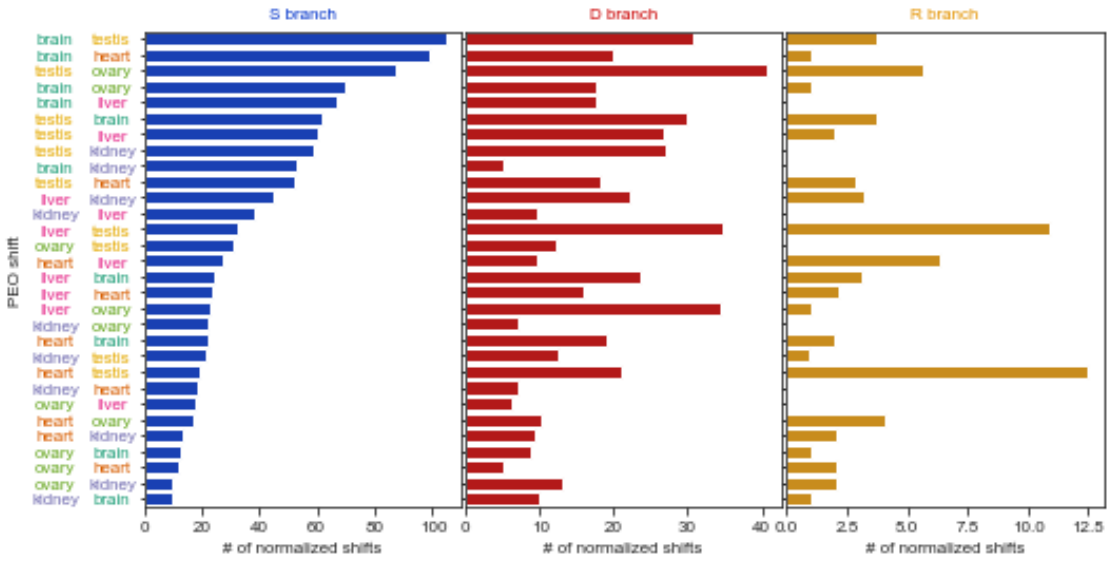

S branch
D branch
R branch
PEO shift
brain heart
testis liver
heart liver
kidney liver
brain liver
liver heart
testis heart
liver kidney
brain testis
testis brain
testis ovary
liver testis
liver brain
testis kidney
heart brain
ovary liver
heart testis
heart kidney
brain kidney
brain ovary
ovary testis
heart ovary
ovary heart
liver ovary
kidney heart
kidney testis
kidney brain
kidney ovary
ovary brain
ovary kidney
0 50 100 150 200
# of normalized shifts
0 25 50 75 100 125
# of normalized shifts
0 10 20 30 40 50
# of normalized shifts

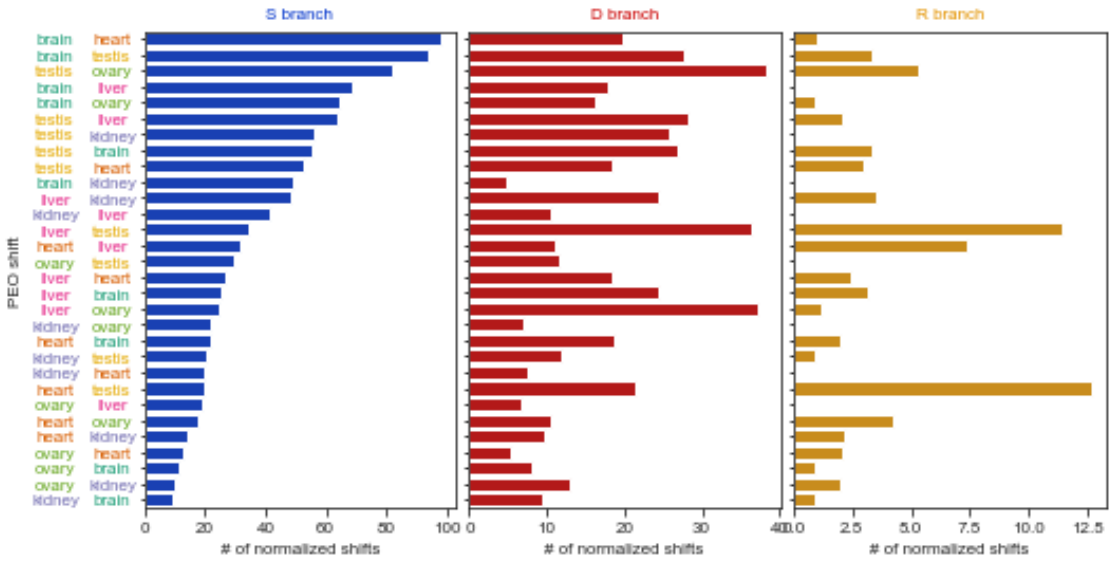

S branch
D branch
R branch
PEO shift
brain testis
brain heart
testis ovary
brain ovary
brain liver
testis liver
brain kidney
testis kidney
testis brain
liver kidney
testis heart
liver testis
kidney liver
heart testis
heart liver
liver ovary
ovary testis
liver heart
kidney ovary
heart brain
liver brain
kidney testis
heart ovary
ovary liver
ovary brain
heart kidney
kidney brain
kidney heart
ovary heart
ovary kidney
0 50 100 150 200
# of normalized shifts
0 20 40 60 80
# of normalized shifts
0 5 10 15 20
# of normalized shifts

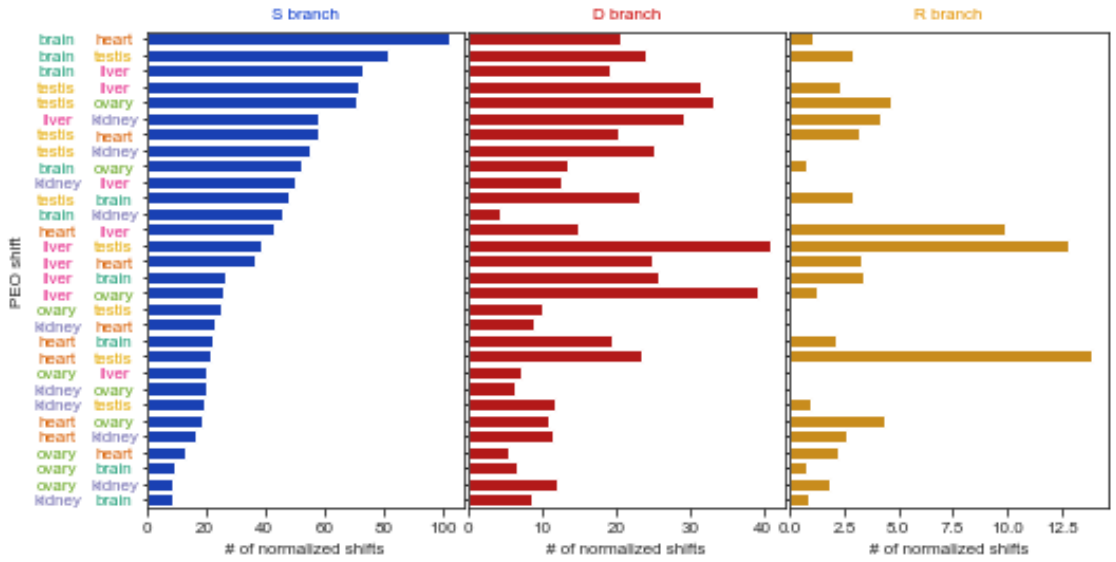

S branch
D branch
R branch
PEO shift
brain heart
brain testis
testis ovary
brain ovary
brain liver
testis liver
brain kidney
testis kidney
liver kidney
testis brain
testis heart
liver testis
kidney liver
heart liver
heart testis
liver ovary
liver heart
ovary testis
liver brain
kidney ovary
heart brain
kidney testis
heart ovary
ovary liver
heart kidney
ovary brain
kidney heart
kidney brain
ovary heart
ovary kidney
0 50 100 150
# of normalized shifts
0 20 40 60
# of normalized shifts
0 5 10 15 20 25
# of normalized shifts

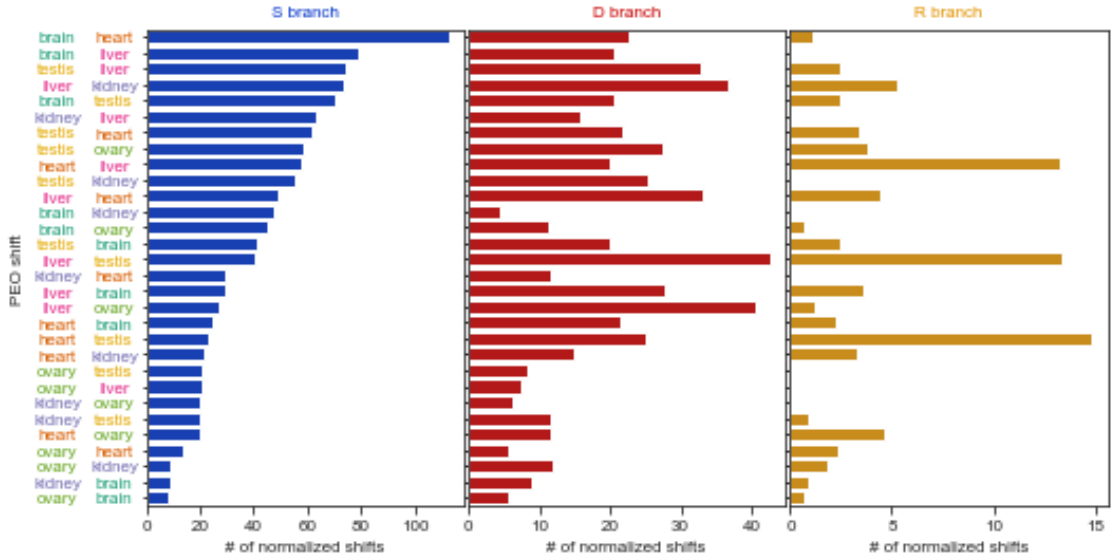

S branch
D branch
R branch
PEO shift
brain heart
brain testis
testis ovary
brain liver
testis liver
liver kidney
brain ovary
brain kidney
testis kidney
kidney liver
testis heart
liver testis
heart liver
liver heart
testis brain
heart testis
liver ovary
liver brain
heart brain
kidney ovary
heart ovary
ovary testis
kidney testis
heart kidney
ovary liver
kidney heart
ovary brain
kidney brain
ovary heart
ovary kidney
0 50 100 150 200
0 20 40 60 80
0 5 10 15 20 25
# of normalized shifts
# of normalized shifts
# of normalized shifts


S branch
D branch
R branch
PEO shift
brain heart
brain liver
liver kidney
testis liver
brain testis
testis ovary
heart liver
kidney liver
liver heart
brain kidney
testis heart
testis kidney
liver testis
brain ovary
heart testis
testis brain
liver ovary
heart brain
liver brain
heart kidney
heart ovary
kidney ovary
kidney heart
kidney testis
ovary liver
ovary testis
kidney brain
ovary heart
ovary brain
ovary kidney
0 50 100 150 200
0 20 40 60 80
0 5 10 15 20 25
# of normalized shifts
# of normalized shifts
# of normalized shifts


S branch
D branch
R branch
PEO shift
brain testis
brain heart
testis ovary
brain ovary
brain liver
testis brain
testis liver
testis kidney
brain kidney
testis heart
liver kidney
kidney liver
liver testis
ovary testis
heart liver
liver brain
liver heart
liver ovary
kidney ovary
heart brain
kidney testis
heart testis
kidney heart
ovary liver
heart ovary
heart kidney
ovary brain
ovary heart
ovary kidney
kidney brain
0 20 40 60 80 100
# of normalized shifts
0 10 20 30 40
# of normalized shifts
0.0 2.5 5.0 7.5 10.0 12.5
# of normalized shifts


S branch
D branch
R branch
PEO shift
brain heart
brain testis
testis ovary
brain liver
brain ovary
testis liver
testis kidney
testis brain
testis heart
brain kidney
liver kidney
kidney liver
liver testis
heart liver
ovary testis
liver heart
liver brain
liver ovary
kidney ovary
heart brain
kidney testis
kidney heart
heart testis
ovary liver
heart ovary
heart kidney
ovary heart
ovary brain
ovary kidney
kidney brain
0 20 40 60 80 100
# of normalized shifts
0 10 20 30 40
# of normalized shifts
0.0 2.5 5.0 7.5 10.0 12.5
# of normalized shifts



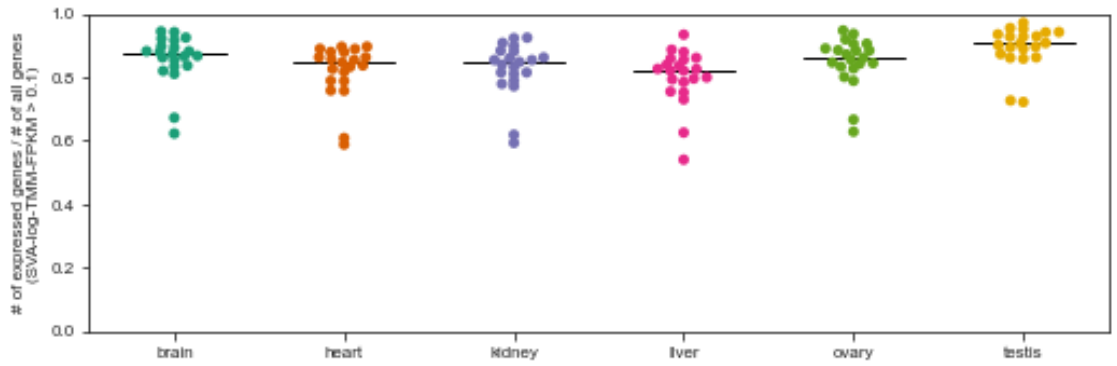


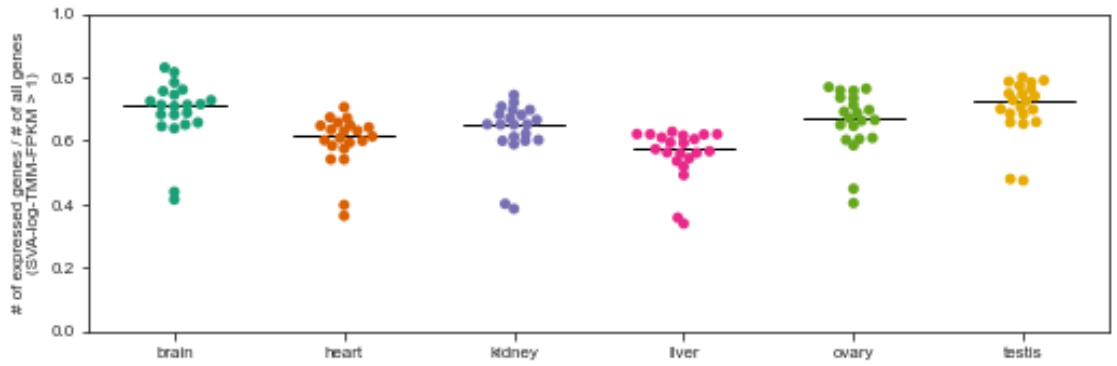
[27]:
```
for threshold in thresholds:
    fig,axes = matplotlib.pyplot.subplots(nrows=1, ncols=1, figsize=(7.2,2.4),␣
↪sharex=False)
    #axes = axes.flat
    tmp1 = expressed_ratio.loc[(expressed_ratio['threshold']==threshold),organs]
    tmp = tmp1.stack().reset_index().drop('level_0', axis=1)
    tmp.columns = ['organ','expressed_gene_ratio']
    median_y = tmp1.median().values
    median_x_from = numpy.arange(len(median_y))-0.3
```

