

# Messina E2B: MessinaSurv vs Others

March 21, 2015

## 1 Preparation

```
library(plyr)
library(messina)
library(maxstat)
library(doMC)

deltaForMargin = function(margin, sigma_epsilon = 1, alpha = 0.05) margin - 2*sigma_epsilon*qnorm(alpha)
marginForDelta = function(delta, sigma_epsilon = 1, alpha = 0.05) delta + 2*sigma_epsilon*qnorm(alpha)

messina_objectives = list("cox.log2" = messinaSurvObj.CoxCoef(log(2)))

e2b.design = expand.grid(
  Delta = seq(0, 5, 0.5),
  R1 = c(1, 2, 4, 8, 16),
  sigma_epsilon = 1,
  p1 = c(0.2, 0.5, 0.8),
  pc = c(0, 0.2, 0.5),
  alpha = 0.2,
  stat.alpha = 0.05,
  messina.objective = "cox.log2",
  messina.minmarg = 1,
  n = c(25, 50, 100),
  reps = 5e1)

e2b.design$margin = marginForDelta(e2b.design$Delta, e2b.design$sigma_epsilon, alpha = e2b.design$alpha)

detector_multicut = function(x, y, ncuts = 10, correct = "none")
{
  if (ncuts == 1)      { correct = "none" }
  if (is.vector(x))    { x = matrix(x, nrow = 1) }

  aapply(x, 1, function(x1) {
    cutpoints = quantile(x1, probs = (1:ncuts)/(ncuts + 1))
    pvals = sapply(cutpoints, function(c) {
      x1c = x1 > c
      test = survdiff(y ~ x1c)
      pval = pchisq(test$chisq, df = 1, lower.tail = FALSE)
      pval
    })
    pvals = p.adjust(pvals, correct)
    pvals[is.na(pvals)] = 1
  })
}
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        min(pvals)
      }, .parallel = FALSE)
    }

e2b.datafun = function(n, p1, pc, Delta, R1, sigma_epsilon, ...)
{
  n1 = round(n*p1)
  n0 = n - n1
  c = rep(c(0, 1), c(n0, n1))
  x = Delta*c + rnorm(n, mean = 0, sd = sigma_epsilon)

  Rc = optimize(function(Rc) abs(integrate(function(t) pexp(t, Rc) * ((1-p1)*dexp(t, 1) + p1*dexp(t, R1)))(0, 1)),
    lower = 0, upper = R1)

  time_event = c(rexp(n0, 1), rexp(n1, R1))
  time_cens = rexp(n, Rc)

  y = Surv(pmin(time_event, time_cens), time_event <= time_cens)

  list(x = x, y = y, c = c)
}

e2b.detfun = function(x, y, stat.alpha, messina.objective, messina.minmarg, ...)
{
  data.maxstat = data.frame(time = y[,1], event = y[,2], x = x)
  test.maxstat = try(maxstat.test(Surv(time, event) ~ x, data = data.maxstat, smethod = "LogRank"), silent = TRUE)
  det.maxstat = ifelse(class(test.maxstat) == "try-error", FALSE, test.maxstat$p.value < stat.alpha)

  det.1cut = detector_multicut(x, y, 1) < stat.alpha
  det.10cut = detector_multicut(x, y, 10) < stat.alpha
  det.10cutHolm = detector_multicut(x, y, 10, "holm") < stat.alpha

  x.messina = rbind(x, x, x)
  fit.messina = messinaSurv(x.messina, y, messina_objectives[[messina.objective]], silent = TRUE)
  det.messina = fit.messina@fits@summary$passed[1] == TRUE && fit.messina@fits@summary$margin[1] > 0
  det.messina.nomarg = fit.messina@fits@summary$passed[1] == TRUE

  c(maxstat = det.maxstat, c1 = det.1cut, c10 = det.10cut, cH10 = det.10cutHolm, m = det.messina, nomarg = det.messina.nomarg)
}

e2b.repfun = function(i, Delta, R1, sigma_epsilon, pc, p1, stat.alpha, messina.minmarg, messina.objective, ...)
{
  data = e2b.datafun(n, p1, pc, Delta, R1, sigma_epsilon)
  dets = try(e2b.detfun(data$x, data$y, stat.alpha, messina.objective, messina.minmarg), silent = TRUE)
  if(class(dets) == "try-error") { return(c(NA, NA, NA, NA, NA, NA)) }
  return(dets)
}

e2b.expfun = function(Delta, R1, sigma_epsilon, pc, p1, stat.alpha, messina.minmarg, messina.objective, ...)
{
  message(date(), "\t", jobindex)
  detections = sapply(1:reps, e2b.repfun, Delta = Delta, R1 = R1, sigma_epsilon = sigma_epsilon, pc = pc, p1 = p1, stat.alpha = stat.alpha, messina.minmarg = messina.minmarg, messina.objective = messina.objective, ...)
  detrate = rowMeans(detections, na.rm = TRUE)
  detrate
}

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}

registerDoMC(32)

e2b.design$jobindex = 1:nrow(e2b.design)
set.seed(20150320)
e2b.det = mply(e2b.design, e2b.expfun, .parallel = TRUE)

e2b.design = rbind(
  cbind(e2b.design, method = "maxstat", detrates = simplify2array(e2b.det)[1,]),
  cbind(e2b.design, method = "c1", detrates = simplify2array(e2b.det)[2,]),
  cbind(e2b.design, method = "c10", detrates = simplify2array(e2b.det)[3,]),
  cbind(e2b.design, method = "cH10", detrates = simplify2array(e2b.det)[4,]),
  cbind(e2b.design, method = "messina", detrates = simplify2array(e2b.det)[5,]),
  cbind(e2b.design, method = "messina_0m", detrates = simplify2array(e2b.det)[6,])
)

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e2b.design2 = expand.grid(
  Delta = seq(0, 5, 0.5),
  R1 = c(1, 4, 16),
  sigma_epsilon = 1,
  p1 = c(0.2, 0.5),
  pc = c(0.2, 0.5),
  alpha = 0.2,
  stat.alpha = 0.05,
  messina.objective = "cox.log2",
  messina.minmarg = 1,
  n = c(25, 50, 100),
  reps = 5e2)

e2b.design2$margin = marginForDelta(e2b.design2$Delta, e2b.design2$sigma_epsilon, alpha = e2b.design2$alpha)

registerDoMC(32)
e2b.design2$jobindex = 1:nrow(e2b.design2)
set.seed(20150321)
e2b.det2 = mply(e2b.design2, e2b.expfun, .parallel = TRUE)

e2b.design2 = rbind(
  cbind(e2b.design2, method = "maxstat", detrates = simplify2array(e2b.det2)[1,]),
  cbind(e2b.design2, method = "c1", detrates = simplify2array(e2b.det2)[2,]),
  cbind(e2b.design2, method = "c10", detrates = simplify2array(e2b.det2)[3,]),
  cbind(e2b.design2, method = "cH10", detrates = simplify2array(e2b.det2)[4,]),
  cbind(e2b.design2, method = "messina", detrates = simplify2array(e2b.det2)[5,]),
  cbind(e2b.design2, method = "messina_0m", detrates = simplify2array(e2b.det2)[6,])
)

