

CHAPTER 1

# Appendix

---

## 1.1 Pharmaceutical duration and level changes plots

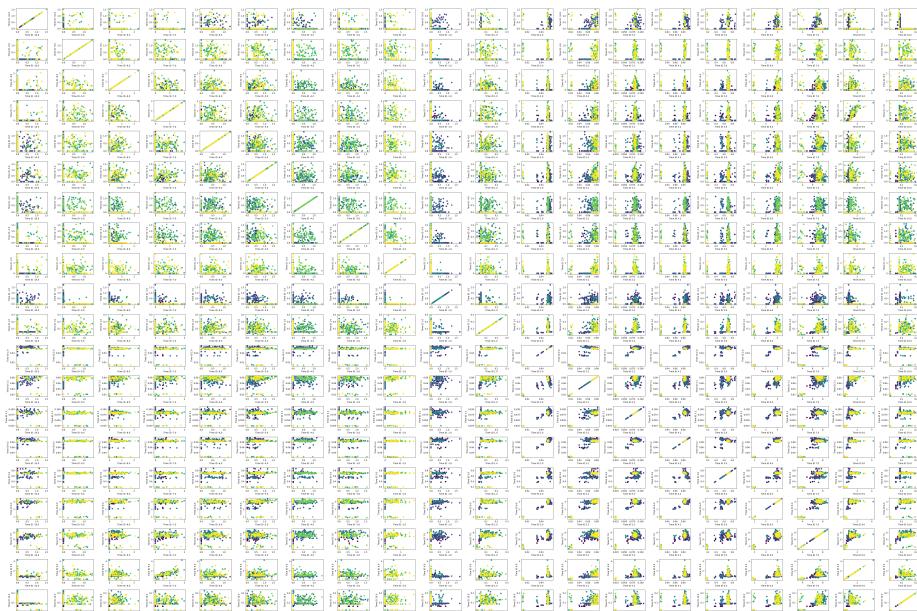


Figure 1.1