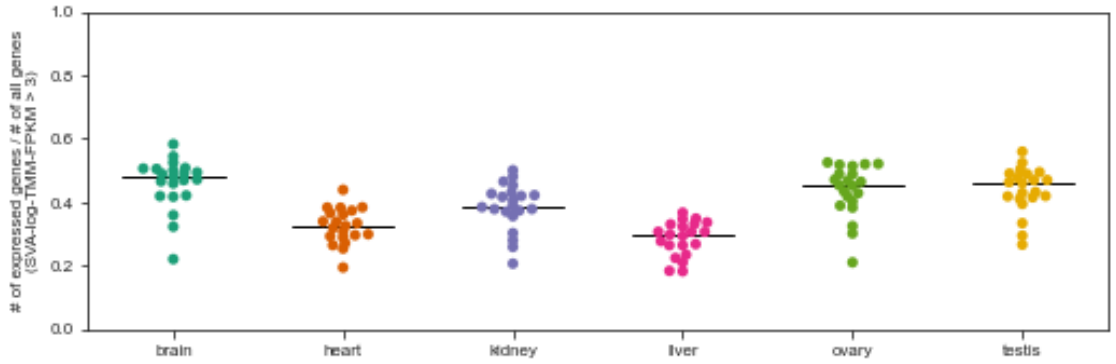
```
    median_x_to = numpy.arange(len(median_y))+0.3

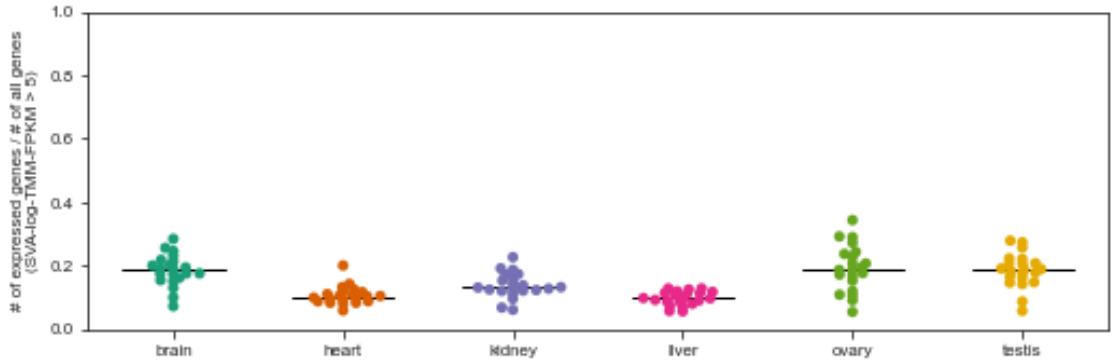
    ax = axes
    seaborn.swarmplot(x='organ', y='expressed_gene_ratio', data=tmp, ax=ax,␣
↪palette=organ_colors)
    ax.plot([median_x_from,median_x_to],[median_y,median_y], color='black',␣
↪lw=1)
    ax.set_ylim(0, 1)
    ax.set_ylabel('# of expressed genes / # of all genes\n(SVA-log-TMM-FPKM >␣
↪'+str(threshold)+')')
    ax.set_xlabel('')

    fig.tight_layout(pad=0.5)
    outbase = 'ExpressedGeneRate_expThreshold'+str(threshold)
    fig.savefig(outbase+".pdf", format='pdf', transparent=True)
    fig.savefig(outbase+".svg", format='svg', transparent=True)
```









[28]:
```
event_combinations = list(itertools.combinations(branch_categories, 2))
print('event_combinations:', event_combinations)

for pp in pcm_prefixes:
    for min_tau in min_taus:
        for min_max_second_mu_ratio in min_max_second_mu_ratios:
            for min_bs in min_bss:
                specificity_term =␣
↪pp+'muRatio'+str(min_max_second_mu_ratio)+'_minTau'+str(min_tau)+'_minBS'+str(min_bs)
                print(specificity_term)
                observed = dict()
                corrected = dict()
                for event in ['S','D','R']:
                    infile =␣
↪'shift_count_observed_'+specificity_term+'_'+event+'.tsv'
                    observed[event] = pandas.read_csv(infile, sep='\t',␣
↪header=0, index_col=0)
                    infile2 =␣
↪'shift_count_corrected_'+specificity_term+'_'+event+'.tsv'
```

```
                    corrected[event] = pandas.read_csv(infile2, sep='\t',␣
↪header=0, index_col=0)

                for event_combination in event_combinations:
                    tested_values = observed
                    e1 = event_combination[0]
                    e2 = event_combination[1]
                    tmp = tested_values[e1]; tmp1 = tmp.values.reshape(tmp.
↪shape[0]*tmp.shape[1])
                    tmp = tested_values[e2]; tmp2 = tmp.values.reshape(tmp.
↪shape[0]*tmp.shape[1])
                    ctable = numpy.array([tmp1,tmp2])
                    ctable = ctable[:,(ctable.sum(axis=0)>0)]
                    out = scipy.stats.chi2_contingency(ctable, correction=True,␣
↪lambda_=None)
                    print('ancestral-derived', e1, e2, 'pvalue =', out[1],␣
↪'chi2 stat =', out[0])

                for event_combination in event_combinations:
                    tested_values = observed
                    e1 = event_combination[0]
                    e2 = event_combination[1]
                    tmp = tested_values[e1]; tmp1 = tmp.values.sum(axis=0)
                    tmp = tested_values[e2]; tmp2 = tmp.values.sum(axis=0)
                    ctable = numpy.array([tmp1,tmp2])
                    ctable = ctable[:,(ctable.sum(axis=0)>0)]
                    out = scipy.stats.chi2_contingency(ctable, correction=True,␣
↪lambda_=None)
                    print('only derived', e1, e2, 'pvalue =', out[1], 'chi2␣
↪stat =', out[0])

                for event in branch_categories:
                    tmp = observed[event]
                    tmp = tmp.values.reshape(tmp.shape[0]*tmp.shape[1])
                    tmp = tmp/tmp.sum()
                    out = scipy.stats.chisquare(tmp)
                    print('ancestral-derived', event, 'pvalue =', out[1], 'chi2␣
↪stat =', out[0])

                for event in branch_categories:
                    tmp = observed[event]
                    tmp = tmp.values.sum(axis=0)
                    tmp = tmp/tmp.sum()
                    out = scipy.stats.chisquare(tmp)
                    print('only derived', event, 'pvalue =', out[1], 'chi2 stat␣
↪=', out[0])
```

```
                for event in branch_categories:
                    tmp = observed[event]
                    dif = 0
                    organs = list(set(tmp.index.tolist()).intersection(set(tmp.
↪columns.tolist())))
                    for i in itertools.combinations(organs, 2):
                        if i[0]!=i[1]:
                            dif = dif + numpy.abs(tmp.loc[i[0],i[1]] - tmp.
↪loc[i[1],i[0]])
                    symmetry = 1 - (dif/tmp.sum().sum())
                    print(event, 'symmetry of the number of shift =', symmetry)

                for event in branch_categories:
                    tmp = corrected[event]
                    dif = 0
                    organs = list(set(tmp.index.tolist()).intersection(set(tmp.
↪columns.tolist())))
                    for i in itertools.combinations(organs, 2):
                        if i[0]!=i[1]:
                            dif = dif + numpy.abs(tmp.loc[i[0],i[1]] - tmp.
↪loc[i[1],i[0]])
                    symmetry = 1 - (dif/tmp.sum().sum())
                    print(event, 'symmetry of the acceleration of shift =',␣
↪symmetry)

                print()
```

```
event_combinations: [('S', 'D'), ('S', 'R'), ('D', 'R')]
l1ou_fpkm_muRatio0_minTau0_minBS0
ancestral-derived S D pvalue = 1.1645425725499324e-33 chi2 stat =
232.6015555526961
ancestral-derived S R pvalue = 3.15741388058073e-54 chi2 stat =
337.26871370739775
ancestral-derived D R pvalue = 7.322841049325359e-27 chi2 stat =
196.83199619773367
only derived S D pvalue = 0.0006312751579895948 chi2 stat = 21.57219097992501
only derived S R pvalue = 5.727871322112838e-17 chi2 stat = 85.56596341989552
only derived D R pvalue = 4.704916901656827e-10 chi2 stat = 52.28968702326899
ancestral-derived S pvalue = 1.0 chi2 stat = 0.3880086372405372
ancestral-derived D pvalue = 1.0 chi2 stat = 0.35234780855959336
ancestral-derived R pvalue = 1.0 chi2 stat = 0.8670298787456246
only derived S pvalue = 0.9999968230540931 chi2 stat = 0.020499147605217337
only derived D pvalue = 0.9999840101891352 chi2 stat = 0.03923108052664371
only derived R pvalue = 0.998601936427763 chi2 stat = 0.24143061475321465
S symmetry of the number of shift = 0.848388033691548
D symmetry of the number of shift = 0.8856664807585053
```

```
R symmetry of the number of shift = 0.5630026809651474
S symmetry of the acceleration of shift = 0.954120276015039
D symmetry of the acceleration of shift = 0.9380191481355096
R symmetry of the acceleration of shift = 0.8420599103110884

l1ou_fpkm_muRatio0_minTau0_minBS99
ancestral-derived S D pvalue = 1.1656647990706282e-19 chi2 stat =
157.77142932826834
ancestral-derived S R pvalue = 4.92143783390324e-28 chi2 stat =
203.0640970783855
ancestral-derived D R pvalue = 3.0619835981501303e-06 chi2 stat =
77.09101926176949
only derived S D pvalue = 7.682996259087532e-06 chi2 stat = 31.4357002043132
only derived S R pvalue = 1.0529379252262355e-06 chi2 stat = 35.776145833250084
only derived D R pvalue = 0.02079599317957807 chi2 stat = 13.291378457948749
ancestral-derived S pvalue = 1.0 chi2 stat = 0.42782374468613504
ancestral-derived D pvalue = 1.0 chi2 stat = 0.3441118851588771
ancestral-derived R pvalue = 1.0 chi2 stat = 0.7244809688581315
only derived S pvalue = 0.9999990983378625 chi2 stat = 0.012372157949220062
only derived D pvalue = 0.9999674762800292 chi2 stat = 0.05221283421048528
only derived R pvalue = 0.9994212998676993 chi2 stat = 0.16789215686274508
S symmetry of the number of shift = 0.8333837314786816
D symmetry of the number of shift = 0.8707557502738226
R symmetry of the number of shift = 0.6274509803921569
S symmetry of the acceleration of shift = 0.9492625829490327
D symmetry of the acceleration of shift = 0.9407586790309318
R symmetry of the acceleration of shift = 0.793684663033914

l1ou_fpkm_muRatio0_minTau0.5_minBS0
ancestral-derived S D pvalue = 8.887362232292662e-18 chi2 stat =
147.27294260834327
ancestral-derived S R pvalue = 2.941578886654832e-31 chi2 stat =
220.05562051022451
ancestral-derived D R pvalue = 3.816019765323653e-14 chi2 stat =
126.51240092175345
only derived S D pvalue = 0.00021515460123787145 chi2 stat = 24.020476732194734
only derived S R pvalue = 1.7443494961517143e-07 chi2 stat = 39.66533050014218
only derived D R pvalue = 0.00011752793086720099 chi2 stat = 25.382482350291024
ancestral-derived S pvalue = 1.0 chi2 stat = 0.7454758872600206
ancestral-derived D pvalue = 1.0 chi2 stat = 0.5753159830046348
ancestral-derived R pvalue = 0.9999999999999999 chi2 stat = 1.9236520877437948
only derived S pvalue = 0.9999883139452478 chi2 stat = 0.03458375249105983
only derived D pvalue = 0.99997347053871 chi2 stat = 0.04809874178551392
only derived R pvalue = 0.9958850594901416 chi2 stat = 0.3791270663483627
S symmetry of the number of shift = 0.6176598521096128
D symmetry of the number of shift = 0.7939508506616257
R symmetry of the number of shift = 0.40268456375838924
S symmetry of the acceleration of shift = 0.878119701406599
```

```
D symmetry of the acceleration of shift = 0.9102296154643834
R symmetry of the acceleration of shift = 0.510984529731863

l1ou_fpkm_muRatio0_minTau0.5_minBS99
ancestral-derived S D pvalue = 5.566817868652583e-12 chi2 stat =
113.72968199442163
ancestral-derived S R pvalue = 2.377658640736338e-17 chi2 stat =
144.86730756686904
ancestral-derived D R pvalue = 0.0004896507293822123 chi2 stat =
60.807030670771894
only derived S D pvalue = 0.0003013618753243799 chi2 stat = 23.257553274337308
only derived S R pvalue = 0.0010603021798619365 chi2 stat = 20.379911822941423
only derived D R pvalue = 0.06363467877368677 chi2 stat = 10.442109989645738
ancestral-derived S pvalue = 1.0 chi2 stat = 0.8074099268155377
ancestral-derived D pvalue = 1.0 chi2 stat = 0.5914845140619438
ancestral-derived R pvalue = 0.9999999999999998 chi2 stat = 1.9888
only derived S pvalue = 0.999995154287944 chi2 stat = 0.02428340213923813
only derived D pvalue = 0.999970025749984 chi2 stat = 0.050523317906728385
only derived R pvalue = 0.996152161078495 chi2 stat = 0.36853333333333327
S symmetry of the number of shift = 0.6044520547945205
D symmetry of the number of shift = 0.7433962264150944
R symmetry of the number of shift = 0.4
S symmetry of the acceleration of shift = 0.8820005458503392
D symmetry of the acceleration of shift = 0.8583233271629571
R symmetry of the acceleration of shift = 0.41545364137615903

l1ou_tpm_muRatio0_minTau0_minBS0
ancestral-derived S D pvalue = 1.2803596852689708e-29 chi2 stat =
211.44194549979858
ancestral-derived S R pvalue = 3.2765565191475903e-44 chi2 stat =
286.7964343857895
ancestral-derived D R pvalue = 1.189506679469606e-24 chi2 stat =
184.99699829145175
only derived S D pvalue = 0.026558245513776127 chi2 stat = 12.68104914518126
only derived S R pvalue = 5.0033486447679886e-26 chi2 stat = 128.47921998711317
only derived D R pvalue = 4.510200345340426e-18 chi2 stat = 90.82403547603904
ancestral-derived S pvalue = 1.0 chi2 stat = 1.027348418530505
ancestral-derived D pvalue = 1.0 chi2 stat = 0.8780762217023703
ancestral-derived R pvalue = 1.0 chi2 stat = 1.7074585586453934
only derived S pvalue = 0.9997000426799068 chi2 stat = 0.1283606011224609
only derived D pvalue = 0.9996496843152228 chi2 stat = 0.13674446020372452
only derived R pvalue = 0.9902825003612684 chi2 stat = 0.5474547031782032
S symmetry of the number of shift = 0.8771346531660873
D symmetry of the number of shift = 0.884692417739628
R symmetry of the number of shift = 0.6030855539971949
S symmetry of the acceleration of shift = 0.946570717472631
D symmetry of the acceleration of shift = 0.9167071309305176
R symmetry of the acceleration of shift = 0.7873259282130881
```

```
l1ou_tpm_muRatio0_minTau0_minBS99
ancestral-derived S D pvalue = 1.0523789030835427e-14 chi2 stat =
129.760188956094
ancestral-derived S R pvalue = 2.2029154641494666e-24 chi2 stat =
183.55598383597146
ancestral-derived D R pvalue = 5.481109524503753e-08 chi2 stat =
88.8422765150004
only derived S D pvalue = 0.00011722731137690391 chi2 stat = 25.388232956822737
only derived S R pvalue = 4.846318953685127e-14 chi2 stat = 71.56207476214485
only derived D R pvalue = 6.954310074482721e-06 chi2 stat = 31.654533039134602
ancestral-derived S pvalue = 1.0 chi2 stat = 1.0224654361332297
ancestral-derived D pvalue = 1.0 chi2 stat = 0.9731807028857056
ancestral-derived R pvalue = 1.0 chi2 stat = 1.695183464188431
only derived S pvalue = 0.9998081177192559 chi2 stat = 0.10702948757777357
only derived D pvalue = 0.999425349627942 chi2 stat = 0.1674097245675057
only derived R pvalue = 0.993818985787964 chi2 stat = 0.4506521390802757
S symmetry of the number of shift = 0.8443305573350417
D symmetry of the number of shift = 0.849360755975542
R symmetry of the number of shift = 0.6227848101265823
S symmetry of the acceleration of shift = 0.9119215046331075
D symmetry of the acceleration of shift = 0.8973572879495197
R symmetry of the acceleration of shift = 0.7334591303407625

l1ou_tpm_muRatio0_minTau0.5_minBS0
ancestral-derived S D pvalue = 1.3961237112388258e-18 chi2 stat =
151.7750466106425
ancestral-derived S R pvalue = 3.0760106664249445e-14 chi2 stat =
127.05739423406402
ancestral-derived D R pvalue = 1.6272885044004317e-08 chi2 stat =
92.26093633030023
only derived S D pvalue = 0.007310476845760265 chi2 stat = 15.841827457785897
only derived S R pvalue = 1.8422147302824774e-07 chi2 stat = 39.547683650746634
only derived D R pvalue = 1.9503892685336116e-05 chi2 stat = 29.382745603784713
ancestral-derived S pvalue = 1.0 chi2 stat = 1.0842219833378124
ancestral-derived D pvalue = 1.0 chi2 stat = 1.0983373256737647
ancestral-derived R pvalue = 0.9999999999999999 chi2 stat = 1.8371511870054145
only derived S pvalue = 0.9996251217498067 chi2 stat = 0.14057847352862132
only derived D pvalue = 0.9996390027501225 chi2 stat = 0.1384304427970715
only derived R pvalue = 0.9850273747764663 chi2 stat = 0.6612522560044426
S symmetry of the number of shift = 0.6885245901639344
D symmetry of the number of shift = 0.8108581436077058
R symmetry of the number of shift = 0.6938775510204082
S symmetry of the acceleration of shift = 0.9038234071657318
D symmetry of the acceleration of shift = 0.8945460653736539
R symmetry of the acceleration of shift = 0.6542436553654958

l1ou_tpm_muRatio0_minTau0.5_minBS99
```

```
ancestral-derived S D pvalue = 1.3431121459082411e-07 chi2 stat =
86.28509322451443
ancestral-derived S R pvalue = 8.085657493226364e-09 chi2 stat =
94.20781351567337
ancestral-derived D R pvalue = 0.006416527451683615 chi2 stat =
51.36161390751743
only derived S D pvalue = 0.08519227067820091 chi2 stat = 9.668488156358054
only derived S R pvalue = 0.001024127642288065 chi2 stat = 20.460015000800386
only derived D R pvalue = 0.021569047499517435 chi2 stat = 13.200677857356986
ancestral-derived S pvalue = 1.0 chi2 stat = 1.1060314403793423
ancestral-derived D pvalue = 1.0 chi2 stat = 0.9854987262394669
ancestral-derived R pvalue = 0.9999999999999982 chi2 stat = 2.2512499999999998
only derived S pvalue = 0.9998467030705749 chi2 stat = 0.0977071600693814
only derived D pvalue = 0.9995873536266715 chi2 stat = 0.14619784813788342
only derived R pvalue = 0.9891192452486938 chi2 stat = 0.5749999999999998
S symmetry of the number of shift = 0.6935086277732128
D symmetry of the number of shift = 0.8007054673721341
R symmetry of the number of shift = 0.675
S symmetry of the acceleration of shift = 0.8607710100595406
D symmetry of the acceleration of shift = 0.8794435751326903
R symmetry of the acceleration of shift = 0.47099265100117405
```