```

```

e2b.design3 = expand.grid(
  Delta = 100,
  R1 = 4,
  sigma_epsilon = 1,
  p1 = seq(0, 1, 0.05),
  pc = 0.2,

```

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    alpha = 0.2,
    stat.alpha = 0.05,
    messina.objective = "cox.log2",
    messina.minmarg = 1,
    n = 50,
    reps = 5e3)

registerDoMC(32)
e2b.design3$jobindex = 1:nrow(e2b.design3)
set.seed(20150321)
e2b.det3 = mply(e2b.design3, e2b.expfun, .parallel = TRUE)

e2b.design3 = rbind(
  cbind(e2b.design3, method = "maxstat", detrates = simplify2array(e2b.det3)[1,]),
  cbind(e2b.design3, method = "c1", detrates = simplify2array(e2b.det3)[2,]),
  cbind(e2b.design3, method = "c10", detrates = simplify2array(e2b.det3)[3,]),
  cbind(e2b.design3, method = "cH10", detrates = simplify2array(e2b.det3)[4,]),
  cbind(e2b.design3, method = "messina", detrates = simplify2array(e2b.det3)[5,]),
  cbind(e2b.design3, method = "messina_0m", detrates = simplify2array(e2b.det3)[6,])
)

```

```

e2b.design4 = expand.grid(
  Delta = 100,
  R1 = 1,
  sigma_epsilon = 1,
  p1 = 0.5,
  pc = 0.2,
  alpha = 0.2,
  stat.alpha = 0.05,
  multicut.n = 1:25,
  n = 50,
  reps = 5e3)

e2b.detfun4 = function(x, y, multicut.n, stat.alpha, ...)
{
  det.multicut = detector_multicut(x, y, multicut.n) < stat.alpha
  det.multicutHolm = detector_multicut(x, y, multicut.n, "holm") < stat.alpha

  c(mc = det.multicut, mcH = det.multicutHolm)
}

e2b.repfun4 = function(i, Delta, R1, sigma_epsilon, pc, p1, multicut.n, stat.alpha, n, ...)
{
  data = e2b.datafun(n, p1, pc, Delta, R1, sigma_epsilon)