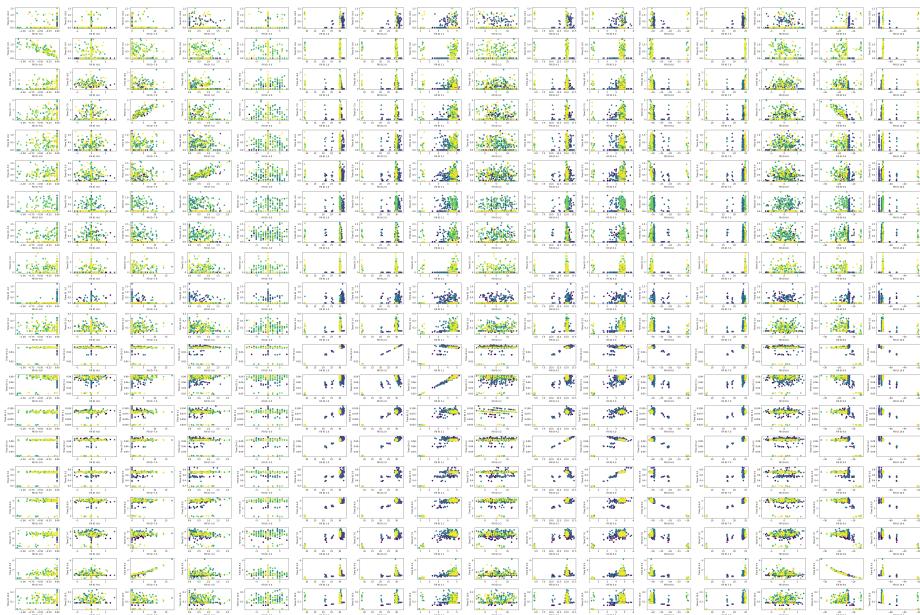


Figure 1.2

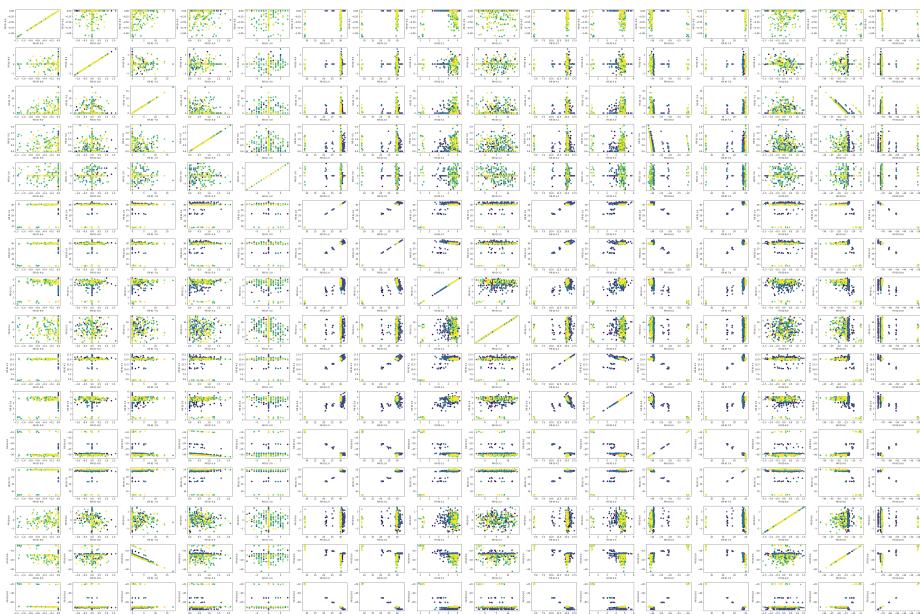
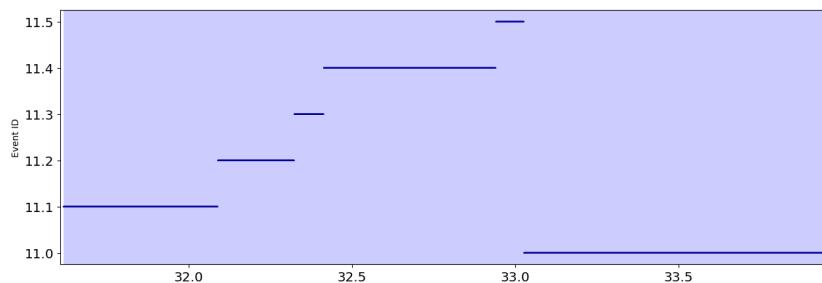
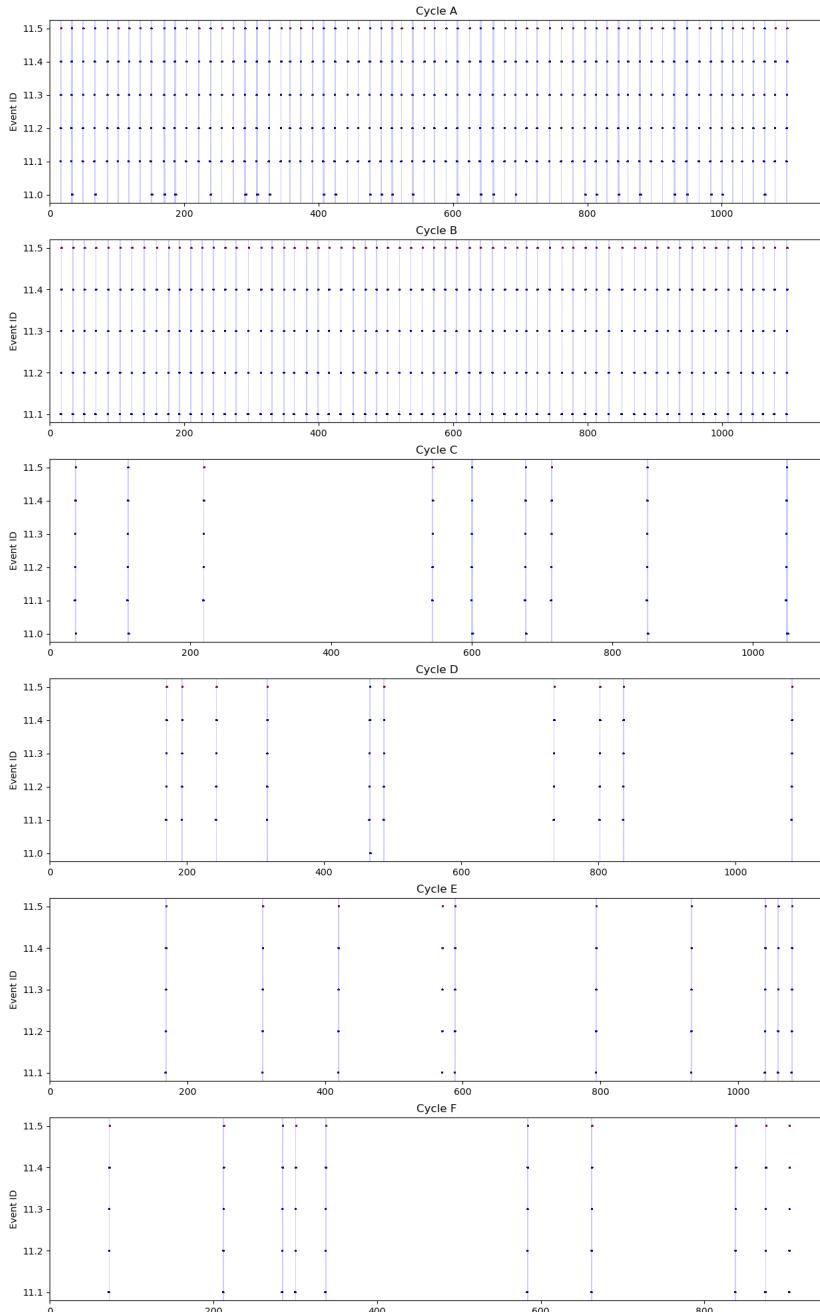