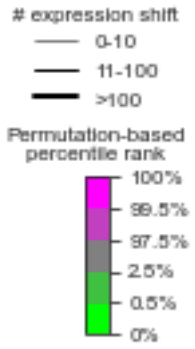
[29]:
```
fig = matplotlib.pyplot.figure(figsize=(1, 2.4))
gs = matplotlib.gridspec.GridSpec(nrows=2, ncols=5)
ax0 = matplotlib.pyplot.subplot(gs[0,:])
ax1 = matplotlib.pyplot.subplot(gs[1,2])

ax = ax0
ax.axis('off')
leg_handles = list()
leg_handles.append(matplotlib.lines.Line2D([], [], color='black', label='0-10',␣
 ↪linewidth=0.5))
leg_handles.append(matplotlib.lines.Line2D([], [], color='black',␣
 ↪label='11-100', linewidth=1))
leg_handles.append(matplotlib.lines.Line2D([], [], color='black', label='>100',␣
 ↪linewidth=2))
leg = ax.legend(handles=leg_handles, loc='upper center', frameon=False,␣
 ↪fontsize=font_size)
leg.set_title('# expression shift', prop={'weight': 'normal'})
leg.get_title().set_fontsize(font_size)
#leg._legend_box.align = "left"

ax = ax1
cmap = matplotlib.colors.ListedColormap(['#00FF00', '#40C040', '#808080',␣
 ↪'#C040C0', '#FF00FF'])
bounds = [1, 2, 3, 4, 5, 6]
```

```
ticks = bounds#[1.5,2.5,3.5,4.5,5.5]
ticklabels = ['0%', '0.5%', '2.5%', '97.5%', '99.5%', '100%']
norm = matplotlib.colors.BoundaryNorm(bounds, cmap.N)
title = 'Permutation-based\npercentile rank'
cbar = matplotlib.colorbar.ColorbarBase(ax, cmap=cmap, norm=norm,␣
 ↪orientation='vertical', ticks=ticks)
cbar.ax.set_yticklabels(ticklabels, ha='left', fontsize=font_size)
ax.set_title(title, ha='center', fontsize=font_size)


fig.savefig('colorbar_lime_magenta.svg', format='svg', transparent=True)
```



[30]:
```
sra_date = '2018_5_1'
dir_tc = os.path.join(dir_ensembl, 'curated_transcriptome/', sra_date+'/')
dir_sra = os.path.join(dir_ensembl, 'sra/', sra_date)
file_sra = os.path.join(dir_sra, 'sra_table_amalgamated_'+sra_date+'.tsv')
df_sra = pandas.read_csv(file_sra, sep='\t', header=0)

pivot = df_sra.loc[:,['scientific_name','tissue','bioproject']].
 ↪drop_duplicates().pivot_table(index='scientific_name', columns='tissue',␣
 ↪aggfunc='count')
pandas.options.display.max_rows=100
IPython.display.display(pivot)
pandas.options.display.max_rows=10
```

	bioproject					
tissue	brain	heart	kidney	liver	ovary	testis
scientific_name						
Ailuropoda melanoleuca	NaN	NaN	NaN	1.0	1.0	1.0
Anas platyrhynchos	1.0	NaN	NaN	5.0	2.0	NaN
Anolis carolinensis	4.0	3.0	2.0	3.0	2.0	2.0
Aotus nancymaae	NaN	1.0	1.0	1.0	1.0	NaN
Astyanax mexicanus	4.0	3.0	3.0	2.0	2.0	2.0

Bos taurus	3.0	5.0	7.0	27.0	7.0	11.0
Callithrix jacchus	3.0	4.0	4.0	7.0	1.0	4.0
Canis lupus	4.0	4.0	8.0	7.0	1.0	8.0
Cavia porcellus	1.0	NaN	2.0	3.0	1.0	1.0
Cercocebus atys	NaN	1.0	1.0	1.0	NaN	NaN
Chinchilla lanigera	1.0	1.0	1.0	1.0	1.0	1.0
Chlorocebus sabaeus	1.0	NaN	1.0	1.0	NaN	NaN
Danio rerio	7.0	5.0	4.0	5.0	4.0	3.0
Dasypus novemcinctus	NaN	1.0	1.0	1.0	NaN	NaN
Drosophila melanogaster	23.0	1.0	NaN	NaN	64.0	28.0
Equus caballus	1.0	NaN	1.0	1.0	NaN	6.0
Erinaceus europaeus	1.0	NaN	1.0	1.0	NaN	NaN
Felis catus	3.0	1.0	2.0	3.0	NaN	2.0
Fukomys damarensis	1.0	NaN	1.0	1.0	1.0	1.0
Gadus morhua	1.0	1.0	1.0	2.0	1.0	1.0
Gallus gallus	8.0	14.0	13.0	26.0	13.0	14.0
Gasterosteus aculeatus	6.0	1.0	5.0	3.0	NaN	1.0
Gorilla gorilla	NaN	1.0	1.0	1.0	NaN	3.0
Homo sapiens	4.0	4.0	5.0	5.0	2.0	4.0
Lepisosteus oculatus	2.0	2.0	2.0	2.0	1.0	2.0
Macaca fascicularis	2.0	1.0	3.0	4.0	NaN	1.0
Macaca mulatta	12.0	10.0	12.0	15.0	2.0	17.0
Macaca nemestrina	1.0	1.0	1.0	1.0	NaN	NaN
Meleagris gallopavo	1.0	1.0	NaN	4.0	NaN	NaN
Mesocricetus auratus	2.0	NaN	2.0	3.0	NaN	NaN
Microcebus murinus	NaN	NaN	1.0	3.0	NaN	NaN
Monodelphis domestica	7.0	5.0	5.0	7.0	4.0	8.0
Mus caroli	1.0	1.0	1.0	2.0	NaN	1.0
Mus musculus	5.0	3.0	4.0	4.0	2.0	3.0
Mus pahari	1.0	1.0	1.0	1.0	NaN	NaN
Oreochromis niloticus	3.0	2.0	3.0	8.0	2.0	2.0
Ornithorhynchus anatinus	4.0	3.0	3.0	2.0	3.0	4.0
Oryctolagus cuniculus	2.0	2.0	3.0	5.0	1.0	2.0
Oryzias latipes	3.0	2.0	1.0	6.0	3.0	4.0
Ovis aries	4.0	5.0	3.0	8.0	9.0	4.0
Pan paniscus	NaN	1.0	1.0	1.0	NaN	1.0
Pan troglodytes	2.0	4.0	4.0	6.0	NaN	3.0
Papio anubis	1.0	3.0	2.0	3.0	NaN	NaN
Petromyzon marinus	2.0	NaN	1.0	2.0	NaN	1.0
Rattus norvegicus	4.0	4.0	5.0	5.0	3.0	4.0
Rhinopithecus bieti	1.0	1.0	1.0	1.0	NaN	NaN
Saimiri boliviensis	1.0	1.0	1.0	1.0	1.0	NaN
Sus scrofa	4.0	8.0	9.0	32.0	10.0	9.0
Taeniopygia guttata	2.0	NaN	NaN	NaN	NaN	1.0
Takifugu rubripes	NaN	NaN	2.0	3.0	1.0	2.0
Tupaia belangeri	1.0	NaN	NaN	2.0	NaN	1.0
Xenopus tropicalis	4.0	3.0	4.0	7.0	3.0	3.0

[31]:
```
spp = b.loc[b.so_event=='L','taxon'].sort_values().unique()
exp_methods = ['tmm_rpkm','tpm']
for exp_method in exp_methods:
    mydir = os.path.join(dir_tc, exp_method+'/', 'sra/')
    files = os.listdir(mydir)
    files = [ f for f in files if f.endswith('.tsv') ]
    dfpiv = pandas.DataFrame()
    for file in files:
        s = pandas.read_csv(mydir+file, sep='\t', header=0)
        s['count'] = 1
        piv = s.pivot_table(index='exclusion', columns='scientific_name',␣
 ↪values='count', aggfunc=sum, fill_value=0)
        dfpiv = pandas.concat([dfpiv, piv], axis=1, sort=True)
    dfpiv = dfpiv.fillna(0).astype(int)
    dfpiv.index = dfpiv.index.str.replace('^no$', 'non_excluded')
    dfpiv = dfpiv.loc[dfpiv.index.sort_values(),dfpiv.columns.sort_values()]
    num_ex = dfpiv.loc[~dfpiv.index.str.contains('non_excluded'),:].sum(axis=0)
    num_nonex = dfpiv.loc['non_excluded',:]
    dfpiv.loc['exclusion_rate (%)',:] = num_ex / (num_ex+num_nonex) * 100
    last_ind = ['non_excluded','exclusion_rate (%)']
    ind = [ i for i in dfpiv.index if i not in last_ind ] + last_ind
    dfpiv = dfpiv.loc[ind,spp]
    dfpiv = dfpiv.loc[dfpiv.sum(axis=1)!=0,:].astype(int)
    outfile = 'exclusion_'+exp_method+'.tsv'
    dfpiv.to_csv(outfile, sep='\t', index=True)
```