  dets = try(e2b.detfun4(data$x, data$y, multicut.n, stat.alpha))
  if(class(dets) == "try-error") { return(c(NA, NA)) }
  return(dets)
}

e2b.expfun4 = function(Delta, R1, sigma_epsilon, pc, p1, multicut.n, stat.alpha, n, reps, ...)
{
  detections = sapply(1:reps, e2b.repfun4, Delta = Delta, R1 = R1, sigma_epsilon = sigma_epsilon,
    detrates = rowMeans(detections, na.rm = TRUE)

```

```

    detraterate
  }

registerDoMC(32)
set.seed(20150321)
e2b.det4 = mply(e2b.design4, e2b.expfun4, .parallel = TRUE)

e2b.design4 = rbind(
  cbind(e2b.design4, method = "mc", detraterate = simplify2array(e2b.det4)[1,]),
  cbind(e2b.design4, method = "mcH", detraterate = simplify2array(e2b.det4)[2,])
)

```

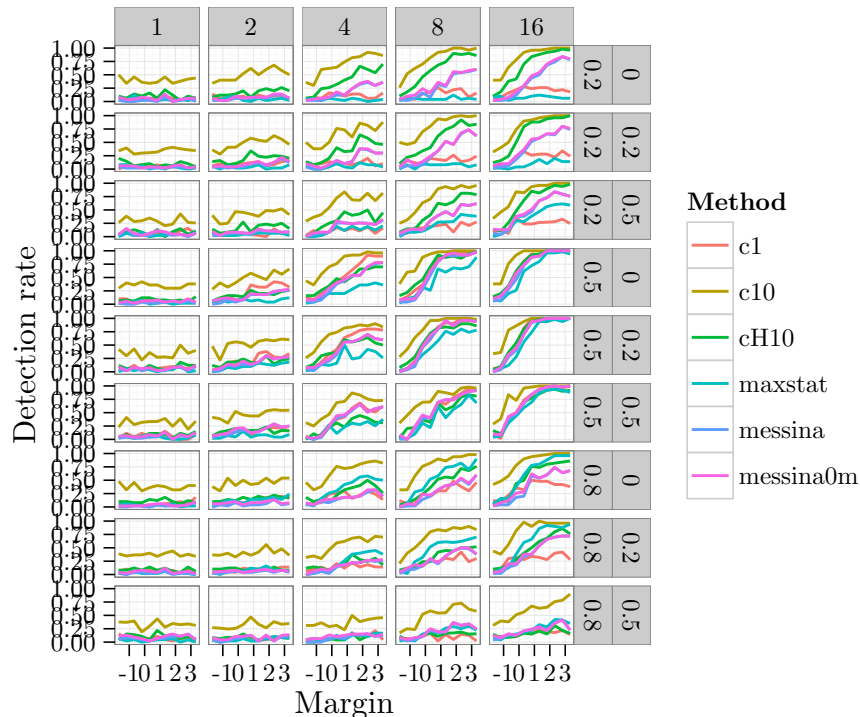
```
library(ggplot2)
```

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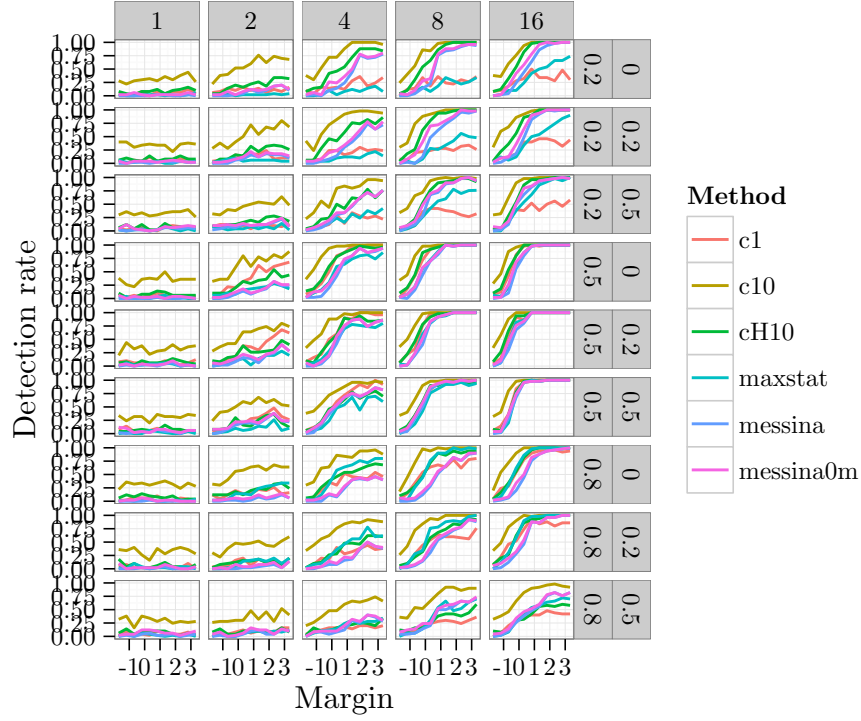
e2b.design$method = as.character(e2b.design$method)
e2b.design$method[e2b.design$method == "messina_0m"] = "messina0m"
e2b.design$method = as.factor(e2b.design$method)
e2b.design2$method = as.character(e2b.design2$method)
e2b.design2$method[e2b.design2$method == "messina_0m"] = "messina0m"
e2b.design2$method = as.factor(e2b.design2$method)
e2b.design3$method = as.character(e2b.design3$method)
e2b.design3$method[e2b.design3$method == "messina_0m"] = "messina0m"
e2b.design3$method = as.factor(e2b.design3$method)
e2b.design4$method = as.character(e2b.design4$method)
e2b.design4$method[e2b.design4$method == "mc"] = "'Optimal'"
e2b.design4$method[e2b.design4$method == "mcH"] = "'Optimal' + MTC"
e2b.design4$method = as.factor(e2b.design4$method)