Figure 1.3

## 1.2 Cleaning operations plots



**Figure 1.4:** A single blue rectangle zoomed in



**Figure 1.5:** Each of the 6 cycles, cleaning (corresponding to `BatchID = 0`). Each (Cleaning Procedure), CIP, is highlighted with an opaque interval (the blue rectangles). The dots marked with red (only ID 11.5, but not all of these are red), is if the Cleaning ID is 0.

### 1.3 Suicide data

1	25	40	83	123	256
1	27	49	84	126	257
1	27	49	84	129	311
5	30	54	84	134	314
7	30	56	90	144	322
8	31	56	91	147	369
8	31	62	92	153	415
13	32	63	93	163	573
14	34	65	93	167	609
14	35	65	103	175	640
17	36	67	103	228	737
18	37	75	111	231	
21	38	76	112	235	
21	39	79	119	242	
22	39	82	122	256	

**Table 1.1:** The length of treatment of control patients in suicide study. The data originates from the Mental Health Enquiry (MHE) of England of Wales and was published in 1967.

### 1.3.1 A better spline

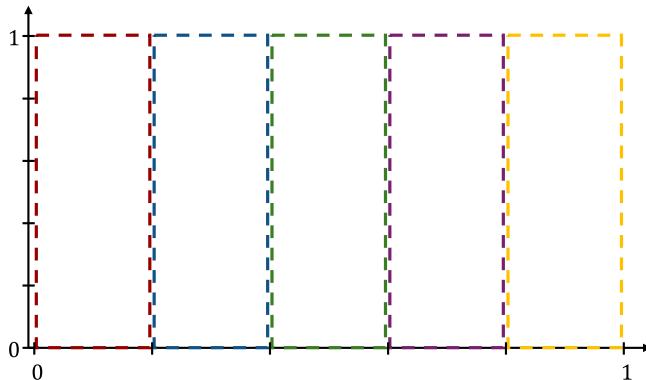
In theory, we could make a set of splines ourselves, that has both of the desired properties of B-splines and M-splines. I.e. a set of piecewise polynomials, which we shall denote  $Q_{i,p}$ , that has both the property that

$$\sum_{i=1}^n Q_{i,p}(t) = 1$$

and

$$\int_0^1 Q_{i,p}(t) dt = \frac{1}{n}$$

Actually, both M- and B-splines satisfies this for  $p = 0$  as they are then both piecewise constant and non-zero on disjoint intervals. From this, one can construct such sets of  $Q_{i,p}$  in the following way. Namely, start with the piecewise constant functions,  $Q_{i,0}$  depicted in Figure 1.6 as boxes in the case  $n = 5$ .