[32]:
```
sra_date = '2018_5_1'
#dir_ks = os.path.join(dir_ensembl, 'kallisto_summary/', sra_date)
#dir_fpkm = os.path.join(dir_ks, 'fpkm.tmm.kallisto.gene.log.tsv/')
#dir_tpm = os.path.join(dir_ks, 'tpm.masked.kallisto.gene.log.tsv/')
dir_tc = os.path.join(dir_ensembl, 'curated_transcriptome/', sra_date+'/')
dir_fpkm = os.path.join(dir_tc, 'tmm_rpkm/', 'tc/')
dir_tpm = os.path.join(dir_tc, 'tpm/', 'tc/')
dir_sra = os.path.join(dir_ensembl, 'sra/', sra_date)
file_sra = os.path.join(dir_sra, 'sra_table_amalgamated_'+sra_date+'.tsv')
df_sra = pandas.read_csv(file_sra, sep='\t', header=0)

nsample = 1000

# GAPDH https://www.ensembl.org/Homo_sapiens/Gene/Compara_Ortholog?db=core;
 ↪g=ENSG00000111640;r=12:6534512-6538374
species_genes = [
    ['Anolis carolinensis','ENSACAG00000006502'],
    ['Astyanax mexicanus','ENSAMXG00000039361'],
    ['Bos taurus','ENSBTAG00000014731'],
    ['Callithrix jacchus','ENSCJAG00000008234'], # spermatogenic
    ['Canis lupus','ENSCAFG00000007743'],
```

```
    ['Chinchilla lanigera','ENSCLAG00000013783'],
    ['Danio rerio','ENSDARG00000043457'],
    ['Gadus morhua','ENSGMOG00000010369'],
    ['Gallus gallus','ENSGALG00000014442'],
    ['Homo sapiens','ENSG00000111640'],
    ['Macaca mulatta','ENSMMUG00000018679'],
    ['Monodelphis domestica','ENSMODG00000011838'],
    ['Mus musculus','ENSMUSG00000057666'],
    ['Oreochromis niloticus','ENSONIG00000012916'],
    ['Ornithorhynchus anatinus','ENSOANG00000004492'],
    ['Oryctolagus cuniculus','ENSOCUG00000025023'],
    ['Oryzias latipes','ENSORLG00000012224'], # or ENSORLG00020000877, or␣
 ↪ENSORLG00015011254
    ['Ovis aries','ENSOARG00000007894'],
    ['Rattus norvegicus','ENSRNOG00000018630'],
    ['Sus scrofa','ENSSSCG00000000694'],
    ['Xenopus tropicalis','ENSXETG00000033975'],
]

def get_subsampled_stat(gene, df_exp, df_sra, nsample, func='median',␣
 ↪verbose=False):
    conditions = True
    conditions = conditions & (df_sra['scientific_name']==sci_name)
    conditions = conditions & (df_sra['tissue']==tissue)
    bioprojects = df_sra.loc[conditions,'bioproject'].unique()
    num_bp = len(bioprojects)
    df_sat = pandas.DataFrame({'num_bp':[],'ave_exp':[]})
    for i in numpy.arange(num_bp)+1:
        flag_permutation = False
        counter = 0
        for bps in itertools.combinations(bioprojects, i):
            counter +=1
            if counter>=nsample:
                flag_permutation = True
                break
        if flag_permutation:
            if verbose:
                print('Combinations of {}. Permutation.'.format(i))
            for j in numpy.arange(0, nsample):
                bps = numpy.random.choice(a=bioprojects, size=i, replace=False)
                runs = df_sra.loc[(df_sra['bioproject'].isin(bps)),'run'].
 ↪unique()
                if func=='mean':
                    ave = df_exp.loc[gene,runs].mean()
                elif func=='median':
                    ave = df_exp.loc[gene,runs].median()
```

```
                df_sat = df_sat.append({'num_bp':i,'ave_exp':ave},␣
↪ignore_index=True)
        else:
            if verbose:
                print('Combinations of {}. Exhaustive. Count of combinations =␣
↪{}'.format(i, counter))
            for bps in itertools.combinations(bioprojects, i):
                runs = df_sra.loc[(df_sra['bioproject'].isin(bps)),'run'].
↪unique()
                if func=='mean':
                    ave = df_exp.loc[gene,runs].mean()
                elif func=='median':
                    ave = df_exp.loc[gene,runs].median()
                df_sat = df_sat.append({'num_bp':i,'ave_exp':ave},␣
↪ignore_index=True)
    df_sat.loc[:,'num_bp'] = df_sat.loc[:,'num_bp'].astype(int)
    return df_sat

dfs = dict()
for sg in species_genes:
    sci_name = sg[0]
    gene = sg[1]
    print(sci_name)
    dfs[sci_name] = pandas.DataFrame()
    for exp_key in ['fpkm','tpm']:
        if exp_key=='fpkm':
            file_fpkm = os.path.join(dir_fpkm, sci_name.replace(' ','_')+'.tc.
↪tsv')
            df_exp = pandas.read_csv(file_fpkm, sep='\t', header=0)
        elif exp_key=='tpm':
            file_tpm = os.path.join(dir_tpm, sci_name.replace(' ','_')+'.tc.
↪tsv')
            df_exp = pandas.read_csv(file_tpm, sep='\t', header=0)
        df_sra2 = df_sra.loc[(df_sra['run'].isin(df_exp.columns)),:]
        if gene in df_exp.index:
            for tissue in tissues:
                #file_fpkm = os.path.join(dir_fpkm, sci_name.replace(' ','_')+'.
↪gene.log.tsv')
                #file_tpm = os.path.join(dir_tpm, sci_name.replace(' ','_')+'.
↪gene.log.tsv')
                tmp = get_subsampled_stat(gene, df_exp, df_sra2, nsample)
                tmp['unit'] = exp_key
                tmp['tissue'] = tissue
                dfs[sci_name] = pandas.concat([dfs[sci_name], tmp],␣
↪ignore_index=True)
        else:
```

```
            print('Gene ID ({}) not found in {}'.format(gene, sci_name))
```

```
Anolis carolinensis
Astyanax mexicanus
Gene ID (ENSAMXG00000039361) not found in Astyanax mexicanus
Gene ID (ENSAMXG00000039361) not found in Astyanax mexicanus
Bos taurus
Callithrix jacchus
Canis lupus
Chinchilla lanigera
Danio rerio
Gadus morhua
Gallus gallus
Homo sapiens
Macaca mulatta
Monodelphis domestica
Mus musculus
Oreochromis niloticus
Ornithorhynchus anatinus
Oryctolagus cuniculus
Oryzias latipes
Ovis aries
Rattus norvegicus
Sus scrofa
Xenopus tropicalis
```

[33]:
```
alpha=1

for sg in species_genes:
    sci_name = sg[0]
    gene = sg[1]
    if dfs[sci_name].shape[0]==0:
        print("{} not found in input.".format(sci_name))
    else:
        print("{} found in input.".format(sci_name))
        fig,axes = matplotlib.pyplot.subplots(nrows=2, ncols=6, figsize=(7.2,2.
↪6), sharex=False, sharey=False)
        axes = axes.flat
        i = 0
        for exp_key,ylabel in␣
↪zip(['fpkm','tpm'],['Mean\nSVA-log-TMM-FPKM','Mean\nSVA-log-TPM']):
            ymin = numpy.inf
            ymax = -numpy.inf
            for tissue in tissues:
                tmp = dfs[sci_name].
↪loc[(dfs[sci_name]['unit']==exp_key)&(dfs[sci_name]['tissue']==tissue),:]
                ymin = min(ymin, tmp['ave_exp'].min())
```

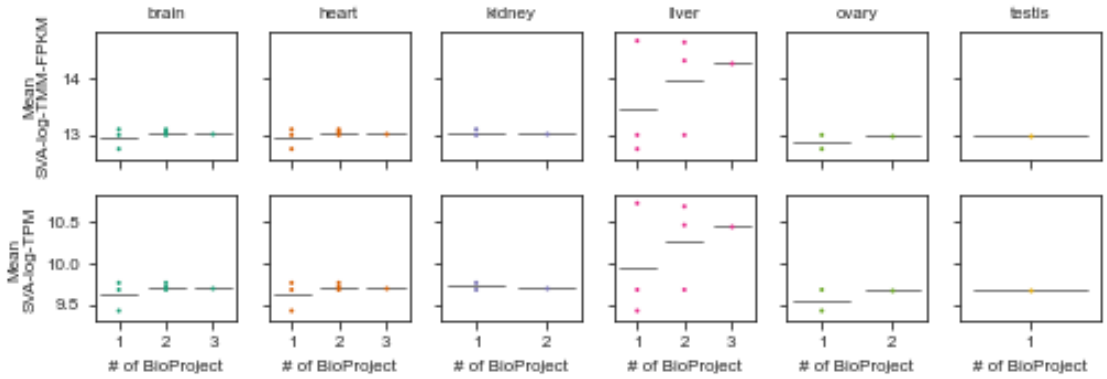
```
                ymax = max(ymax, tmp['ave_exp'].max())
                yunit = (ymax-ymin)*0.025
                ymin = ymin - yunit
                ymax = ymax + yunit
            for j,tissue in enumerate(tissues):
                ax = axes[i]
                tmp = dfs[sci_name].
↪loc[(dfs[sci_name]['unit']==exp_key)&(dfs[sci_name]['tissue']==tissue),:]
                count = tmp.groupby('num_bp').count()
                lower_count = count.index[count['ave_exp'] < 10].tolist()
                is_lower = (tmp['num_bp'].isin(lower_count))
                tmp2 = tmp.copy()
                tmp2.loc[~is_lower,'ave_exp'] = numpy.nan
                seaborn.swarmplot('num_bp', 'ave_exp', data=tmp2, ax=ax, size=2,
                                  color=organ_colors[j])
                for num_bp in tmp2['num_bp'].unique():
                    y = tmp2.loc[tmp2['num_bp']==num_bp,'ave_exp'].mean()
                    ax.plot([num_bp-1.4,num_bp-0.6], [y,y], lw=0.5,␣
↪color='black')
                if any(~is_lower):
                    tmp2 = tmp.copy()
                    tmp2.loc[is_lower,'ave_exp'] = numpy.nan
                    seaborn.boxplot('num_bp', 'ave_exp', data=tmp2, ax=ax,
                                    color=organ_colors[j], linewidth=0.5,␣
↪fliersize=0)
                #ax = change_seaborn_boxplot_linecolors(ax,␣
↪col=organ_colors[j])
                ax.set_ylim(ymin, ymax)
                if exp_key=='fpkm':
                    ax.set_title(tissue)
                    ax.set_xlabel('')
                    ax.set_xticklabels(['',] * len(ax.get_xticklabels()))
                else:
                    ax.set_xlabel('# of BioProject')
                if j==0:
                    ax.set_ylabel(ylabel)
                else:
                    ax.set_ylabel('')
                    ax.set_yticklabels(['',] * len(ax.get_yticklabels()))
                while len(ax.get_xticklabels())>8:
                    xticks = ax.get_xticks()[0::2]
                    xticklabels = [ tl._text for tl in ax.get_xticklabels()[0::
↪2] ]
                    ax.set_xticks(ticks=xticks)
                    ax.set_xticklabels(labels=xticklabels)
                i += 1
        fig.tight_layout()
```

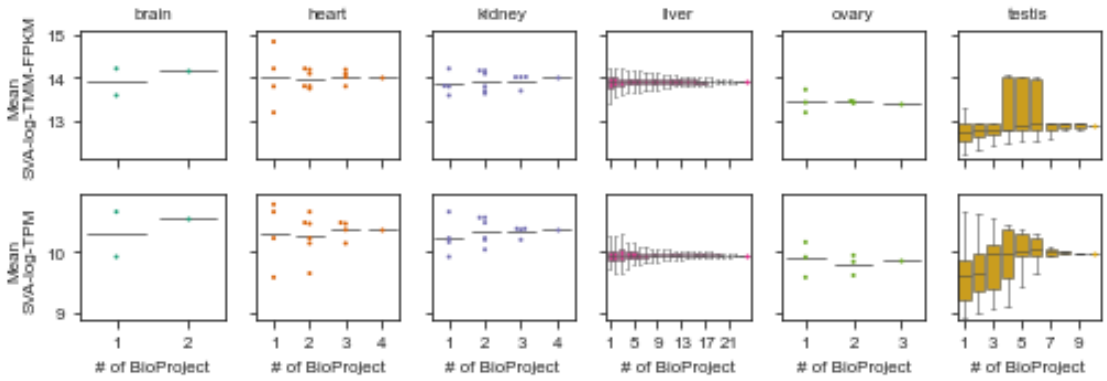
```
        outbase = 'mean_reversion_'+sci_name.replace(' ','_')+"_"+gene
        fig.savefig(outbase+".pdf", format='pdf', transparent=True)
        fig.savefig(outbase+".svg", format='svg', transparent=True)
```

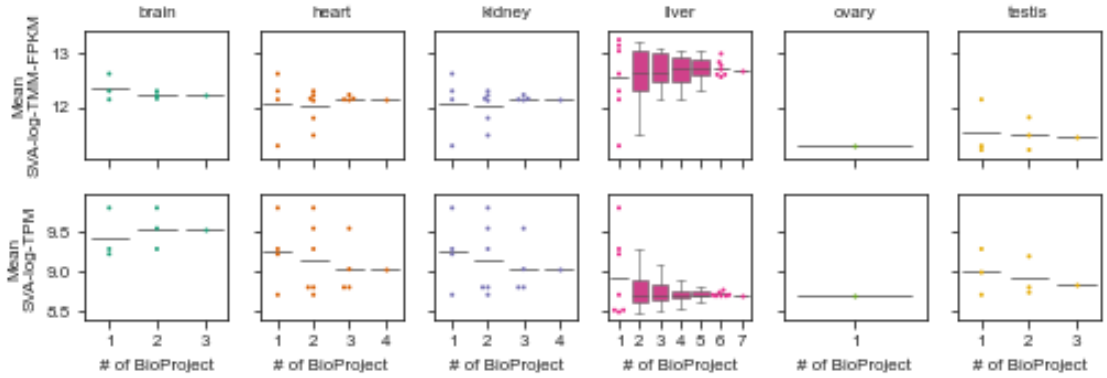
```
Anolis carolinensis found in input.
Astyanax mexicanus not found in input.
Bos taurus found in input.
Callithrix jacchus found in input.
Canis lupus found in input.
Chinchilla lanigera found in input.
```

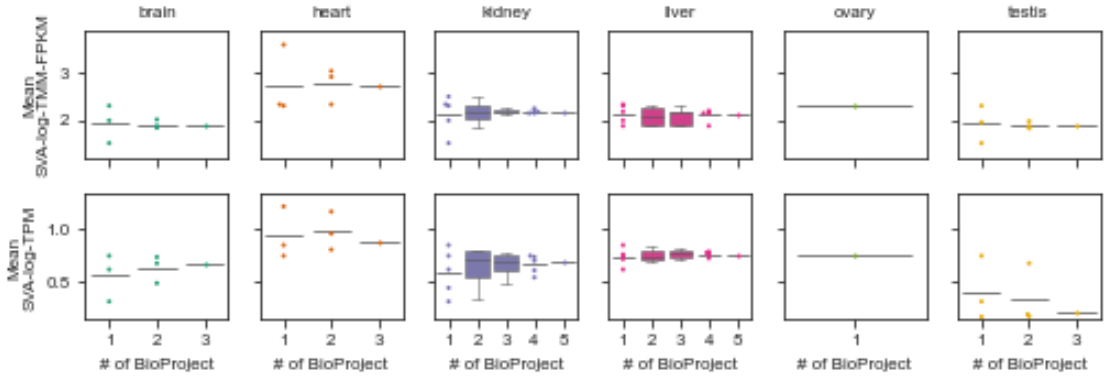
```
/Users/kef74yk/anaconda3/lib/python3.6/site-packages/ipykernel_launcher.py:42:
UserWarning: Attempting to set identical bottom == top == 14.64062997997635
results in singular transformations; automatically expanding.
/Users/kef74yk/anaconda3/lib/python3.6/site-packages/ipykernel_launcher.py:42:
UserWarning: Attempting to set identical bottom == top == 10.759435623 results
in singular transformations; automatically expanding.
```

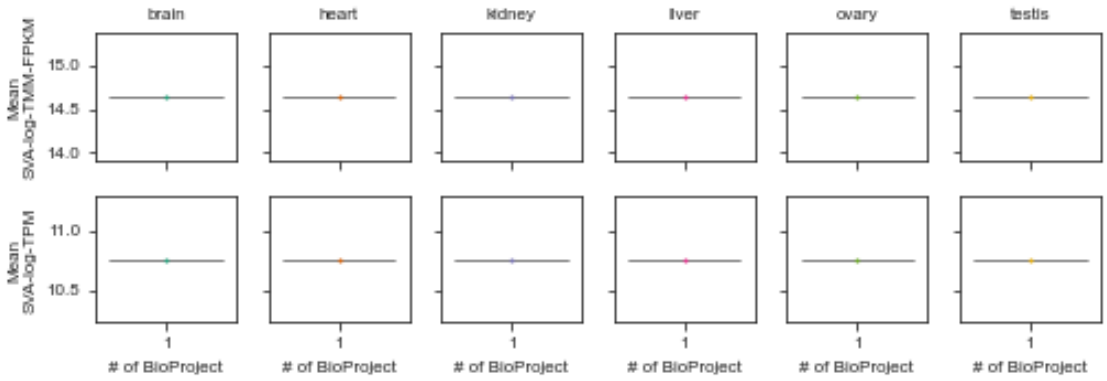
```
Danio rerio found in input.
Gadus morhua found in input.
Gallus gallus found in input.
Homo sapiens found in input.
Macaca mulatta found in input.
Monodelphis domestica found in input.
Mus musculus found in input.
Oreochromis niloticus found in input.
Ornithorhynchus anatinus found in input.
Oryctolagus cuniculus found in input.
Oryzias latipes found in input.
Ovis aries found in input.
Rattus norvegicus found in input.
Sus scrofa found in input.
Xenopus tropicalis found in input.
```