```

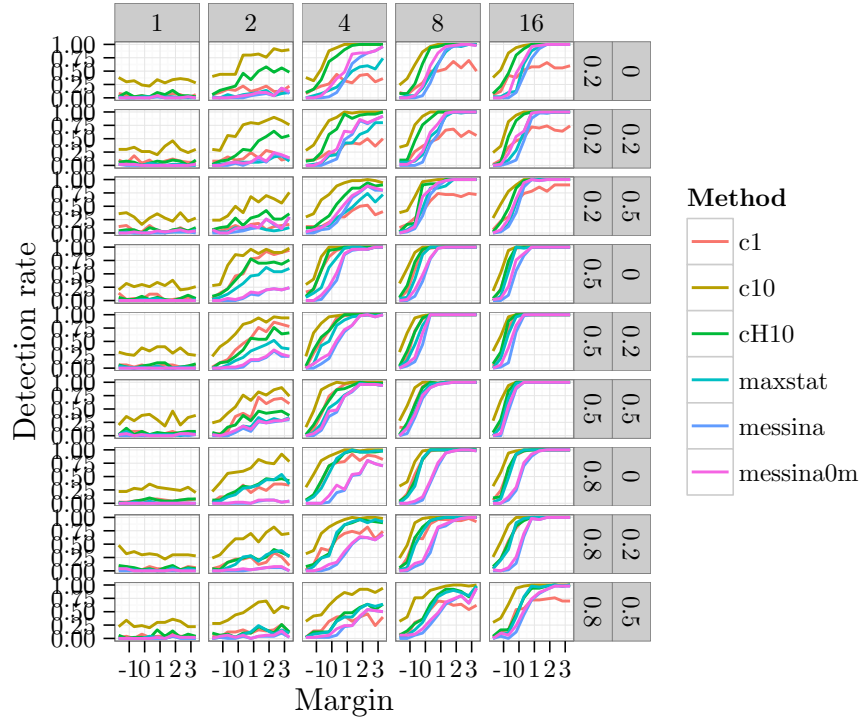
```
ggplot(e2b.design[e2b.design$n == 25,], aes(x = margin, y = detraterate, colour = factor(method))) + geom_line()
```



