The R/qtlcmst package

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SISG 2012

July 10, 2012

Simulate data

We first use the **SimCrossCausal** function to simulate a cross object with 3 phenotypes, y_1, y_2 and y_3, where y_1 has a causal effect on both y_2 and y_3.

```
> set.seed(987654321)
> Cross <- SimCrossCausal(n.ind = 100,
+                         len = rep(100, 3),
+                         n.mar = 101,
+                         beta = rep(0.5, 2),
+                         add.eff = 1,
+                         dom.eff = 0,
+                         sig2.1 = 0.4,
+                         sig2.2 = 0.1,
+                         eq.spacing = FALSE,
+                         cross.type = "bc",
+                         normalize = TRUE)
```
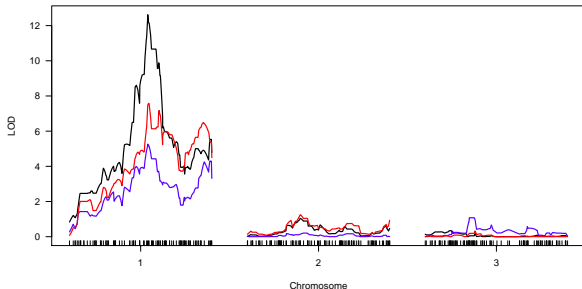
QTL mapping

Compute the genotype conditional probabilities setting the maximum distance between positions at which genotype probabilities were calculated to 1cM.

```
> Cross <- calc.genoprob(Cross, step = 1)
```

Perform QTL mapping using Haley-Knott regression.

```
> Scan <- scanone(Cross, pheno.col = 1:3, method = "hk")
> plot(Scan, lodcolumn = 1:3, ylab = "LOD")
```


Black, blue and red curves represent phenos y_1, y_2 and y_3, respectively.

QTL mapping

Summarize the results for the 3 phenotypes.

```
> summary(Scan[, c(1, 2, 3)], thr = 3)
         chr pos   y1
c1.loc55   1  55 12.6
> summary(Scan[, c(1, 2, 4)], thr = 3)
         chr pos   y2
c1.loc55   1  55 5.27
> summary(Scan[, c(1, 2, 5)], thr = 3)
      chr  pos   y3
D1M50   1 55.5 7.58
```

y_1 and y_2 map to the same QTL at position 55 cM on chr 1, y_3 maps to a distinct position.

Which QTL should we use as causal anchor?

QTL mapping

Our approach is to compute the joint LOD profile of both phenos and use the QTL detected by this joint approach as the causal anchor.

```
> commqtls <- GetCommonQtls(Cross,
+                           pheno1 = "y1",
+                           pheno2 = "y3",
+                           thr = 3,
+                           peak.dist = 5,
+                           addcov1 = NULL,
+                           addcov2 = NULL,
+                           intcov1 = NULL,
+                           intcov2 = NULL)
> commqtls
         Q Q.chr Q.pos
1 c1.loc55     1    55
```

CMST tests

Fit the CMST tests.

```
> nms <- names(Cross$pheno)
> out1 <- CMSTtests(Cross,
+                   pheno1 = nms[1],
+                   pheno2 = nms[2],
+                   Q.chr = 1,
+                   Q.pos = 55,
+                   addcov1 = NULL,
+                   addcov2 = NULL,
+                   intcov1 = NULL,
+                   intcov2 = NULL,
+                   cross.type = "bc",
+                   method = "all",
+                   penalty = "both")
```

CMST tests - output

```
> out1[1:6]
$pheno1
[1] "y1"

$pheno2
[1] "y2"

$n.ind
[1] 100

$loglik
[1] -123.5318 -140.4604 -141.5803 -123.4834

$model.dim
[1] 6 6 6 7

$R2
[1] 0.4407170 0.2153583
```

CMST tests - output

Covariance matrix of the log-likelihood scores.

```
> out1[7]
$S.hat
            [,1]          [,2]         [,3]          [,4]          [,5]
[1,]  0.26221327 -0.01323094  0.010924311 -0.275444212 -0.251288963
[2,] -0.01323094  0.36275299  0.012080993  0.375983930  0.025311930
[3,]  0.01092431  0.01208099  0.001115354  0.001156681 -0.009808958
[4,] -0.27544421  0.37598393  0.001156681  0.651428142  0.276600893
[5,] -0.25128896  0.02531193 -0.009808958  0.276600893  0.241480006
[6,]  0.02415525 -0.35067200 -0.010965639 -0.374827248 -0.035120888
            [,6]
[1,]  0.02415525
[2,] -0.35067200
[3,] -0.01096564
[4,] -0.37482725
[5,] -0.03512089
[6,]  0.33970636
```

CMST tests - output

```
> out1[8:12]
$BICs
[1] 274.6946 308.5518 310.7917 279.2030

$Z.bic
     [,1]    [,2]      [,3]      [,4]
[1,]   NA 3.305926 2.9966507  6.749745
[2,]   NA      NA 0.1387598 -2.986200
[3,]   NA      NA        NA -2.709873
[4,]   NA      NA        NA        NA

$pvals.p.BIC
[1] 0.001364817 0.999526684 0.998635183 1.000000000

$pvals.np.BIC
[1] 6.289575e-06 9.999977e-01 9.999999e-01 1.000000e+00

$pvals.j.BIC
[1] 0.003779558 0.999946885 0.999669186 1.000000000
```

CMST tests - output

```
> out1[13:17]
$AICs
[1] 259.0636 292.9208 295.1606 260.9668

$Z.aic
     [,1]    [,2]      [,3]       [,4]
[1,]  NA 3.305926 2.9966507  2.849429
[2,]  NA      NA 0.1387598 -3.251273
[3,]  NA      NA        NA -2.933361
[4,]  NA      NA        NA        NA

$pvals.p.AIC
[1] 0.002189889 0.999526684 0.998635183 0.997810111

$pvals.np.AIC
[1] 6.289575e-06 9.999977e-01 1.000000e+00 9.999977e-01

$pvals.j.AIC
[1] 0.005993868 0.999946885 0.999669186 1.000000000
```

CMST tests

Fit one phenotype against a list of phenotypes.

```
> out2 <- CMSTtestsList(Cross,
+                       pheno1 = nms[1],
+                       phenos = nms[-1],
+                       Q.chr = 1,
+                       Q.pos = 55,
+                       addcov1 = NULL,
+                       addcov2 = NULL,
+                       intcov1 = NULL,
+                       intcov2 = NULL,
+                       cross.type = "bc",
+                       method = "par",
+                       penalty = "bic")
```

CMST tests

```
> out2
$R2s
     R2.Y1 ~ Q R2.Y2 ~ Q
y1_y2  0.440717 0.2153583
y1_y3  0.440717 0.2914979

$BIC.stats
         BIC.1    BIC.2    BIC.3    BIC.4     z.12     z.13     z.14
y1_y2 274.6946 308.5518 310.7917 279.2030 3.305926 2.996651 6.749745
y1_y3 270.4445 294.0943 325.3707 274.6665 2.339472 4.207872 3.446223
          z.23     z.24     z.34
y1_y2 0.1387598 -2.986200 -2.709873
y1_y3 1.9587743 -2.126754 -4.070649

$pvals.p.BIC
           pval.1    pval.2    pval.3    pval.4
y1_y2 0.001364817 0.9995267 0.9986352 1.0000000
y1_y3 0.009655499 0.9903445 0.9999871 0.9997158
```