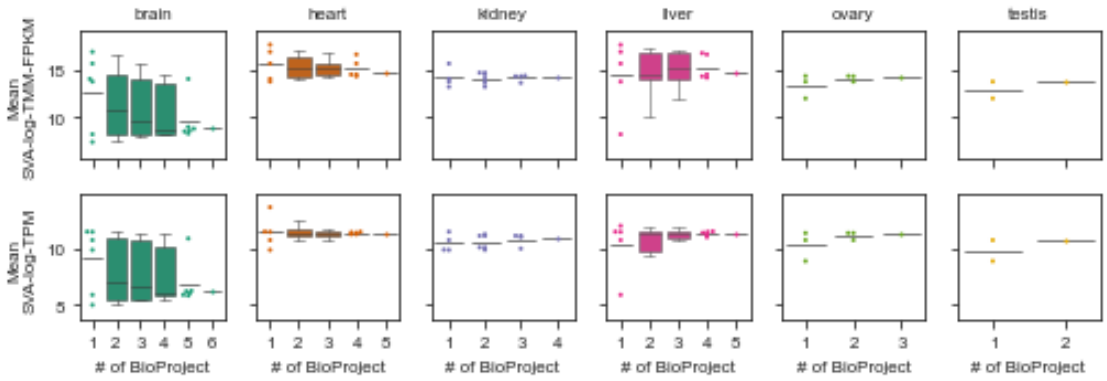


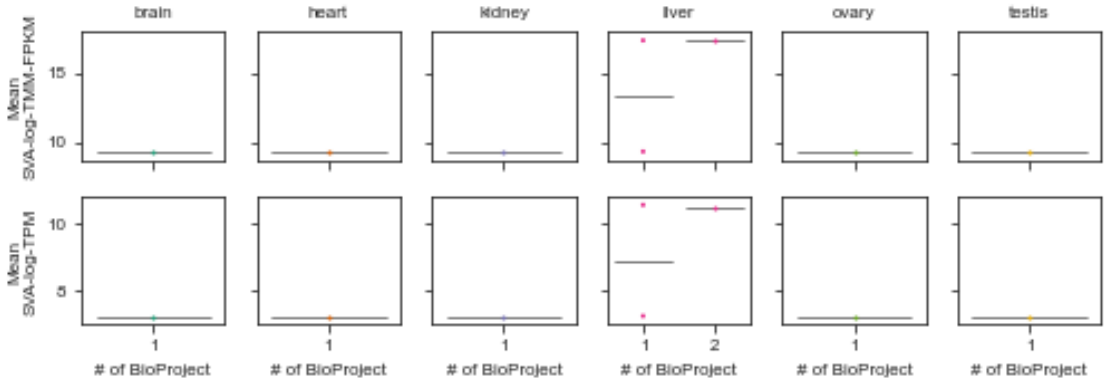

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject

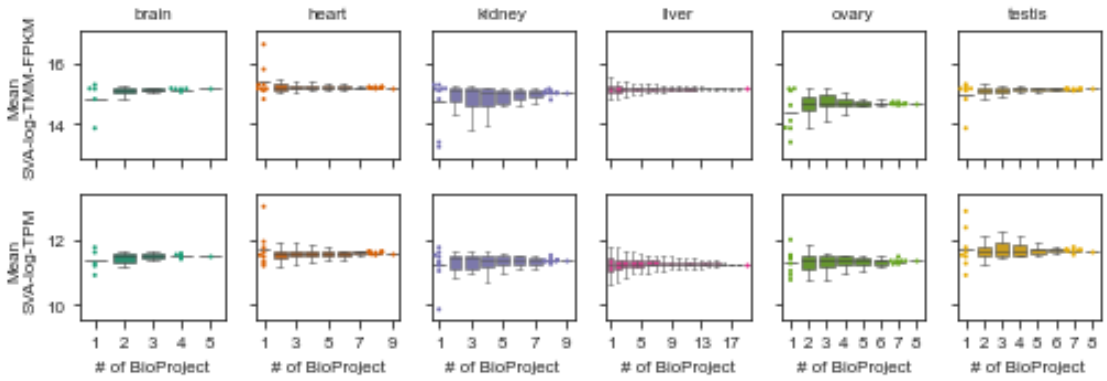

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject

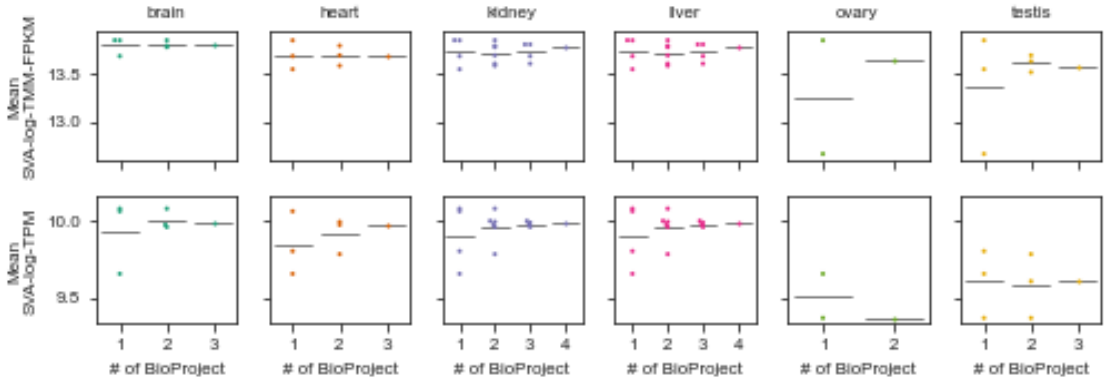

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject

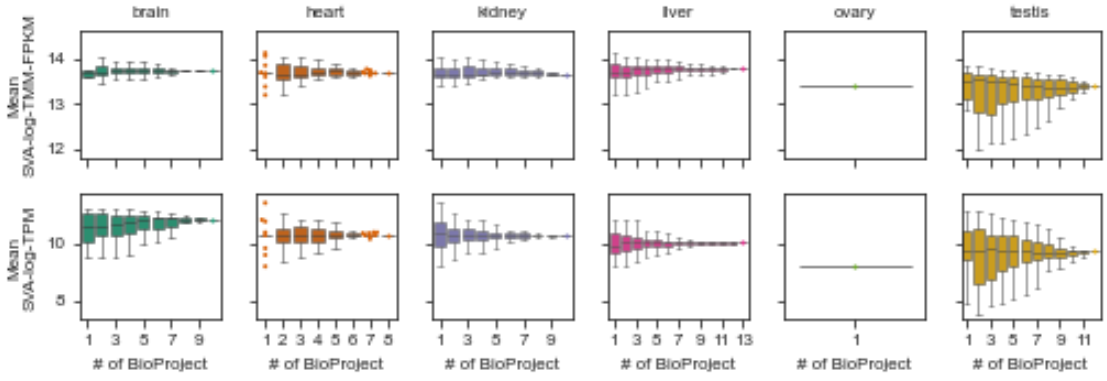

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
15.0
14.5
14.0
Mean SVA-log-TPM
11.0
10.5
1
# of BioProject

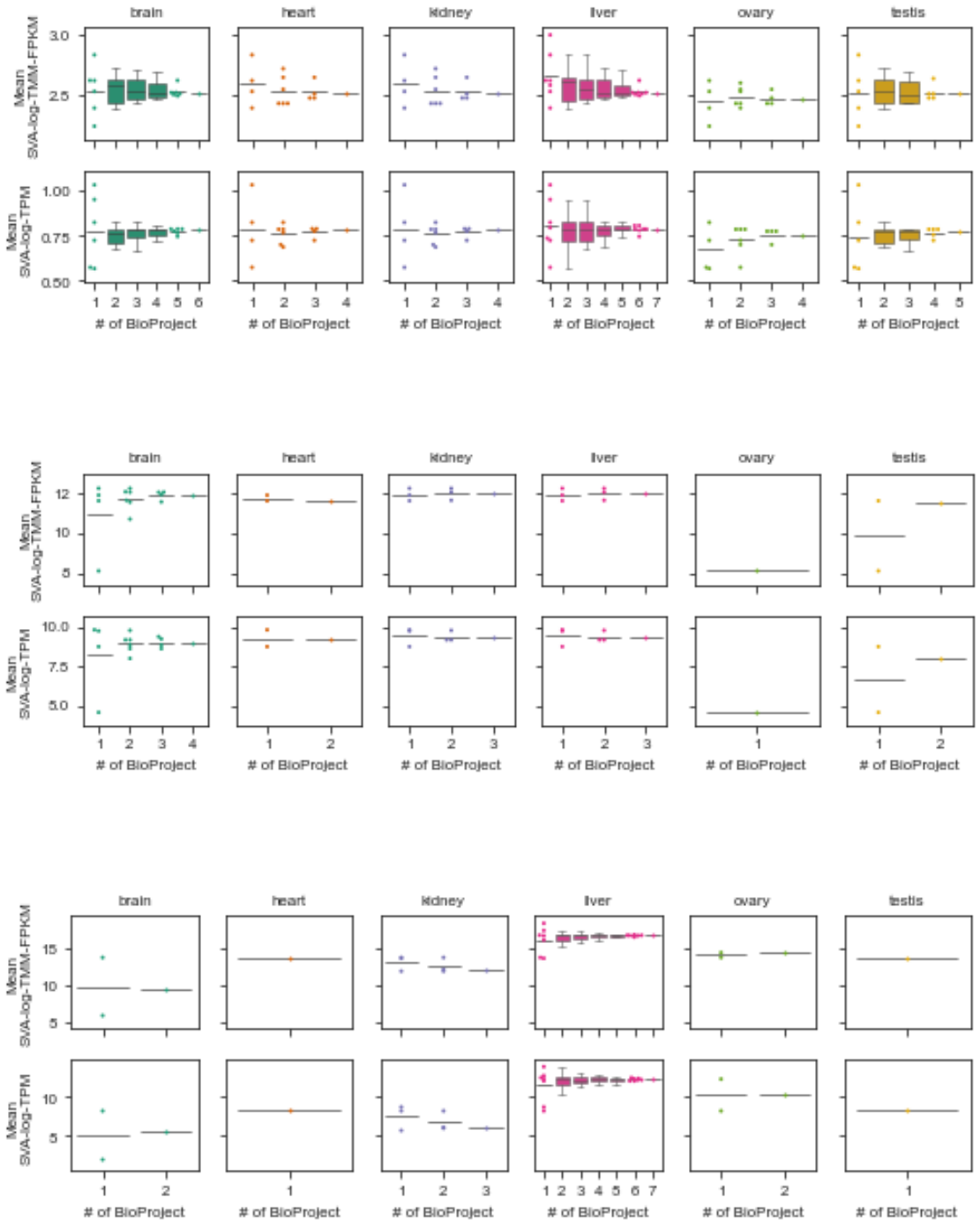

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
15
10
Mean SVA-log-TPM
10
5
1 2 3 4 5 6
1 2 3 4 5
1 2 3 4
1 2 3
1 2
# of BioProject

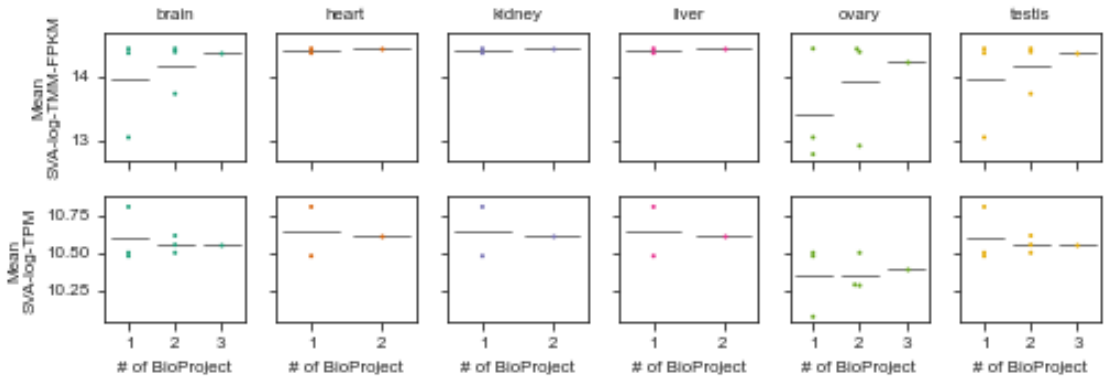

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
15
10
Mean SVA-log-TPM
10
5
1
2
# of BioProject

