

# The R/qtIcmst package

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## 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)
```

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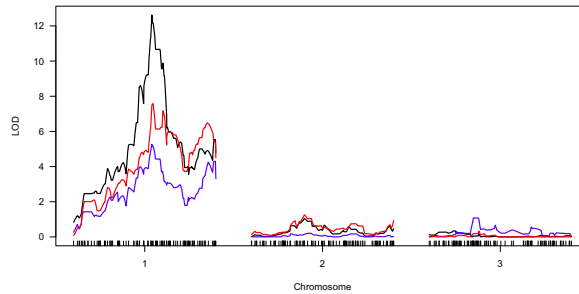
## QTL mapping

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.

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## 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?

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## 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
```

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## 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")
```

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## 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
```

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## 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
```

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## 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
```

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## 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
```

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## 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")
```

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## 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
```

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