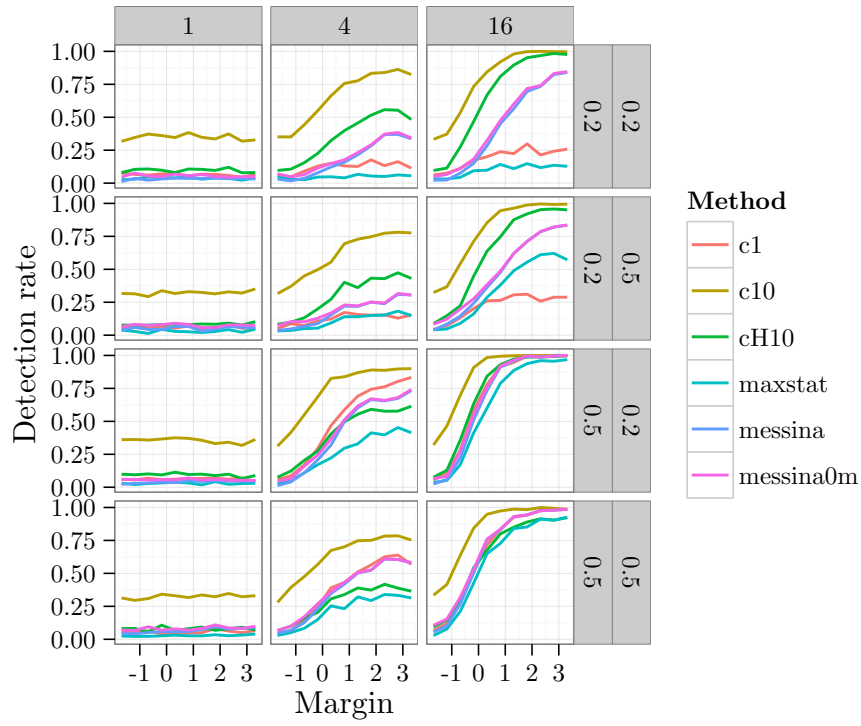
```
ggplot(e2b.design[e2b.design$n == 50,], aes(x = margin, y = detrare, colour = factor(method))) + geom_line()
```



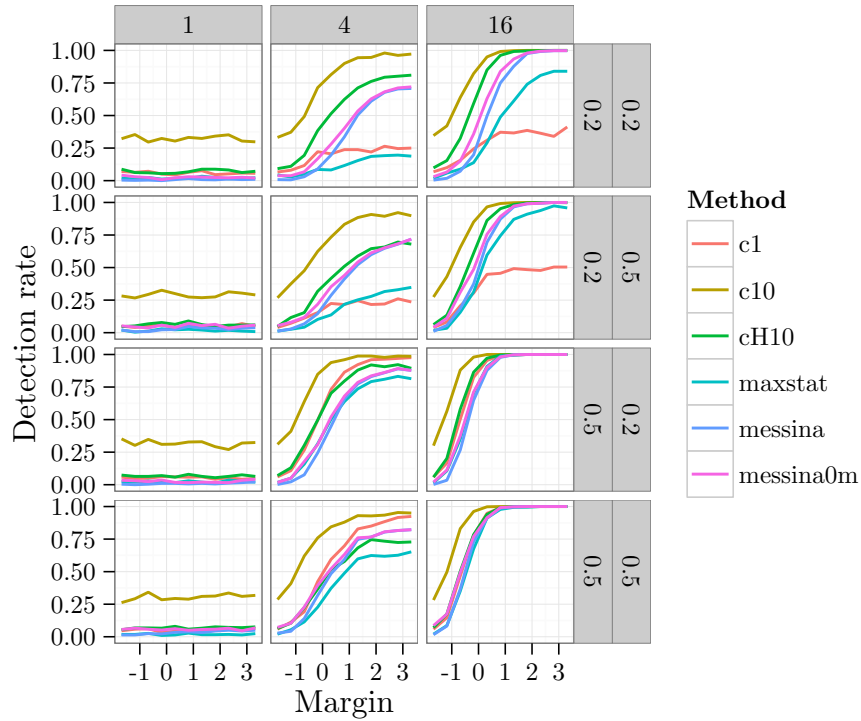
```
ggplot(e2b.design[e2b.design$n == 100,], aes(x = margin, y = detrare, colour = factor(method))) + geom_line()
```



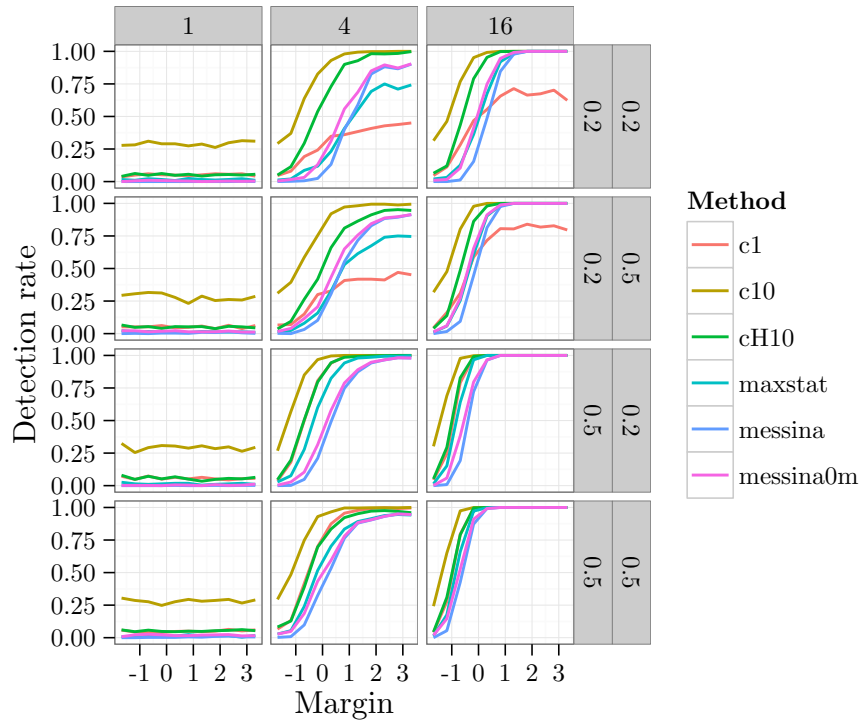
```
ggplot(e2b.design2[e2b.design2$n == 25,], aes(x = margin, y = detrare, colour = factor(method))) + geom_line()
```



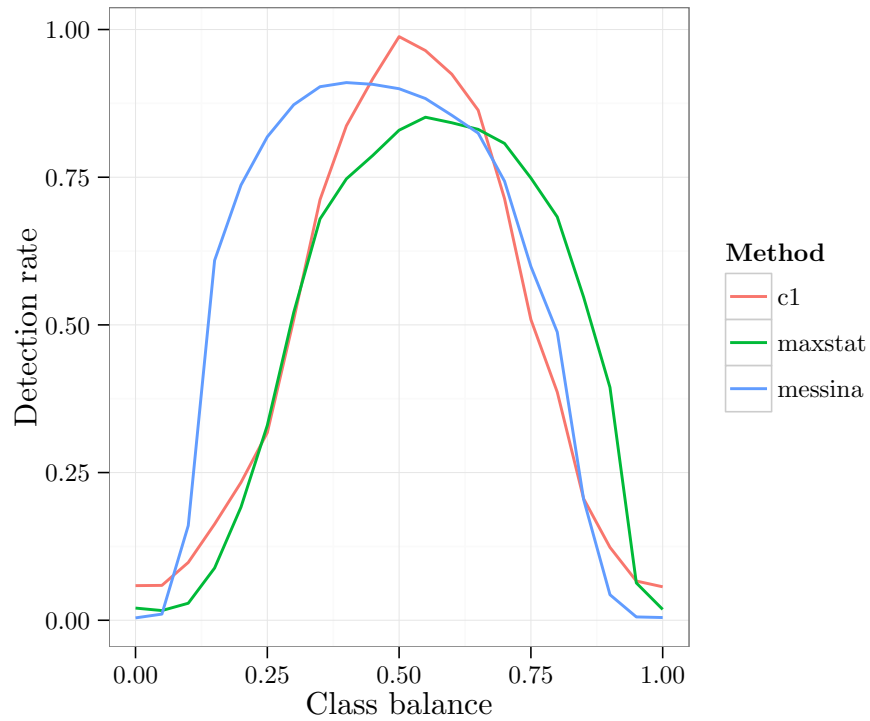
```
ggplot(e2b.design2[e2b.design2$n == 50,], aes(x = margin, y = detrates, colour = factor(method))) + geom_line()
```



```
ggplot(e2b.design2[e2b.design2$n == 100,], aes(x = margin, y = detrates, colour = factor(method))) + geom_line()
```



```
ggplot(e2b.design3[e2b.design3$method %in% c("c1", "maxstat", "messina"),], aes(x = p1, y = detrare, col = method))
```



```
ggplot(e2b.design4, aes(x = multicut.n, y = detrare, colour = factor(method))) + geom_line(lwd = 1) + xlab("multicut.n")
```