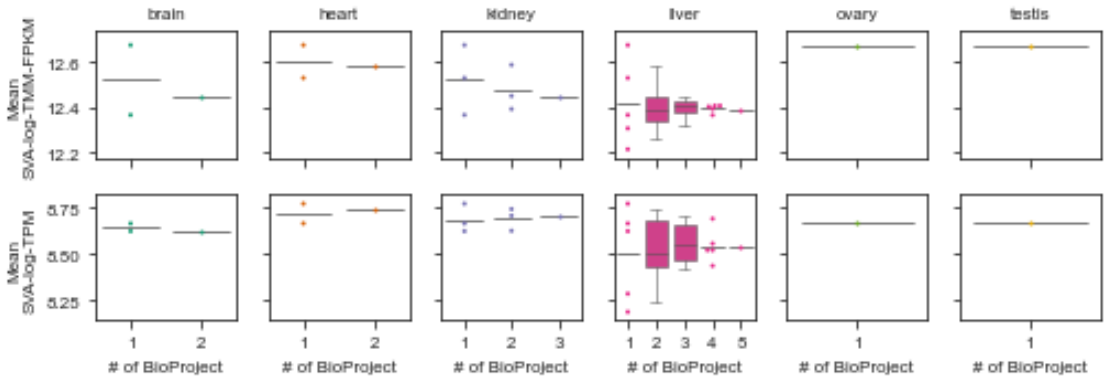

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject

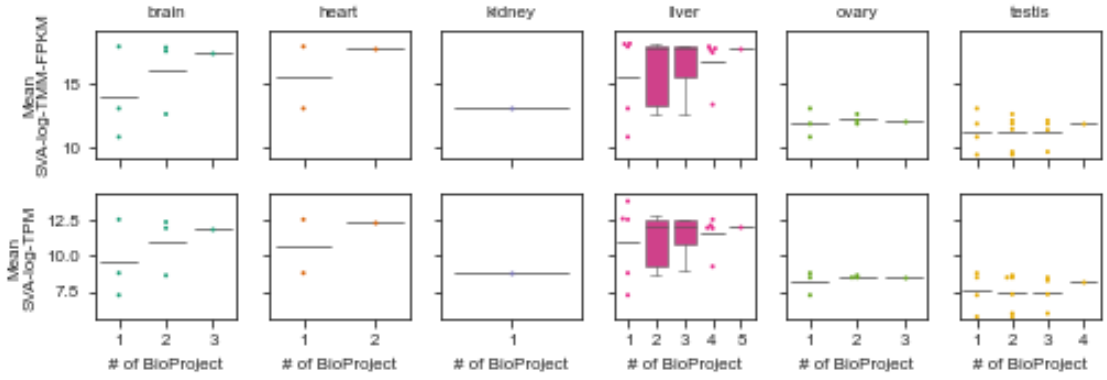

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject

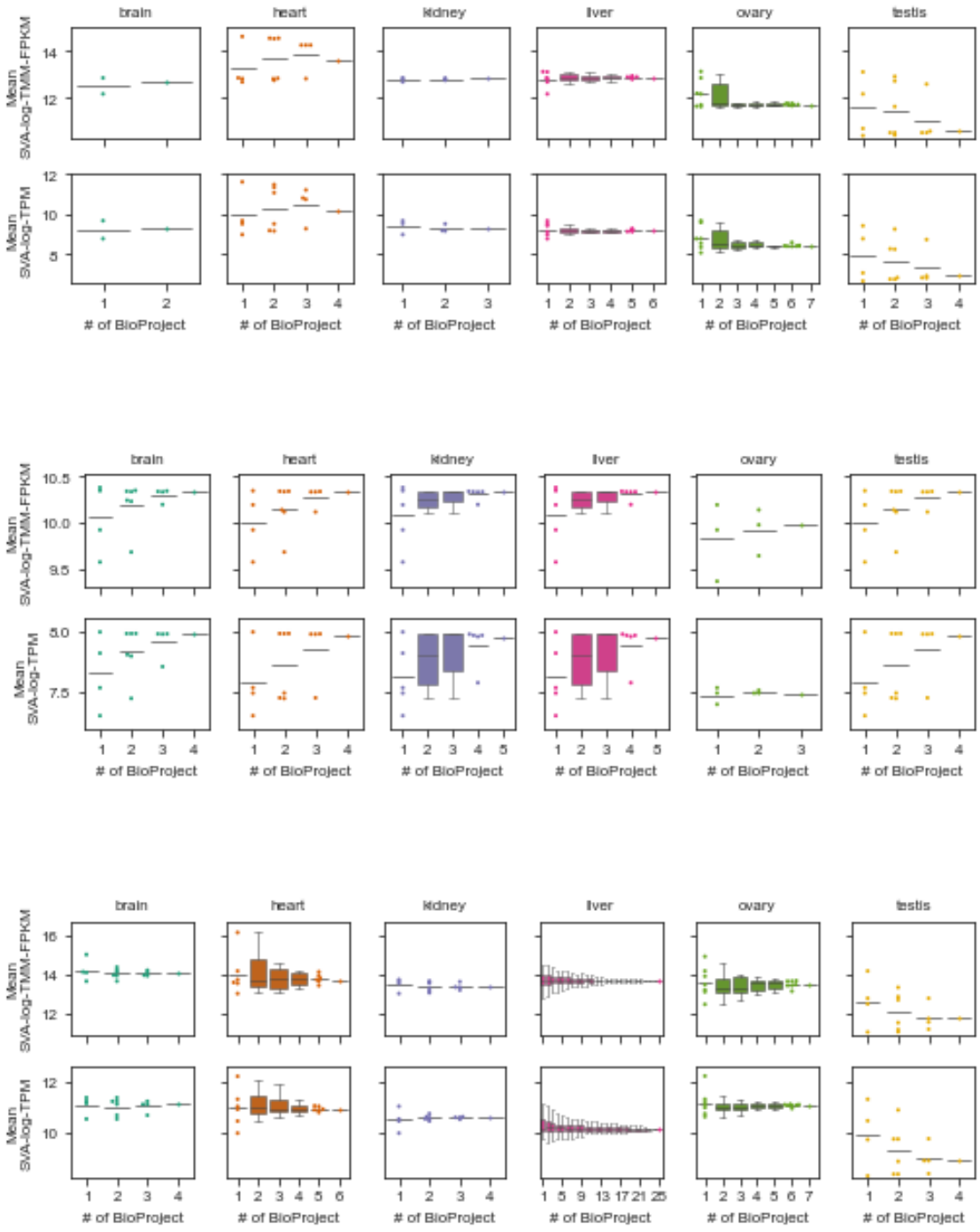

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject

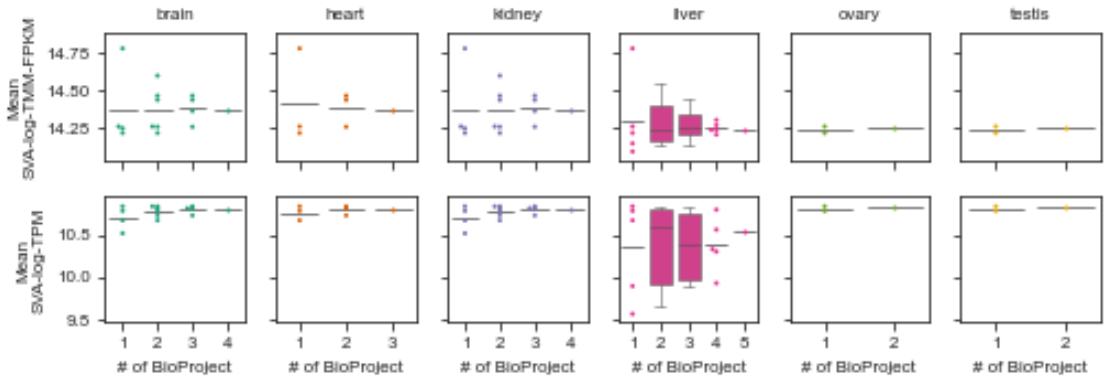

brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject


brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject


brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject


brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject


brain
heart
kidney
liver
ovary
testis
Mean SVA-log-TMM-FPKM
Mean SVA-log-TPM
# of BioProject



[34]:
```
import gseapy
import mygene

#library_names = gseapy.get_library_name()

library_names = [
    'KEGG_2019_Human',
    'KEGG_2019_Mouse',
]

bidirectionals = [True,False]
pcm_prefixes = ['l1ou_fpkm_','l1ou_tpm_']
min_taus = [0,0.5]


mg = mygene.MyGeneInfo()
taxids = ','.join(b.taxid.unique().astype(str))

new_wd = os.path.join(wd+'GO_specificity_shift')
if not os.path.exists(new_wd):
    os.mkdir(new_wd)
os.chdir(new_wd)


b_leaf = b.loc[(b['so_event']=='L'),:]

for pp,bidirectional,min_tau in itertools.product(pcm_prefixes, bidirectionals,␣
 ↪min_taus):
    organ1s = b['parent_'+pp+'max_organ'].dropna().unique()
    organ2s = b[pp+'max_organ'].dropna().unique()
    events = ['All','S','D','R']

    conditions = True
```

```
    conditions = conditions&(b['l1ou_intersect_is_shift']==1)
    conditions = conditions&(b['spnode_coverage']!='root')
    conditions = conditions&(b[pp+'tau']>=min_tau)
    conditions = conditions&(b['parent_'+pp+'tau']>=min_tau)
    b2 = b.loc[conditions,:].reset_index()
    if bidirectional:
        organ_combinat = list(itertools.combinations(set(organ1s).
↪union(set(organ2s)), 2))
        iters = [ [ev,]+list(o) for ev in events for o in organ_combinat ]
    else:
        iters = itertools.product(events, organ1s, organ2s)
    for ev,organ1,organ2 in iters:
        if organ1==organ2:
            continue
        elif organ1>organ2:
            organ1prev = organ1
            organ2prev = organ2
            organ1 = organ2prev
            organ2 = organ1prev
        conditions = True
        if ev!='All':
            conditions = conditions&(b2['branch_category']==ev)
        if bidirectional:
            is_organ_combinat1 =␣
↪(b2['parent_'+pp+'max_organ']==organ1)&(b2[pp+'max_organ']==organ2)
            is_organ_combinat2 =␣
↪(b2['parent_'+pp+'max_organ']==organ2)&(b2[pp+'max_organ']==organ1)
            conditions = conditions&(is_organ_combinat1|is_organ_combinat2)
        else:
            conditions = conditions&(b2['parent_'+pp+'max_organ']==organ1)
            conditions = conditions&(b2[pp+'max_organ']==organ2)
        b3 = b2.loc[conditions,['orthogroup',pp+'regime']].
↪reset_index(drop=True)
        if b3.shape[0]==0:
            continue
        gene_ids = pandas.DataFrame()
        for i in b3.index:
            if i%1000==0:
                print(i)
            regime = b3.loc[i,pp+'regime']
            og = b3.loc[i,'orthogroup']
            tmp_gene_ids = b_leaf.
↪loc[(b_leaf[pp+'regime']==regime)&(b_leaf['orthogroup']==og),['orthogroup','node_name']]
            gene_ids = pandas.concat([gene_ids,tmp_gene_ids], sort=False,␣
↪ignore_index=True)
```

```
        gene_ids = gene_ids.drop_duplicates().
↪sort_values(by=['orthogroup','node_name'])
        for sp in ['Homo_sapiens','Mus_musculus']:
            outdir=pp+sp+'_minTau'+str(min_tau)+'_'+organ1+'_'+organ2+'_'+ev
            if bidirectional:
                outdir = 'bidirectional_'+outdir
            df_sp = gene_ids.loc[(gene_ids['node_name'].str.startswith(sp)),:]
            if df_sp.shape[0]==0:
                continue
            df_sp.loc[:,'node_name'] = df_sp.loc[:,'node_name'].replace('.
↪*_','', regex=True)
            df_sp.columns = ['orthogroup','gene_id']
            if not os.path.exists(outdir):
                os.mkdir(outdir)
            df_sp.to_csv(os.path.join(outdir, outdir+'.geneid.tsv'), sep='\t',␣
↪index=False)
            sp_gene_ids = df_sp.loc[:,'gene_id'].tolist()
            b_mygene = mg.querymany(sp_gene_ids, scopes='ensembl.gene',␣
↪fields='symbol', species=taxids, as_dataframe=True)
            if b_mygene.columns[0]=='notfound':
                b_mygene = pandas.DataFrame()
            if b_mygene.shape[0]==0:
                continue
            for ln in library_names:
                if (sp=='Homo_sapiens')&('Mouse' in ln):
                    continue
                if (sp=='Mus_musculus')&('Human' in ln):
                    continue
                txt = '{} min_tau={} {} {}-{} {}: #shift={}, #leaf={},␣
↪#queryGene={}, {}'
                if bidirectional:
                    txt = txt+' bidirectional'
                else:
                    txt = txt+' unidirectional'
                txt = txt.format(pp, min_tau, ev,organ1,organ2,sp,b3.
↪shape[0],len(gene_ids),len(sp_gene_ids),ln)
                if os.path.isfile(outdir+'/'+ln+'.'+outdir+'.enrichr.reports.
↪txt'):
                    print('Skipped.', txt)
                    continue
                print(txt)
                try:
                    out = gseapy.enrichr(gene_list=b_mygene['symbol'].
↪astype(str).tolist(), description=outdir, gene_sets=ln, outdir=outdir,␣
↪cutoff=0.05)
                except:
```

```
                    print('Error and retry.')
                    try:
                        out = gseapy.enrichr(gene_list=b_mygene['symbol'].
↪astype(str).tolist(), description=outdir, gene_sets=ln, outdir=outdir,␣
↪cutoff=0.05)
                    except:
                        time.sleep(3)
                        print('The retry failed. Skipped.')
        print('')
print('Done!')

del b_leaf

os.chdir(wd)
```

```
0
```

```
/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/pandas/core/indexing.py:1048: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
Try using .loc[row_indexer,col_indexer] = value instead

See the caveats in the documentation: https://pandas.pydata.org/pandas-
docs/stable/user_guide/indexing.html#returning-a-view-versus-a-copy
  self.obj[item_labels[indexer[info_axis]]] = value
```

```
querying 1-140…done.
Finished.
```

```
/Users/kef74yk/anaconda3/lib/python3.6/site-
packages/biothings_client/base.py:143: FutureWarning:
pandas.io.json.json_normalize is deprecated, use pandas.json_normalize instead
  df = json_normalize(obj)
```

```
140 input query terms found no hit:
        ['ENSG00000204577', 'ENSG00000244482', 'ENSG00000273991',
'ENSG00000274587', 'ENSG00000275290', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-107…done.
Finished.
107 input query terms found no hit:
        ['ENSMUSG00000089942', 'ENSMUSG00000095088', 'ENSMUSG00000073968',
'ENSMUSG00000048076', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-86…done.
```

```
Finished.
86 input query terms found no hit:
        ['ENSG00000211947', 'ENSG00000211966', 'ENSG00000255374',
'ENSG00000255837', 'ENSG00000273092', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-83…done.
Finished.
83 input query terms found no hit:
        ['ENSMUSG00000076823', 'ENSMUSG00000076839', 'ENSMUSG00000076846',
'ENSMUSG00000076858', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-229…done.
Finished.
229 input query terms found no hit:
        ['ENSG00000276033', 'ENSG00000276848', 'ENSG00000240764',
'ENSG00000172466', 'ENSG00000275528', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-181…done.
Finished.
181 input query terms found no hit:
        ['ENSMUSG00000057439', 'ENSMUSG00000051469', 'ENSMUSG00000020676',
'ENSMUSG00000045534', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-110…done.
Finished.
110 input query terms found no hit:
        ['ENSG00000104970', 'ENSG00000180573', 'ENSG00000211788',
'ENSG00000075624', 'ENSG00000163017', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-95…done.
Finished.
95 input query terms found no hit:
        ['ENSMUSG00000094420', 'ENSMUSG00000058818', 'ENSMUSG00000093969',
'ENSMUSG00000096106', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-392…done.
```

```
Finished.
392 input query terms found no hit:
        ['ENSG00000125498', 'ENSG00000167633', 'ENSG00000240403',
'ENSG00000242019', 'ENSG00000243772', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-152…done.
Finished.
152 input query terms found no hit:
        ['ENSMUSG00000073913', 'ENSMUSG00000078808', 'ENSMUSG00000115644',
'ENSMUSG00000047246', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-138…done.
Finished.
138 input query terms found no hit:
        ['ENSG00000211959', 'ENSG00000259261', 'ENSG00000204642',
'ENSG00000206452', 'ENSG00000225691', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-117…done.
Finished.
117 input query terms found no hit:
        ['ENSMUSG00000053338', 'ENSMUSG00000025479', 'ENSMUSG00000040583',
'ENSMUSG00000040650', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-174…done.
Finished.
174 input query terms found no hit:
        ['ENSG00000277177', 'ENSG00000206435', 'ENSG00000228299',
'ENSG00000203747', 'ENSG00000198211', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-112…done.
Finished.
112 input query terms found no hit:
        ['ENSMUSG00000073406', 'ENSMUSG00000020440', 'ENSMUSG00000021877',
'ENSMUSG00000051853', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-136…done.
```

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Finished.
136 input query terms found no hit:
        ['ENSG00000233999', 'ENSG00000239819', 'ENSG00000242580',
'ENSG00000243063', 'ENSG00000282310', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-125…done.
Finished.
125 input query terms found no hit:
        ['ENSMUSG00000074521', 'ENSMUSG00000078889', 'ENSMUSG00000078901',
'ENSMUSG00000043091', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

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1000
querying 1-186…done.
Finished.
186 input query terms found no hit:
        ['ENSG00000273884', 'ENSG00000274311', 'ENSG00000274513',
'ENSG00000277317', 'ENSG00000277398', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-196…done.
Finished.
196 input query terms found no hit:
        ['ENSMUSG00000056782', 'ENSMUSG00000066263', 'ENSMUSG00000066269',
'ENSMUSG00000094520', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-146…done.
Finished.
146 input query terms found no hit:
        ['ENSG00000276798', 'ENSG00000127362', 'ENSG00000256436',
'ENSG00000263097', 'ENSG00000282612', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-129…done.
Finished.
129 input query terms found no hit:
        ['ENSMUSG00000076778', 'ENSMUSG00000074955', 'ENSMUSG00000007097',
'ENSMUSG00000033161', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
```