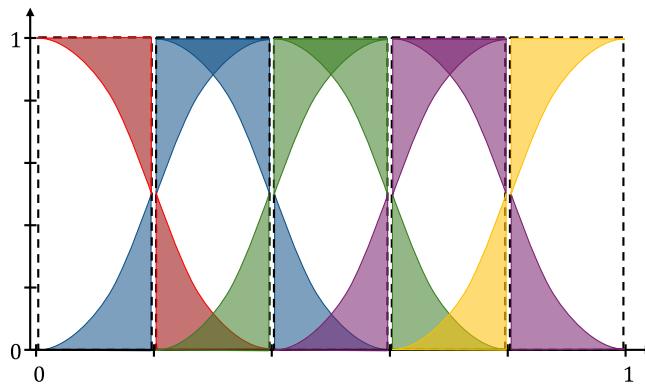


**Figure 1.6**

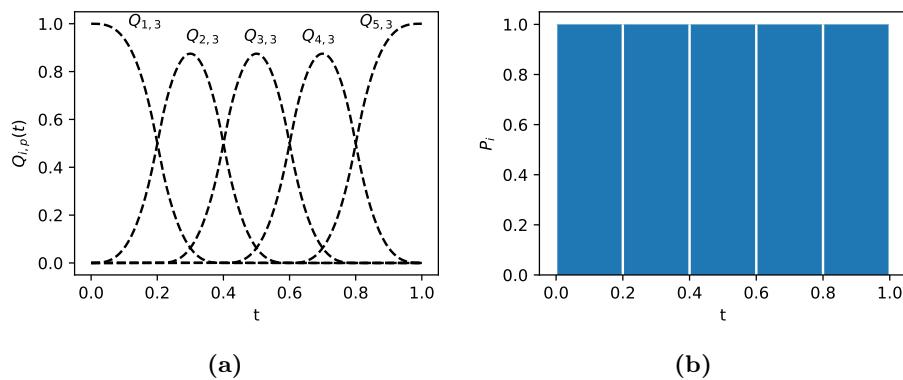
A better spline

Cut off function has derivative 0 at top and is halfway down at the sides

This example does however not work well for many bins, in particular, due to the splines not overlapping that much i.e. a poor regularization on the smoothness. However, the method used for constructing this set of splines can be extended to bleed into multiple neighboring bins just as for B- and M-splines.



**Figure 1.7**



**Figure 1.8:**  $P_i$  is area of each rectangle i.e. 0.2.

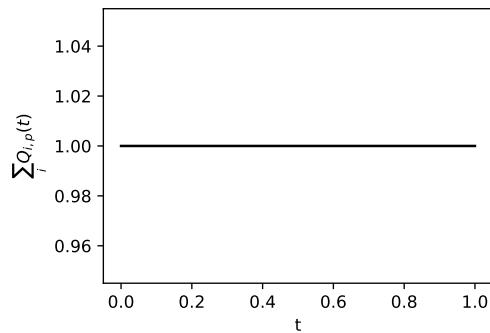


Figure 1.9

## 1.4 M-spline based MI estimation

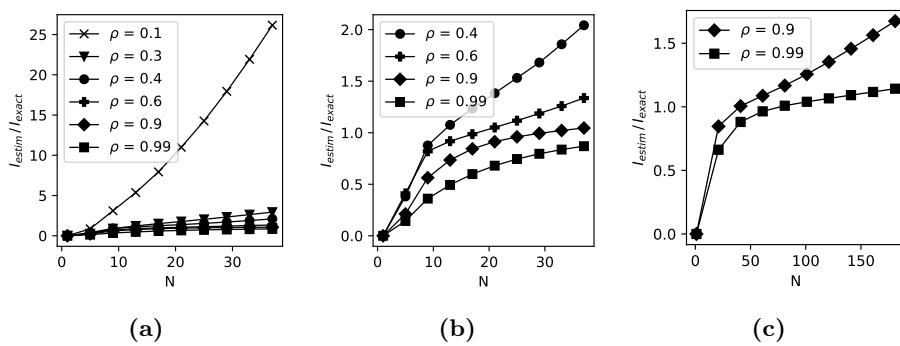


Figure 1.10

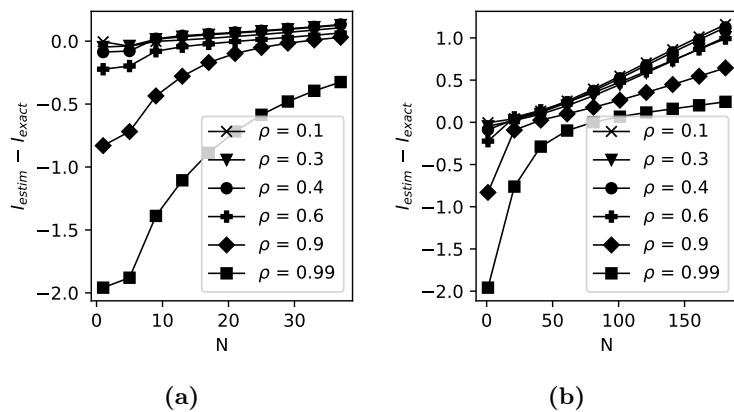


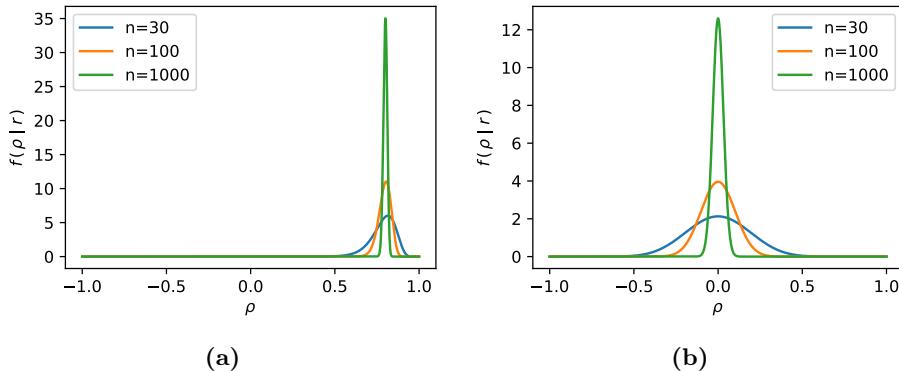
Figure 1.11

## 1.5 Confidence interval for absolute correlation in bivariate Gaussian

From [?], given a bivariate Gaussian, the confidence distribution of  $\rho$  given the empirical correlation  $r$  based on  $n$  observations is given by

$$f(\rho | r, \nu) = \frac{\nu(\nu - 1)\Gamma(\nu - 1)}{\sqrt{2\pi}\Gamma(\nu + \frac{1}{2})} \frac{(1 - r^2)^{\frac{\nu-1}{2}}}{(1 - r\rho)^{\frac{2\nu-1}{2}}} F\left(\frac{3}{2}, -\frac{1}{2}, \nu + \frac{1}{2}, \frac{1 + r\rho}{2}\right)$$

where  $F(a, b, c, z)$  is the Gaussian hypergeometric function and  $\nu = n - 1$ . That is, given a sample correlation  $r$ , what is the confidence in  $\rho$  in terms of a distribution. In the following figure, a sample correlation  $r = 0.8$  and  $r = 0$  has been used with varying number of observations (degrees of freedom) in figures Figure 1.12a and Figure 1.12b respectively. A key property is that  $f$  is even



**Figure 1.12:**  $f(\rho | r, \nu)$  shown for  $r = 0.8$  and  $r = 0$  in (a) and (b) with  $n \in \{30, 100, 1000\}$ . As one would expect, the power i.e. the width of the peak decreases with increasing  $n$  and for correlations closer to 0, the width is the largest.

symmetric in  $\rho, r$ . That is  $f(\rho | r) = f(-\rho | -r)$ . Thus, a confidence interval for  $\rho$  given  $r$  is the negative of the confidence interval given  $-r$ . In particular, if we only observe  $|r|$ , we can calculate a confidence interval for  $\rho$  up to the sign of the bounds of the interval. Furthermore, as we want a CI for  $|\rho|$ , it does not matter if  $r$  is negative or positive. Hence, without loss of generality, we assume that  $r \geq 0$ . At this point, to construct a confidence interval for  $|\rho|$  we list the following desired properties. Firstly, it should be an exact confidence interval, meaning that for a given significance level  $\alpha$ , the CI includes the true value exactly  $1 - \alpha$  fraction of the times. Secondly, if for a given  $r$ , it can not be rejected that  $\rho$  is 0, 0 should also be contained in the interval. Finally, if we reject

that  $\rho = 0$ , we shall have  $\alpha/2$  probability mass above and below the bounds of the interval. The above is enough to uniquely define a confidence interval in all cases. Before continuing with how this CI is calculated, we mention that as  $r$  is an unbiased estimator of  $\rho$ , we would preferably want  $|r| \in CI_{1-\alpha}(|\rho|)$  (where  $CI_{1-\alpha}(|\rho|)$  denotes the  $1 - \alpha$  confidence interval for  $|\rho|$ ). However, although this will in almost every scenario be the case, we can not be sure of this from the above properties and in fact examples with large  $\alpha$  can be constructed such that  $|r|$  lies just outside the constructed CI.

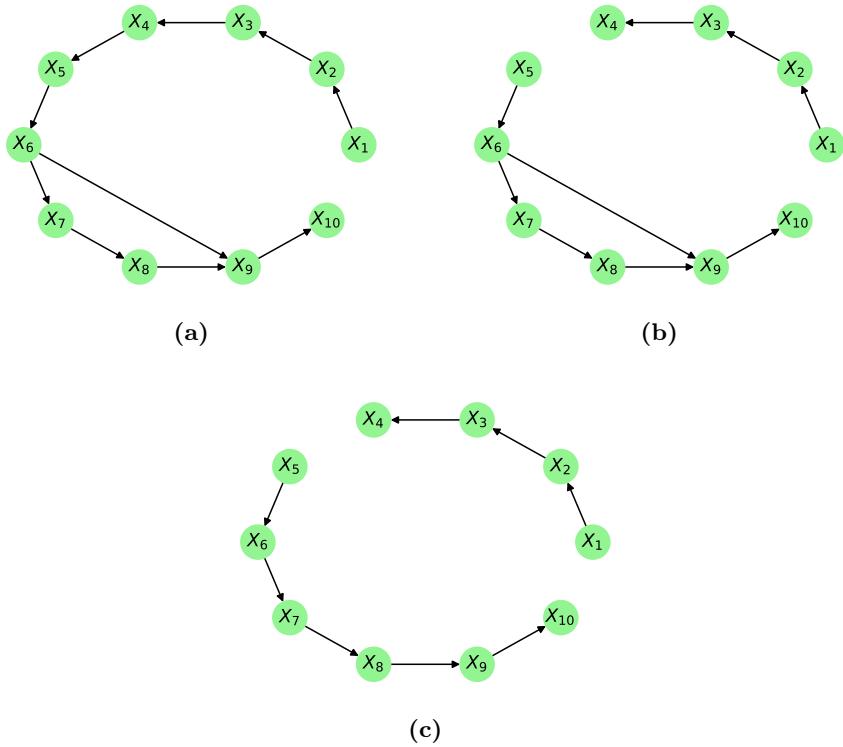
First, to conform with the second desired property, if it can not be rejected that  $\rho = 0$  on a significance level  $\alpha$ , we will initially compute a CI for  $\rho$  (not  $|\rho|$ ) based on  $r$  (wlog chosen to be non-negative). This CI will just be a symmetric CI in the sense that  $\alpha/2$  of the probability mass will lie below the lower bound of the CI and above the upper bound of the CI respectively. If 0 is contained in this CI, we can not reject that  $\rho = 0$  and vice versa on an  $\alpha$  significance level. Thus, if 0 is contained in this initial CI for  $\rho$ , we will start the CI for  $|\rho|$  at 0 and determine and upper bound  $b$  such that  $\alpha$  probability mass is above this  $b$ . Otherwise, we shall find  $a$  and  $b$  such that  $\alpha/2$  probability mass is below  $a$  and above  $b$  respectively. Choosing  $a$  and  $b$  this way also conforms with the third property. Finally, to ensure that the CI contains exactly  $1 - \alpha$ , we define  $\tilde{f}$  as the reflected  $f$  in  $\rho$  such that

$$\tilde{f}(\rho_a | r_a, \nu) = f(\rho_a | r_a, \nu) + f(-\rho_a | r_a, \nu), \quad \rho_a, r \in [0, 1]$$

where  $\rho_a$  and  $r_a$  is the absolute correlation and empirical correlation respectively. With this  $\tilde{f}$ , the density at  $\rho_a$  is both the density for the negative and positive correlation ensuring that the  $\tilde{f}$  has probability mass 1. Thus, if  $a = 0$  (i.e. the CI must contain 0), we find  $b$  as the  $1 - \alpha$  percentile of  $\tilde{f}$  and if  $a \neq 0$ , we take  $a$  as the  $\alpha/2$  percentile and  $b$  as the  $1 - \alpha/2$  percentile of  $\tilde{f}$ .

As an example, suppose  $r_a = 0.06$  with 1000 observations. Then a 95% CI for  $|\rho|$  is  $[0, 0.11164]$  whereas if one had observed  $r_a = 0.07$  the CI would be  $[0.01071, 0.1314]$ . These CI could then be used to test the absolute correlation of a bivariate Gaussian i.e. for  $r_a = 0.07$  based on 1000 observations would be rejected as stemming from a Gaussian with absolute correlation 0.01 on a 5% significance level.

## 1.6 Gaussian chain deconvolution



**Figure 1.13:** Triangular, mutual information, cutoff  $2 \cdot 10^{-10}$ ,  $2.1 \cdot 10^{-2}$  and  $4.51 \cdot 10^{-2}$ .

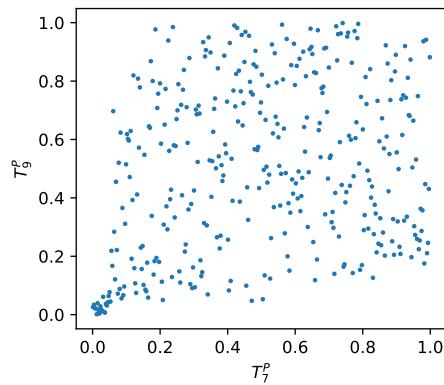
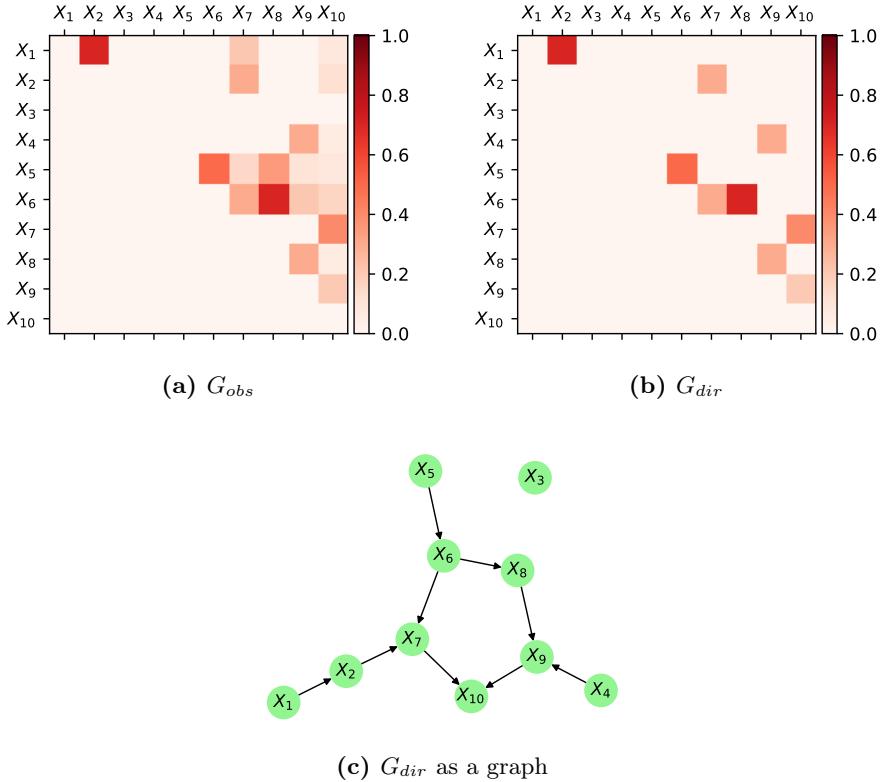


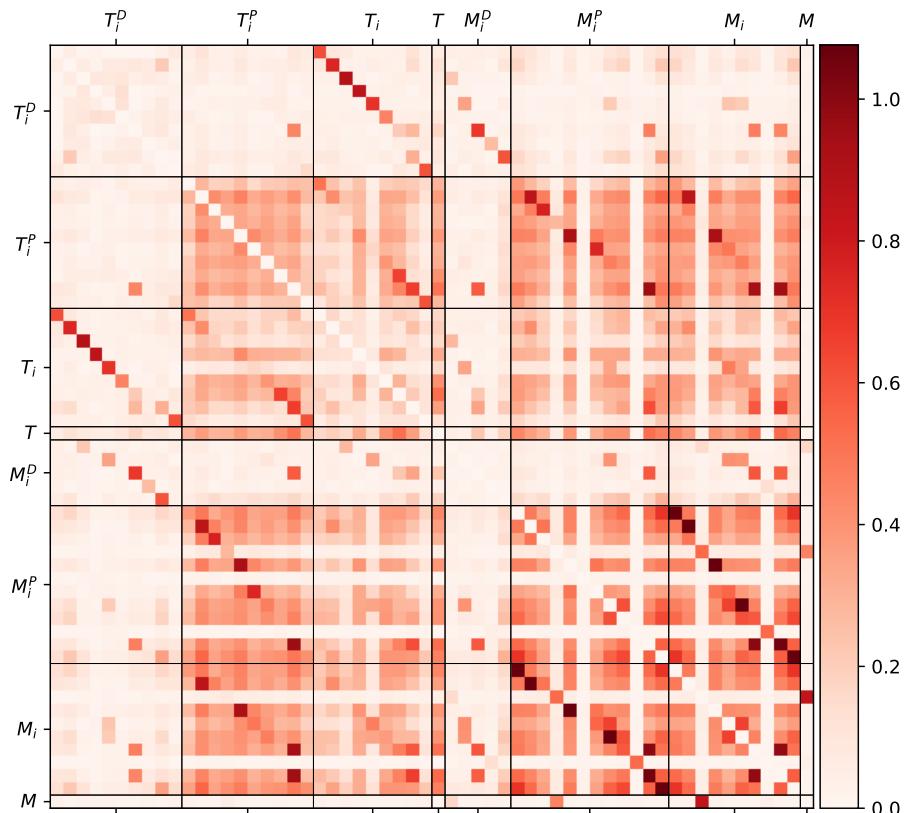
Figure 1.14

## 1.7 Gaussian network deconvolution

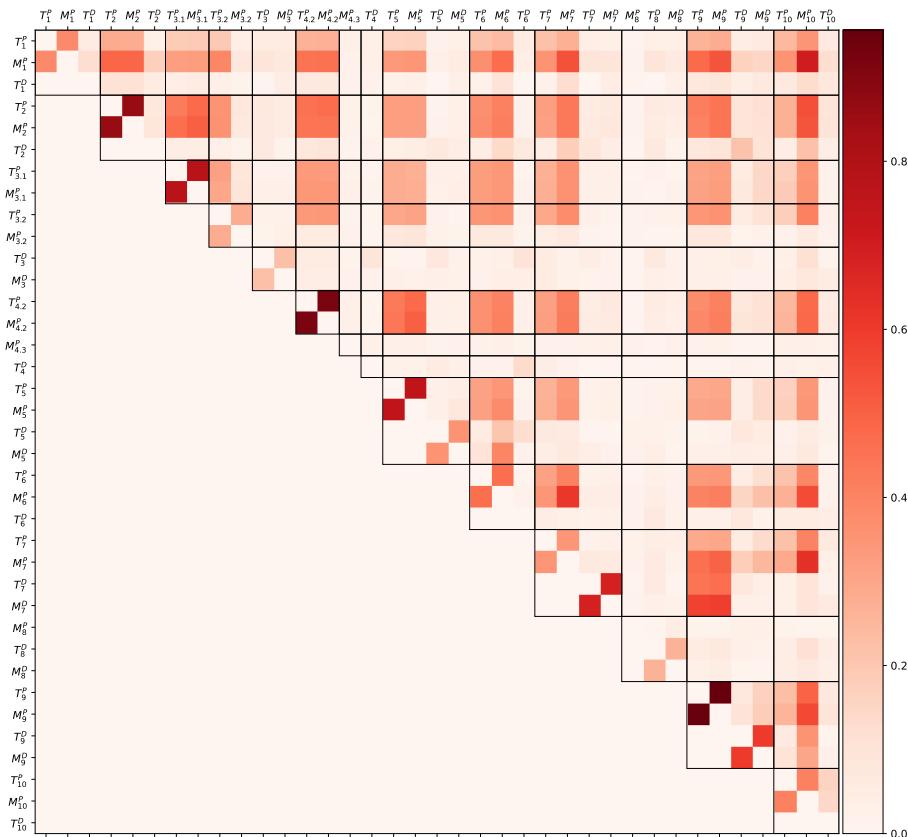


**Figure 1.15:** For the linear network defined in ??, using a triangular  $G_{obs}$  (a) with the true topological structure we are able to perfectly rediscover the causal structure as seen in (b) and (c).

## 1.8 Pharmaceutical process deconvolution



**Figure 1.16:**  $G_{obs}$  from pharmaceutical production data. Strong dependencies between variables and the related accumulated variables are observed.



**Figure 1.17:**  $G_{obs}$  for both durations, delays and level changes for the simulated data from [?]. Labels related to the same process are divided by lines vertically and horizontally to easier observe what is related to what.