```
querying 1-187…done.
Finished.
187 input query terms found no hit:
        ['ENSG00000211957', 'ENSG00000282045', 'ENSG00000282211',
'ENSG00000282305', 'ENSG00000211599', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-164…done.
Finished.
164 input query terms found no hit:
        ['ENSMUSG00000073028', 'ENSMUSG00000076500', 'ENSMUSG00000076501',
'ENSMUSG00000076505', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-117…done.
Finished.
117 input query terms found no hit:
        ['ENSG00000184698', 'ENSG00000273539', 'ENSG00000278042',
'ENSG00000282425', 'ENSG00000282651', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-135…done.
Finished.
135 input query terms found no hit:
        ['ENSMUSG00000050085', 'ENSMUSG00000058200', 'ENSMUSG00000094531',
'ENSMUSG00000096773', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-158…done.
Finished.
158 input query terms found no hit:
        ['ENSG00000005001', 'ENSG00000282937', 'ENSG00000127366',
'ENSG00000276541', 'ENSG00000165527', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-120…done.
Finished.
120 input query terms found no hit:
        ['ENSMUSG00000044147', 'ENSMUSG00000049758', 'ENSMUSG00000074946',
'ENSMUSG00000109528', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
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1000
querying 1-235…done.
Finished.
235 input query terms found no hit:
        ['ENSG00000276114', 'ENSG00000227739', 'ENSG00000151079',
'ENSG00000169432', 'ENSG00000188613', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-259…done.
Finished.
259 input query terms found no hit:
        ['ENSMUSG00000094076', 'ENSMUSG00000043366', 'ENSMUSG00000073973',
'ENSMUSG00000094822', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

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1000
querying 1-262…done.
Finished.
262 input query terms found no hit:
        ['ENSG00000276590', 'ENSG00000124635', 'ENSG00000197903',
'ENSG00000184260', 'ENSG00000170465', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-199…done.
Finished.
199 input query terms found no hit:
        ['ENSMUSG00000043948', 'ENSMUSG00000073962', 'ENSMUSG00000046932',
'ENSMUSG00000095632', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-83…done.
Finished.
83 input query terms found no hit:
        ['ENSG00000179144', 'ENSG00000090659', 'ENSG00000143226',
'ENSG00000088881', 'ENSG00000094963', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-66…done.
Finished.
66 input query terms found no hit:
        ['ENSMUSG00000062421', 'ENSMUSG00000078606', 'ENSMUSG00000017756',
'ENSMUSG00000063694', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

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0
querying 1-53…done.
Finished.
53 input query terms found no hit:
        ['ENSG00000108691', 'ENSG00000213719', 'ENSG00000223639',
'ENSG00000226248', 'ENSG00000226417', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-55…done.
Finished.
55 input query terms found no hit:
        ['ENSMUSG00000076823', 'ENSMUSG00000076839', 'ENSMUSG00000076846',
'ENSMUSG00000094562', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-120…done.
Finished.
120 input query terms found no hit:
        ['ENSG00000240764', 'ENSG00000130037', 'ENSG00000114279',
'ENSG00000120049', 'ENSG00000101144', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-105…done.
Finished.
105 input query terms found no hit:
        ['ENSMUSG00000020676', 'ENSMUSG00000045534', 'ENSMUSG00000090841',
'ENSMUSG00000025221', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-73…done.
Finished.
73 input query terms found no hit:
        ['ENSG00000180573', 'ENSG00000213139', 'ENSG00000257529',
'ENSG00000188778', 'ENSG00000160447', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-66…done.
Finished.
66 input query terms found no hit:
        ['ENSMUSG00000037820', 'ENSMUSG00000042842', 'ENSMUSG00000043613',
'ENSMUSG00000021702', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

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0
querying 1-328…done.
Finished.
328 input query terms found no hit:
        ['ENSG00000125498', 'ENSG00000167633', 'ENSG00000240403',
'ENSG00000242019', 'ENSG00000243772', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-72…done.
Finished.
72 input query terms found no hit:
        ['ENSMUSG00000073913', 'ENSMUSG00000031085', 'ENSMUSG00000040752',
'ENSMUSG00000053093', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-83…done.
Finished.
83 input query terms found no hit:
        ['ENSG00000224305', 'ENSG00000225824', 'ENSG00000226165',
'ENSG00000228254', 'ENSG00000228813', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-72…done.
Finished.
72 input query terms found no hit:
        ['ENSMUSG00000053338', 'ENSMUSG00000025479', 'ENSMUSG00000023122',
'ENSMUSG00000071866', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-94…done.
Finished.
94 input query terms found no hit:
        ['ENSG00000198211', 'ENSG00000215048', 'ENSG00000229295',
'ENSG00000230708', 'ENSG00000010438', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-65…done.
Finished.
65 input query terms found no hit:
        ['ENSMUSG00000108827', 'ENSMUSG00000049680', 'ENSMUSG00000041453',
'ENSMUSG00000037419', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

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0
querying 1-87…done.
Finished.
87 input query terms found no hit:
        ['ENSG00000246705', 'ENSG00000105388', 'ENSG00000090382',
'ENSG00000215472', 'ENSG00000211792', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-75…done.
Finished.
75 input query terms found no hit:
        ['ENSMUSG00000058260', 'ENSMUSG00000069516', 'ENSMUSG00000062328',
'ENSMUSG00000090451', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-76…done.
Finished.
76 input query terms found no hit:
        ['ENSG00000230413', 'ENSG00000233095', 'ENSG00000235346',
'ENSG00000235680', 'ENSG00000237216', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-79…done.
Finished.
79 input query terms found no hit:
        ['ENSMUSG00000056782', 'ENSMUSG00000066263', 'ENSMUSG00000066269',
'ENSMUSG00000066850', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-75…done.
Finished.
75 input query terms found no hit:
        ['ENSG00000127362', 'ENSG00000070831', 'ENSG00000136531',
'ENSG00000163399', 'ENSG00000157388', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-80…done.
Finished.
80 input query terms found no hit:
        ['ENSMUSG00000074955', 'ENSMUSG00000033161', 'ENSMUSG00000019302',
'ENSMUSG00000033295', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

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0
querying 1-131…done.
Finished.
131 input query terms found no hit:
        ['ENSG00000211599', 'ENSG00000211611', 'ENSG00000211623',
'ENSG00000211625', 'ENSG00000211626', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-130…done.
Finished.
130 input query terms found no hit:
        ['ENSMUSG00000073028', 'ENSMUSG00000076500', 'ENSMUSG00000076501',
'ENSMUSG00000076505', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-59…done.
Finished.
59 input query terms found no hit:
        ['ENSG00000184698', 'ENSG00000169777', 'ENSG00000115386',
'ENSG00000117335', 'ENSG00000212657', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-72…done.
Finished.
72 input query terms found no hit:
        ['ENSMUSG00000050085', 'ENSMUSG00000058200', 'ENSMUSG00000094531',
'ENSMUSG00000096773', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-94…done.
Finished.
94 input query terms found no hit:
        ['ENSG00000127366', 'ENSG00000186767', 'ENSG00000139675',
'ENSG00000156508', 'ENSG00000211643', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-78…done.
Finished.
78 input query terms found no hit:
        ['ENSMUSG00000074946', 'ENSMUSG00000109528', 'ENSMUSG00000037742',
'ENSMUSG00000027669', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

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0
querying 1-138…done.
Finished.
138 input query terms found no hit:
        ['ENSG00000151079', 'ENSG00000169432', 'ENSG00000188613',
'ENSG00000132681', 'ENSG00000155511', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-149…done.
Finished.
149 input query terms found no hit:
        ['ENSMUSG00000043366', 'ENSMUSG00000073973', 'ENSMUSG00000094822',
'ENSMUSG00000064259', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-171…done.
Finished.
171 input query terms found no hit:
        ['ENSG00000184260', 'ENSG00000170465', 'ENSG00000170477',
'ENSG00000185479', 'ENSG00000205420', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-135…done.
Finished.
135 input query terms found no hit:
        ['ENSMUSG00000043948', 'ENSMUSG00000073962', 'ENSMUSG00000037737',
'ENSMUSG00000059430', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-57…done.
Finished.
57 input query terms found no hit:
        ['ENSG00000204577', 'ENSG00000244482', 'ENSG00000273991',
'ENSG00000274587', 'ENSG00000275290', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-37…done.
Finished.
37 input query terms found no hit:
        ['ENSMUSG00000089942', 'ENSMUSG00000095088', 'ENSMUSG00000073968',
'ENSMUSG00000048076', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

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0
querying 1-33…done.
Finished.
33 input query terms found no hit:
        ['ENSG00000211947', 'ENSG00000211966', 'ENSG00000255374',
'ENSG00000255837', 'ENSG00000273092', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-28…done.
Finished.
28 input query terms found no hit:
        ['ENSMUSG00000076858', 'ENSMUSG00000096908', 'ENSMUSG00000095074',
'ENSMUSG00000001847', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-108…done.
Finished.
108 input query terms found no hit:
        ['ENSG00000276033', 'ENSG00000276848', 'ENSG00000172466',
'ENSG00000275528', 'ENSG00000223865', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-70…done.
Finished.
70 input query terms found no hit:
        ['ENSMUSG00000057439', 'ENSMUSG00000051469', 'ENSMUSG00000022949',
'ENSMUSG00000109033', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-35…done.
Finished.
35 input query terms found no hit:
        ['ENSG00000104970', 'ENSG00000211788', 'ENSG00000075624',
'ENSG00000163017', 'ENSG00000184009', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-27…done.
Finished.
27 input query terms found no hit:
        ['ENSMUSG00000094420', 'ENSMUSG00000058818', 'ENSMUSG00000093969',
'ENSMUSG00000096106', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

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0
querying 1-59…done.
Finished.
59 input query terms found no hit:
        ['ENSG00000158373', 'ENSG00000248496', 'ENSG00000026950',
'ENSG00000111801', 'ENSG00000154370', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-60…done.
Finished.
60 input query terms found no hit:
        ['ENSMUSG00000078808', 'ENSMUSG00000115644', 'ENSMUSG00000076760',
'ENSMUSG00000060981', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-54…done.
Finished.
54 input query terms found no hit:
        ['ENSG00000211959', 'ENSG00000259261', 'ENSG00000204642',
'ENSG00000206452', 'ENSG00000225691', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-43…done.
Finished.
43 input query terms found no hit:
        ['ENSMUSG00000040583', 'ENSMUSG00000040650', 'ENSMUSG00000040660',
'ENSMUSG00000066704', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-77…done.
Finished.
77 input query terms found no hit:
        ['ENSG00000277177', 'ENSG00000206435', 'ENSG00000228299',
'ENSG00000203747', 'ENSG00000004059', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-44…done.
Finished.
44 input query terms found no hit:
        ['ENSMUSG00000073406', 'ENSMUSG00000020440', 'ENSMUSG00000021877',
'ENSMUSG00000051853', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

```
0
querying 1-49…done.
Finished.
49 input query terms found no hit:
        ['ENSG00000233999', 'ENSG00000239819', 'ENSG00000242580',
'ENSG00000243063', 'ENSG00000282310', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-45…done.
Finished.
45 input query terms found no hit:
        ['ENSMUSG00000074521', 'ENSMUSG00000078889', 'ENSMUSG00000078901',
'ENSMUSG00000043091', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-101…done.
Finished.
101 input query terms found no hit:
        ['ENSG00000273884', 'ENSG00000274311', 'ENSG00000274513',
'ENSG00000277317', 'ENSG00000277398', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-104…done.
Finished.
104 input query terms found no hit:
        ['ENSMUSG00000094520', 'ENSMUSG00000060024', 'ENSMUSG00000061829',
'ENSMUSG00000094898', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-70…done.
Finished.
70 input query terms found no hit:
        ['ENSG00000276798', 'ENSG00000256436', 'ENSG00000263097',
'ENSG00000282612', 'ENSG00000206302', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-48…done.
Finished.
48 input query terms found no hit:
        ['ENSMUSG00000076778', 'ENSMUSG00000007097', 'ENSMUSG00000028664',
'ENSMUSG00000032537', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

```
0
querying 1-54…done.
Finished.
54 input query terms found no hit:
        ['ENSG00000211957', 'ENSG00000282045', 'ENSG00000282211',
'ENSG00000282305', 'ENSG00000168148', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-28…done.
Finished.
28 input query terms found no hit:
        ['ENSMUSG00000078851', 'ENSMUSG00000069265', 'ENSMUSG00000069267',
'ENSMUSG00000069273', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-54…done.
Finished.
54 input query terms found no hit:
        ['ENSG00000273539', 'ENSG00000278042', 'ENSG00000282425',
'ENSG00000282651', 'ENSG00000211786', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-56…done.
Finished.
56 input query terms found no hit:
        ['ENSMUSG00000061296', 'ENSMUSG00000115170', 'ENSMUSG00000115253',
'ENSMUSG00000030196', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-62…done.
Finished.
62 input query terms found no hit:
        ['ENSG00000005001', 'ENSG00000282937', 'ENSG00000276541',
'ENSG00000165527', 'ENSG00000163221', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-40…done.
Finished.
40 input query terms found no hit:
        ['ENSMUSG00000044147', 'ENSMUSG00000049758', 'ENSMUSG00000001020',
'ENSMUSG00000033208', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
```

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0
querying 1-94…done.
Finished.
94 input query terms found no hit:
        ['ENSG00000276114', 'ENSG00000227739', 'ENSG00000206290',
'ENSG00000138758', 'ENSG00000164402', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-105…done.
Finished.
105 input query terms found no hit:
        ['ENSMUSG00000094076', 'ENSMUSG00000096516', 'ENSMUSG00000091652',
'ENSMUSG00000094553', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-89…done.
Finished.
89 input query terms found no hit:
        ['ENSG00000276590', 'ENSG00000124635', 'ENSG00000197903',
'ENSG00000183785', 'ENSG00000198033', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-60…done.
Finished.
60 input query terms found no hit:
        ['ENSMUSG00000046932', 'ENSMUSG00000115404', 'ENSMUSG00000090581',
'ENSMUSG00000095730', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-4…done.
Finished.
4 input query terms found no hit:
        ['ENSMUSG00000110469', 'ENSMUSG00000078153', 'ENSMUSG00000060019',
'ENSMUSG00000073640']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0

0
querying 1-5…done.
Finished.
5 input query terms found no hit:
```

```
        ['ENSMUSG00000092086', 'ENSMUSG00000096156', 'ENSMUSG00000113255',
'ENSMUSG00000096486', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-1…done.
Finished.
1 input query terms found no hit:
        ['ENSG00000125817']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-2…done.
Finished.
2 input query terms found no hit:
        ['ENSMUSG00000068267', 'ENSMUSG00000069622']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-5…done.
Finished.
5 input query terms found no hit:
        ['ENSG00000180138', 'ENSG00000170950', 'ENSG00000163114',
'ENSG00000189401', 'ENSG00000212643']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-17…done.
Finished.
17 input query terms found no hit:
        ['ENSMUSG00000059343', 'ENSMUSG00000063129', 'ENSMUSG00000073730',
'ENSMUSG00000078154', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-2…done.
Finished.
2 input query terms found no hit:
        ['ENSMUSG00000044424', 'ENSMUSG00000069324']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-3…done.
Finished.
3 input query terms found no hit:
        ['ENSG00000226784', 'ENSG00000174599', 'ENSG00000188021']
```

```
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-3…done.
Finished.
3 input query terms found no hit:
        ['ENSMUSG00000044528', 'ENSMUSG00000050148', 'ENSMUSG00000061619']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-1…done.
Finished.
1 input query terms found no hit:
        ['ENSMUSG00000048040']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-9…done.
Finished.
9 input query terms found no hit:
        ['ENSG00000177688', 'ENSG00000165496', 'ENSG00000276380',
'ENSG00000112273', 'ENSG00000253626', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-13…done.
Finished.
13 input query terms found no hit:
        ['ENSMUSG00000046173', 'ENSMUSG00000051732', 'ENSMUSG00000060499',
'ENSMUSG00000098559', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-1…done.
Finished.
1 input query terms found no hit:
        ['ENSG00000178597']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-1…done.
Finished.
1 input query terms found no hit:
        ['ENSMUSG00000043430']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
```

```
querying 1-1…done.
Finished.
1 input query terms found no hit:
        ['ENSG00000211675']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-1…done.
Finished.
1 input query terms found no hit:
        ['ENSMUSG00000067608']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-3…done.
Finished.
3 input query terms found no hit:
        ['ENSG00000229937', 'ENSG00000120329', 'ENSG00000189134']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-5…done.
Finished.
5 input query terms found no hit:
        ['ENSMUSG00000100296', 'ENSMUSG00000036463', 'ENSMUSG00000092305',
'ENSMUSG00000046717', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-1…done.
Finished.
1 input query terms found no hit:
        ['ENSG00000188042']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-1…done.
Finished.
1 input query terms found no hit:
        ['ENSMUSG00000049866']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-2…done.
Finished.
2 input query terms found no hit:
        ['ENSG00000177144', 'ENSG00000137040']
Pass "returnall=True" to return complete lists of duplicate or missing query
```

```
terms.
querying 1-5…done.
Finished.
5 input query terms found no hit:
        ['ENSMUSG00000099787', 'ENSMUSG00000064063', 'ENSMUSG00000074909',
'ENSMUSG00000051255', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-2…done.
Finished.
2 input query terms found no hit:
        ['ENSG00000228075', 'ENSG00000250254']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-2…done.
Finished.
2 input query terms found no hit:
        ['ENSMUSG00000054117', 'ENSMUSG00000112039']
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-25…done.
Finished.
25 input query terms found no hit:
        ['ENSG00000090659', 'ENSG00000143226', 'ENSG00000231555',
'ENSG00000094963', 'ENSG00000169908', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-25…done.
Finished.
25 input query terms found no hit:
        ['ENSMUSG00000089942', 'ENSMUSG00000110469', 'ENSMUSG00000090877',
'ENSMUSG00000074179', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-13…done.
Finished.
13 input query terms found no hit:
        ['ENSG00000100170', 'ENSG00000223609', 'ENSG00000102048',
'ENSG00000148180', 'ENSG00000109062', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-11…done.
```

```
Finished.
11 input query terms found no hit:
        ['ENSMUSG00000031384', 'ENSMUSG00000002900', 'ENSMUSG00000052911',
'ENSMUSG00000027219', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-79…done.
Finished.
79 input query terms found no hit:
        ['ENSG00000223865', 'ENSG00000226826', 'ENSG00000237710',
'ENSG00000130037', 'ENSG00000159212', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-68…done.
Finished.
68 input query terms found no hit:
        ['ENSMUSG00000045534', 'ENSMUSG00000022949', 'ENSMUSG00000028773',
'ENSMUSG00000025221', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-16…done.
Finished.
16 input query terms found no hit:
        ['ENSG00000183801', 'ENSG00000106483', 'ENSG00000274194',
'ENSG00000277025', 'ENSG00000277733', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-13…done.
Finished.
13 input query terms found no hit:
        ['ENSMUSG00000037820', 'ENSMUSG00000011257', 'ENSMUSG00000043613',
'ENSMUSG00000010830', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-28…done.
Finished.
28 input query terms found no hit:
        ['ENSG00000248496', 'ENSG00000105679', 'ENSG00000206383',
'ENSG00000236251', 'ENSG00000006047', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-39…done.
```

```
Finished.
39 input query terms found no hit:
        ['ENSMUSG00000031085', 'ENSMUSG00000079271', 'ENSMUSG00000096793',
'ENSMUSG00000101653', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-32…done.
Finished.
32 input query terms found no hit:
        ['ENSG00000197838', 'ENSG00000231939', 'ENSG00000167755',
'ENSG00000005471', 'ENSG00000073734', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-54…done.
Finished.
54 input query terms found no hit:
        ['ENSMUSG00000053338', 'ENSMUSG00000025479', 'ENSMUSG00000040583',
'ENSMUSG00000040650', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-61…done.
Finished.
61 input query terms found no hit:
        ['ENSG00000203747', 'ENSG00000134287', 'ENSG00000230763',
'ENSG00000236693', 'ENSG00000010438', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-35…done.
Finished.
35 input query terms found no hit:
        ['ENSMUSG00000073406', 'ENSMUSG00000051853', 'ENSMUSG00000071517',
'ENSMUSG00000028645', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-24…done.
Finished.
24 input query terms found no hit:
        ['ENSG00000276192', 'ENSG00000174156', 'ENSG00000136689',
'ENSG00000121552', 'ENSG00000197142', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-34…done.
```

```
Finished.
34 input query terms found no hit:
        ['ENSMUSG00000074521', 'ENSMUSG00000078889', 'ENSMUSG00000078901',
'ENSMUSG00000058260', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-65…done.
Finished.
65 input query terms found no hit:
        ['ENSG00000277317', 'ENSG00000139648', 'ENSG00000167768',
'ENSG00000170454', 'ENSG00000170484', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-73…done.
Finished.
73 input query terms found no hit:
        ['ENSMUSG00000022986', 'ENSMUSG00000023041', 'ENSMUSG00000046834',
'ENSMUSG00000048699', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-41…done.
Finished.
41 input query terms found no hit:
        ['ENSG00000276798', 'ENSG00000206302', 'ENSG00000136531',
'ENSG00000018625', 'ENSG00000105409', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-37…done.
Finished.
37 input query terms found no hit:
        ['ENSMUSG00000076778', 'ENSMUSG00000007097', 'ENSMUSG00000033161',
'ENSMUSG00000024597', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-17…done.
Finished.
17 input query terms found no hit:
        ['ENSG00000052344', 'ENSG00000175793', 'ENSG00000211675',
'ENSG00000229077', 'ENSG00000232180', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-12…done.
```

```
Finished.
12 input query terms found no hit:
        ['ENSMUSG00000024727', 'ENSMUSG00000012187', 'ENSMUSG00000021263',
'ENSMUSG00000030498', 'ENSMUSG000
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.

0
querying 1-37…done.
Finished.
37 input query terms found no hit:
        ['ENSG00000211786', 'ENSG00000115386', 'ENSG00000279804',
'ENSG00000282212', 'ENSG00000179344', 'ENS
Pass "returnall=True" to return complete lists of duplicate or missing query
terms.
querying 1-49…


      ␣
↪---------------------------------------------------------------------------

        HTTPError                                 Traceback (most recent call␣
↪last)

        <ipython-input-34-0fd6712b8370> in <module>
         84             df_sp.to_csv(os.path.join(outdir, outdir+'.geneid.tsv'),␣
↪sep='\t', index=False)
         85             sp_gene_ids = df_sp.loc[:,'gene_id'].tolist()
    ---> 86             b_mygene = mg.querymany(sp_gene_ids, scopes='ensembl.
↪gene', fields='symbol', species=taxids, as_dataframe=True)
         87             if b_mygene.columns[0]=='notfound':
         88                 b_mygene = pandas.DataFrame()


        ~/anaconda3/lib/python3.6/site-packages/biothings_client/base.py in␣
↪_querymany(self, qterms, scopes, **kwargs)
        535         li_query = []
        536         def query_fn(qterms): return self._querymany_inner(qterms,␣
↪verbose=verbose, **kwargs)
    --> 537         for hits in self._repeated_query(query_fn, qterms,␣
↪verbose=verbose):
        538             if return_raw:
        539                 out.append(hits)   # hits is the raw response text


        ~/anaconda3/lib/python3.6/site-packages/biothings_client/base.py in␣
↪_repeated_query(self, query_fn, query_li, verbose, **fn_kwargs)
```

```
      219                 print("querying {0}-{1}…".format(i + 1, cnt), end="")
      220             i = cnt
  --> 221             from_cache, query_result = query_fn(batch, **fn_kwargs)
      222             yield query_result
      223             if verbose:


      ~/anaconda3/lib/python3.6/site-packages/biothings_client/base.py in␣
↪query_fn(qterms)
      534         li_dup = []
      535         li_query = []
  --> 536         def query_fn(qterms): return self._querymany_inner(qterms,␣
↪verbose=verbose, **kwargs)
      537         for hits in self._repeated_query(query_fn, qterms,␣
↪verbose=verbose):
      538             if return_raw:


      ~/anaconda3/lib/python3.6/site-packages/biothings_client/base.py in␣
↪_querymany_inner(self, qterms, verbose, **kwargs)
      481         _kwargs.update(kwargs)
      482         _url = self.url + self._query_endpoint
  --> 483         return self._post(_url, params=_kwargs, verbose=verbose)
      484
      485     def _querymany(self, qterms, scopes=None, **kwargs):


      ~/anaconda3/lib/python3.6/site-packages/biothings_client/base.py in␣
↪_post(self, url, params, verbose)
      175         if self.raise_for_status:
      176             # raise requests.exceptions.HTTPError if not 200
  --> 177             res.raise_for_status()
      178         if return_raw:
      179             return from_cache, res


      ~/anaconda3/lib/python3.6/site-packages/requests/models.py in␣
↪raise_for_status(self)
      939
      940         if http_error_msg:
  --> 941             raise HTTPError(http_error_msg, response=self)
      942
      943     def close(self):


      HTTPError: 502 Server Error: Bad Gateway for url: http://mygene.info/v3/
↪query/
```

[35]:
```
#method = ['pvalue', 0.05]
method = ['top', 10]

new_wd = os.path.join(wd+'GO_specificity_shift')

if ('b' in vars()):
    organ1s = b['parent_'+pp+'max_organ'].dropna().unique()
    organ2s = b[pp+'max_organ'].dropna().unique()
else:
    organs = ['brain','heart','kidney','liver','ovary','testis']
    organ1s = organs
    organ2s = organs
events = ['All','S','D','R']

for ln in library_names:
    for sp in ['Homo_sapiens','Mus_musculus']:
        for pp,bidirectional,min_tau in itertools.product(pcm_prefixes,␣
↪bidirectionals, min_taus):
            if bidirectional:
                summary_wd = os.path.join(new_wd,␣
↪'summary_bidirectional_'+method[0]+str(method[1]))
            else:
                summary_wd = os.path.join(new_wd,␣
↪'summary_unidirectional_'+method[0]+str(method[1]))
            if not os.path.exists(summary_wd):
                os.mkdir(summary_wd)
            outfile =␣
↪'summary_'+ln+'_'+pp+sp+'_minTau'+str(min_tau)+'_'+method[0]+str(method[1])+'.
↪tsv'
            print(outfile)
            dfln = pandas.DataFrame()
            if pp=='l1ou_fpkm_':
                expression_metrics = 'SVA-log-TMM-FPKM'
            elif pp=='l1ou_tpm_':
                expression_metrics = 'SVA-log-TPM'
            if bidirectional:
                organ_combinat = list(itertools.combinations(set(organ1s).
↪union(set(organ2s)), 2))
                iters = [ [ev,]+list(o) for ev in events for o in␣
↪organ_combinat ]
            else:
                iters = itertools.product(events, organ1s, organ2s)
            for ev,organ1,organ2 in iters:
                if organ1==organ2:
                    continue
```

```
                elif organ1>organ2:
                    organ1prev = organ1
                    organ2prev = organ2
                    organ1 = organ2prev
                    organ2 = organ1prev
                outdir=pp+sp+'_minTau'+str(min_tau)+'_'+organ1+'_'+organ2+'_'+ev
                if bidirectional:
                    outdir = 'bidirectional_'+outdir
                ln_file = os.path.join(new_wd, outdir+'/'+ln+'.'+outdir+'.
↪enrichr.reports.txt')
                if os.path.isfile(ln_file):
                    tmp = pandas.read_csv(ln_file, sep='\t', header=0)
                    if method[0]=='pvalue':
                        tmp_sig = tmp.loc[(tmp['Adjusted P-value']<method[1]),:]
                    elif method[0]=='top':
                        tmp_sig = tmp.sort_values(by='Combined Score',␣
↪ascending=False).iloc[0:method[1],:]
                    if tmp_sig.shape[0]!=0:
                        tmp_sig.loc[:,'branch_category'] = ev
                        tmp_sig.loc[:,'organ1'] = organ1
                        tmp_sig.loc[:,'organ2'] = organ2
                        dfln = pandas.concat([dfln, tmp_sig],␣
↪ignore_index=True, sort=False)
            dfln.to_csv(os.path.join(summary_wd, outfile), sep='\t',␣
↪index=False)
```

```
summary_KEGG_2019_Human_l1ou_fpkm_Homo_sapiens_minTau0_top10.tsv
summary_KEGG_2019_Human_l1ou_fpkm_Homo_sapiens_minTau0.5_top10.tsv
summary_KEGG_2019_Human_l1ou_fpkm_Homo_sapiens_minTau0_top10.tsv
summary_KEGG_2019_Human_l1ou_fpkm_Homo_sapiens_minTau0.5_top10.tsv
summary_KEGG_2019_Human_l1ou_tpm_Homo_sapiens_minTau0_top10.tsv
summary_KEGG_2019_Human_l1ou_tpm_Homo_sapiens_minTau0.5_top10.tsv
summary_KEGG_2019_Human_l1ou_tpm_Homo_sapiens_minTau0_top10.tsv
summary_KEGG_2019_Human_l1ou_tpm_Homo_sapiens_minTau0.5_top10.tsv
summary_KEGG_2019_Human_l1ou_fpkm_Mus_musculus_minTau0_top10.tsv
summary_KEGG_2019_Human_l1ou_fpkm_Mus_musculus_minTau0.5_top10.tsv
summary_KEGG_2019_Human_l1ou_fpkm_Mus_musculus_minTau0_top10.tsv
summary_KEGG_2019_Human_l1ou_fpkm_Mus_musculus_minTau0.5_top10.tsv
summary_KEGG_2019_Human_l1ou_tpm_Mus_musculus_minTau0_top10.tsv
summary_KEGG_2019_Human_l1ou_tpm_Mus_musculus_minTau0.5_top10.tsv
summary_KEGG_2019_Human_l1ou_tpm_Mus_musculus_minTau0_top10.tsv
summary_KEGG_2019_Human_l1ou_tpm_Mus_musculus_minTau0.5_top10.tsv
summary_KEGG_2019_Mouse_l1ou_fpkm_Homo_sapiens_minTau0_top10.tsv
summary_KEGG_2019_Mouse_l1ou_fpkm_Homo_sapiens_minTau0.5_top10.tsv
summary_KEGG_2019_Mouse_l1ou_fpkm_Homo_sapiens_minTau0_top10.tsv
summary_KEGG_2019_Mouse_l1ou_fpkm_Homo_sapiens_minTau0.5_top10.tsv
summary_KEGG_2019_Mouse_l1ou_tpm_Homo_sapiens_minTau0_top10.tsv
```

```
summary_KEGG_2019_Mouse_l1ou_tpm_Homo_sapiens_minTau0.5_top10.tsv
summary_KEGG_2019_Mouse_l1ou_tpm_Homo_sapiens_minTau0_top10.tsv
summary_KEGG_2019_Mouse_l1ou_tpm_Homo_sapiens_minTau0.5_top10.tsv
summary_KEGG_2019_Mouse_l1ou_fpkm_Mus_musculus_minTau0_top10.tsv
summary_KEGG_2019_Mouse_l1ou_fpkm_Mus_musculus_minTau0.5_top10.tsv
summary_KEGG_2019_Mouse_l1ou_fpkm_Mus_musculus_minTau0_top10.tsv
summary_KEGG_2019_Mouse_l1ou_fpkm_Mus_musculus_minTau0.5_top10.tsv
summary_KEGG_2019_Mouse_l1ou_tpm_Mus_musculus_minTau0_top10.tsv
summary_KEGG_2019_Mouse_l1ou_tpm_Mus_musculus_minTau0.5_top10.tsv
summary_KEGG_2019_Mouse_l1ou_tpm_Mus_musculus_minTau0_top10.tsv
summary_KEGG_2019_Mouse_l1ou_tpm_Mus_musculus_minTau0.5_top10.tsv
```

[ ]:

[ ]: