Optimal design, orthogonal polynomials and random matrices

Holger Dette

joint work with F. Bretz, S. Delvaux, L. Imhof, W.J. Studden

1 Novartis, Basel
2 Katholieke Universiteit Leuven
3 University of Bonn
4 Purdue University
5 Ruhr-University Bochum

September 2011, Köln
Contents

- Motivating example: dose finding experiment
- Some optimal design theory
- Optimal design for weighted polynomial regression
- Weak asymptotics of optimal designs
Contents

- Motivating example: dose finding experiment
- Some optimal design theory
- Optimal design for weighted polynomial regression
- Weak asymptotics of optimal designs
- Random matrices - the Gaussian ensemble
- Random band matrices
- Matrix orthogonal polynomials
- The limiting spectrum of random band matrices
Motivating example: drug development (clinical phase)

pre-clinic | clinic | market

phase I | phase II | phase III

first experiments with humans | efficacy, dose finding, safety ... | (large) clinical trials (proof of efficacy, side effects)

- Phase I: 20 – 40 patients
- Phase II: 100 – 300 patients
- Phase III: 1000 – 10000 patients

What dose level should be used in the phase III trial?
Motivating Example: drug development

- Confirmatory trial (phase II) to determine the appropriate target dose
- Main goal: estimation of the minimum effective dose level (target dose), which produces at least the clinically relevant effect
- Mathematical (extremely simplified) description of the dose response relationship (Michaelis Menten model)
(Nonlinear) regression model

\[ Y = \eta(x, \theta) + \sigma(x, \theta) \varepsilon, \quad x \in \mathcal{X} \]

- \( \mathcal{X} \) denotes the design space
- \( \varepsilon \) random error, \( E[\varepsilon] = 0 \), \( E[\varepsilon^2] = 1 \)
- \( m \) independent observations \( Y_1, \ldots, Y_m \) at experimental conditions \( x_1, \ldots, x_m \) to estimate the vector of parameters \( \theta \)
- Expectation of \( Y \) (at experimental condition \( x \)) is given by \( \eta(x, \theta) \)
- Variance of \( Y \) (at experimental condition \( x \)) is given by \( \sigma^2(x, \theta) \)
- **Example:** Michaelis Menten model

\[ \eta(x, \theta) = \frac{\theta_1 x}{x + \theta_2} \quad , \quad \sigma(x, \theta) = \frac{\theta_1 x}{x + \theta_2} \quad , \quad x \in \mathcal{X} = (0, \infty) \]
Problem: At which points $x_i$ should we take observations?

**Definition:** An approximate design $\xi$ is a probability measure on the design space $\mathcal{X}$.

**Example:**

$$\xi = \left( \begin{array}{ccc} 25 & 80 & 150 \\ \frac{1}{3} & \frac{1}{3} & \frac{1}{3} \end{array} \right)$$

$\Rightarrow$ $1/3$ of the total observations at each point 25, 80 and 150

- $m = 30 \Rightarrow 10, 10, 10$
- $m = 40 \Rightarrow 13, 14, 13$
Measuring the quality of designs

- **Weighted** least squares estimator: $\hat{\theta}$

\[
\Rightarrow \text{Cov}(\hat{\theta}) \sim \frac{1}{m} M^{-1}(\xi)
\]

where

\[
M(\xi) = \int_x \frac{1}{\sigma^2(x, \theta)} \left( \frac{\partial \eta(x, \theta)}{\partial \theta} \right)^T \frac{\partial \eta(x, \theta)}{\partial \theta} + \frac{1}{2\sigma^4(x, \theta)} \left( \frac{\partial \sigma^2(x, \theta)}{\partial \theta} \right)^T \frac{\partial \sigma^2(x, \theta)}{\partial \theta} d\xi(x)
\]

denotes the **information matrix** of the design $\xi$ (this measure refers to the normality assumption).
Measuring the quality of designs

- **Weighted** least squares estimator: \( \hat{\theta} \)

\[
\Rightarrow \text{Cov}(\hat{\theta}) \sim \frac{1}{m} M^{-1}(\xi)
\]

where

\[
M(\xi) = \int_X \left( \frac{1}{\sigma^2(x, \theta)} \left( \frac{\partial \eta(x, \theta)}{\partial \theta} \right) \right)^T \frac{\partial \eta(x, \theta)}{\partial \theta} + \frac{1}{2\sigma^4(x, \theta)} \left( \frac{\partial \sigma^2(x, \theta)}{\partial \theta} \right)^T \frac{\partial \sigma^2(x, \theta)}{\partial \theta} d\xi(x)
\]

denotes the **information matrix** of the design \( \xi \) (this measure refers to the normality assumption).

**Goal:**

- Maximize \( M(\xi) \) w.r.t. the choice of the design \( \xi \) (impossible!!)
Optimality criteria

- Only a partial ordering in the space of nonnegative definite matrices
- Maximize real valued (statistical meaningful) functions of $M(\xi) \rightarrow$ optimality criteria

The application determines the criterion $c$-optimality (MED-estimation)

$$\xi^* = \arg \max_{\xi} \left( c^T M c - \frac{1}{M(\xi)} (c^T c) \right)$$

where $c$ is a vector determined by the regression model.

$D$-optimality (precise estimation of all parameters)

$$\xi^* = \arg \max_{\xi} |M(\xi)|$$

In this talk we will only consider $D$-optimal designs and polynomial models!
Optimality criteria

- Only a partial ordering in the space of nonnegative definite matrices
- Maximize real valued (statistical meaningful) functions of $M(\xi) \rightarrow$ optimality criteria
- The application determines the criterion
  - $c$-optimality (MED-estimation)
    $\xi^* = \arg \max_{\xi} (c^T M^{-1}(\xi) c)^{-1}$
    where $c$ is a vector determined by the regression model.
  - $D$-optimality (precise estimation of all parameters)
    $\xi^* = \arg \max_{\xi} |M(\xi)|$

- In this talk we will only consider $D$-optimal designs and polynomial models!
Classical (weighted) polynomial regression model

- Polynomial regression model \([\theta = (\theta_0, \ldots, \theta_{n-1})^T, x \in (-\infty, \infty)]\)

\[\eta(x, \theta) = \sum_{j=0}^{n-1} \theta_j x^j\]

\[\sigma^2(x, \theta) = e^{x^2}\]

- Example: \(n = 2\), linear regression model (with heteroscedastic error)

\[\frac{\partial}{\partial \theta}\eta(x, \theta) = (1, x, \ldots, x^{n-1})^T, \quad \frac{\partial}{\partial \theta}\sigma^2(x, \theta) = 0\]
**D-optimal design problem** (weighted polynomial regression)

A D-optimal design maximizes the determinant

\[
|M(\xi)| = \left|\left(\int_{\mathbb{R}} x^i e^{-x^2} d\xi(x)\right)_{i,j=0,\ldots,n-1}\right|
\]

in the class of all probability measures of \(\mathbb{R}\).
D-optimal design problem

**Theorem 1:** The $D$-optimal design $\xi^*$ is a uniform distribution on the set

$$ \left\{ z \mid H_n(z) = 0 \right\} $$

where $H_n$ denotes the $n$-th Hermite polynomial, orthogonal with respect to the measure

$$ e^{-x^2} \, dx $$

**Two Proofs:**

- Equivalence theorems (from design theory) and second order differential equations (Stieltjes)
- Moment theory
Optimal Design

Proof; Step 1 (idea): identification of the weights

- **Equivalence theorem for $D$-optimality (Kiefer and Wolfowitz, 1960):**
  
  $\xi^*$ is $D$-optimal if and only if
  \[
  \forall x \in \mathbb{R} \quad e^{-x^2}(1, x, \ldots, x^{n-1})M^{-1}(\xi^*)(1, x, \ldots, x^{n-1})^T \leq n
  \]

  Moreover, there is equality for all support points of the $D$-optimal design.
Proof; Step 1 (idea): identification of the weights

- **Equivalence theorem for $D$-optimality** (Kiefer and Wolfowitz, 1960): 
  $\xi^*$ is $D$-optimal if and only if

  \[
  \forall x \in \mathbb{R} \quad e^{-x^2}(1, x, \ldots, x^{n-1})M^{-1}(\xi^*)(1, x, \ldots, x^{n-1})^T \leq n
  \]

  Moreover, there is equality for all support points of the $D$-optimal design.

- **Example**: weighted polynomial regression of degree 7 ($n = 8$)
  - $D$-optimal design (solid curve)
  - Equidistant design on 10 points in the interval $[-4, 4]$
  - **Note**: $D$-optimal design has 8 support points (saturated)
Proof; Step 1 (idea): identification of the weights

- **Equivalence theorem for $D$-optimality:** $\xi^*$ is $D$-optimal if and only if

\[
\forall x \in \mathbb{R} \quad e^{-x^2}(1, x, \ldots, x^{n-1})M^{-1}(\xi^*)(1, x, \ldots, x^{n-1})^T \leq n
\]

Moreover, there is equality for all support points of the $D$-optimal design.

- The optimal design has $n$ support points

\[
\Rightarrow \quad \xi^* = \begin{pmatrix}
    x_1 & x_2 & \cdots & x_n \\
    w_1 & w_2 & \cdots & w_n
\end{pmatrix}
\]
Proof; Step 1 (idea): identification of the weights

- **Equivalence theorem for D-optimality:** $\xi^*$ is $D$-optimal if and only if

  $$\forall x \in \mathbb{R} \quad e^{-x^2}(1, x, \ldots, x^{n-1})M^{-1}(\xi^*)(1, x, \ldots, x^{n-1})^T \leq n$$

  Moreover, there is equality for all support points of the $D$-optimal design.

- The optimal design has $n$ support points

  $$\Rightarrow \quad \xi^* = \left( \begin{array}{cccc} x_1 & x_2 & \cdots & x_n \\ w_1 & w_2 & \cdots & w_n \end{array} \right)$$

- 

  $$|M(\xi^*)| = \prod_{1 \leq i < j \leq n} (x_i - x_j)^2 \prod_{i=1}^{n} e^{-x_i^2} \prod_{i=1}^{n} w_i$$

  $$\rightarrow \max_{x_i, w_i}$$

  $$\rightarrow w_i = \frac{1}{n}, \quad i = 1, \ldots, n$$
Proof; Step 2 (idea): identification of the support

- Let
  
  \[ f(x) = (x - x_1)(x - x_2) \ldots (x - x_n) \]

  denote the **supporting polynomial**.

- The necessary condition for an extremum yields a system of \( n \) non-linear equations
  
  \[ f''(x_j) - 2x_j f'(x_j) = 0 \quad j = 1, \ldots n \]
Proof; Step 2 (idea): identification of the support

- Let
  \[ f(x) = (x - x_1) \ldots (x - x_n) \]
  denote the **supporting polynomial**.

- The necessary condition for an extremum yields a system of \( n \) non-linear equations
  \[ f''(x_j) - 2x_j f'(x_j) = 0 \quad j = 1, \ldots, n \]

- Derive a differential equation for the supporting polynomial
  \[ f'''(x) - 2xf'(x) = -2nf(x) \]

- This differential equation has exactly **one** polynomial solution
  \[ f(x) = cH_n(x) \]
Weak asymptotics of roots of Hermite polynomials:

- **Theorem 2:**

\[
\xi^*_n((0, t]) = \frac{1}{n} \# \left\{ z \leq t \mid H_n(\sqrt{n}z) = 0 \right\}
\]

If \( n \to \infty \), then: \( \xi^*_n \) converges weakly to an absolute continuous measure \( \mu^* \) with density

\[
\frac{d\mu^*}{dx} = \frac{1}{\pi} \sqrt{2 - x^2} I_{[-\sqrt{2}, \sqrt{2}]}(x)
\]

- \( \mu^* \) is called the **Wigner semi-circle law**
Proof (idea):

- Use the differential equation for Hermite polynomials to derive a recurrence relation for the moments of the uniform distribution $\xi_n^*$ on the set

$$\{ z \leq t \mid H_n(\sqrt{n}z) = 0 \}$$

that is

$$\mu_{2r,n} = \frac{1}{2} \left\{ \sum_{\nu=0}^{r-1} \mu_{2r-2\nu-2,n} \mu_{2\nu,n} - \frac{2r-1}{n} \mu_{2r-2,n} \right\}$$

- Recurrence relation in the limit ($n \to \infty$)

$$\mu_{2r}^* = \frac{1}{2} \sum_{\nu=0}^{r-1} \mu_{2r-2\nu-2}^* \mu_{2\nu}^*$$

- Identify the moments and the limit distribution

$$\mu_{2r}^* = \frac{1}{r+1} \left( \frac{1}{2} \right)^r \binom{2r}{r} = \frac{1}{\pi} \int_{-\sqrt{2}}^{\sqrt{2}} x^{2r} \sqrt{2-x^2} \, dx$$
**Elementary random matrix theory**

- $M_n \in \mathbb{R}^{n \times n}$ symmetric matrix with i.i.d. entries $M_n(i, j) \sim \mathcal{N}(0, \frac{1}{2})$

- **Problem:** location of the eigenvalues of the random matrix $M_n$?

The joint density of the (random) eigenvalues $\lambda_1 \leq \lambda_2 \leq \ldots \leq \lambda_n$ of the matrix $M_n$ is given by

$$h(\lambda) = c \prod_{1 \leq i < j \leq n} |\lambda_i - \lambda_j|^{\frac{1}{2}} \prod_{i=1}^{n} e^{-\lambda_i^2}.$$  

(Maximum likelihood) Typical locations are the points where the density is maximal!

D-optimal design theory tells us: look at roots of the Hermite polynomial $H_n(z)$

Note: If $n \to \infty$ the roots of $H_n(\sqrt{n}z)$ become dense in $[-\sqrt{2}, \sqrt{2}]$.  


Elementary random matrix theory

- $M_n \in \mathbb{R}^{n \times n}$ symmetric matrix with i.i.d. entries $M_n(i, j) \sim \mathcal{N}(0, \frac{1}{2})$

- **Problem:** location of the eigenvalues of the random matrix $M_n$?

- The joint density of the (random) eigenvalues $\lambda_1 \leq \lambda_2 \leq \ldots \leq \lambda_n$ of the matrix $M_n$ is given by

$$h(\lambda) = c \prod_{1 \leq i < j \leq n} |\lambda_i - \lambda_j| \prod_{i=1}^{n} e^{-\frac{\lambda_i^2}{2}},$$

- (Maximum likelihood) Typical locations are the points where the density is maximal!
**Elementary random matrix theory**

- $M_n \in \mathbb{R}^{n \times n}$ symmetric matrix with i.i.d. entries $M_n(i, j) \sim \mathcal{N}(0, \frac{1}{2})$

- **Problem:** location of the eigenvalues of the random matrix $M_n$?

- The joint density of the (random) eigenvalues $\lambda_1 \leq \lambda_2 \leq \ldots \leq \lambda_n$ of the matrix $M_n$ is given by

  $$h(\lambda) = c \prod_{1 \leq i < j \leq n} |\lambda_i - \lambda_j| \prod_{i=1}^{n} e^{-\frac{\lambda_i^2}{2}},$$

- (Maximum likelihood) Typical locations are the points where the density is maximal!

- **$D$-optimal design theory tells us:** look at roots of the Hermite polynomial $H_n(z)$

- **Note:** If $n \rightarrow \infty$ the roots of $H_n(\sqrt{n}z)$ become dense in $[-\sqrt{2}, \sqrt{2}]$. 
Semi-circle law for the Gaussian ensemble

**Theorem 3** Let $\lambda_1^{(n)} \leq \lambda_2^{(n)} \leq \ldots \leq \lambda_n^{(n)}$ denote the eigenvalues of the random matrix

$$\frac{1}{\sqrt{n}} M_n$$

and by

$$\mu_n = \frac{1}{n} \sum_{j=1}^{n} \delta_{\lambda_j^{(n)}}$$

the empirical eigenvalue distribution ($\delta_x$ is the Dirac measure), then for any $t \in [-\sqrt{2}, \sqrt{2}]$

$$\lim_{n \to \infty} \mu_n((-\sqrt{2}, t]) = \frac{1}{\pi} \int_{-\sqrt{2}}^{t} \sqrt{2 - x^2} dx \quad a.s.$$
Eigenvalues of a $5000 \times 5000$ matrix

Figure: Left panel: histogram of the simulated eigenvalues. Right panel: asymptotic distribution.
Eigenvalues of a $5000 \times 5000$ matrix

Figure: *Histogram of the simulated eigenvalues and the asymptotic distribution*
\( \beta \)-ensembles

The \( \beta \)-ensemble (\( \beta > 0 \)) is defined by the density

\[
h(\lambda) = c \prod_{1 \leq i < j \leq n} |\lambda_i - \lambda_j|^{\beta} \prod_{i=1}^{n} e^{-\frac{\lambda_i^2}{2}},
\]  

Density of the eigenvalues of a \( n \times n \) matrix with normally distributed random variables [Dyson (1962)], where

\[
\begin{align*}
\beta &= 1: \quad \text{real entries} \\
\beta &= 2: \quad \text{complex entries} \\
\beta &= 4: \quad \text{quaternion entries}
\end{align*}
\]
The $\beta$-ensemble ($\beta > 0$) is defined by the density

$$h(\lambda) = c \prod_{1 \leq i < j \leq n} |\lambda_i - \lambda_j|^\beta \prod_{i=1}^{n} e^{-\frac{\lambda_i^2}{2}}, \quad (1)$$

Density of the eigenvalues of a $n \times n$ matrix with normally distributed random variables [Dyson (1962)], where

- $\beta = 1$: real entries
- $\beta = 2$: complex entries
- $\beta = 4$: quaternion entries

Is there any random matrix whose eigenvalue distribution is given by (1) for any $\beta > 0$?
The $\beta$-ensemble ($\beta > 0$) is defined by the density

$$h(\lambda) = c \prod_{1 \leq i < j \leq n} |\lambda_i - \lambda_j|^\beta \prod_{i=1}^{n} e^{-\frac{\lambda_i^2}{2}},$$

(1)

Density of the eigenvalues of a $n \times n$ matrix with normally distributed random variables [Dyson (1962)], where

- $\beta = 1$: real entries
- $\beta = 2$: complex entries
- $\beta = 4$: quaternion entries

Is there any random matrix whose eigenvalue distribution is given by (1) for any $\beta > 0$?

The answer is positive [Dumitriu and Edelman, 2004]

The matrix can be chosen in a tridiagonal form (Householder transformations)!
Tridiagonal matrix representation for the $\beta$-ensemble

$$G_n^{(1)} = \frac{1}{\sqrt{2}} \begin{bmatrix}
\sqrt{2}N_1 & \mathcal{X}_{(n-1)\beta} \\
\mathcal{X}_{(n-1)\beta} & \sqrt{2}N_2 & \mathcal{X}_{(n-2)\beta} \\
& \ddots & \ddots & \ddots \\
& & \mathcal{X}_{2\beta} & \sqrt{2}N_{n-1} & \mathcal{X}_{\beta} \\
& & & \mathcal{X}_\beta & \sqrt{2}N_n
\end{bmatrix}$$

Note:

- $N_1, N_2, \ldots, N_n$ are standard normal distributed ($N_j \sim \mathcal{N}(0, 1)$)

- For $j = 1, \ldots, n - 1$ the random variable $\mathcal{X}_{j\beta}^2$ is chi-square distributed with "$j\beta$ degrees of freedom" ($\mathcal{X}_{j\beta}^2 \sim \chi^2(j\beta)$)

- All random variables are independent
Theorem 4: [D., Imhof, 2007] If

\[ \lambda_1^{(n)} \leq \lambda_2^{(n)} \leq \ldots \leq \lambda_n^{(n)} \]

denote the eigenvalues of the matrix \( \frac{1}{\sqrt{n}} G_n^{(1)} \) and

\[ \xi_1^{(n)} < \xi_2^{(n)} < \ldots < \xi_n^{(n)} \]

denote the zeros of the polynomial \( H_n(\sqrt{n}\beta z) \), then \( (n \to \infty) \)

\[ \max_{1 \leq j \leq n} |\lambda_j^{(n)} - \xi_j^{(n)}| = O\left( \left( \frac{\log n}{n} \right)^{1/2} \right) \quad \text{a.s.} \]
Idea of a proof of Theorem 4

- Expectation of chi-square distribution $\mathbb{E}[\chi_{j\beta}^2] = j\beta$. Approximate
  
  $$\mathbb{E}[\chi_{j\beta}] \approx \sqrt{j\beta}$$

- Consider the (non-random) matrix

  $$E[G_n^{(1)}] \approx F_n = \sqrt{\frac{\beta}{2}} \begin{bmatrix}
  0 & \sqrt{n-1} & \sqrt{n-2} & \cdots & \cdots & \cdots \\
  \sqrt{n-1} & 0 & \sqrt{n-2} & \cdots & \cdots & \cdots \\
  \sqrt{n-2} & \sqrt{n-2} & \sqrt{n-2} & \cdots & \cdots & \cdots \\
  \vdots & \vdots & \vdots & \ddots & \ddots & \ddots \\
  \sqrt{2} & 0 & 1 & \cdots & \cdots & \cdots \\
  1 & 0 & & & & 
  \end{bmatrix}$$

- Note: by the three term recurrence relation for Hermite polynomials we have:

  $$\det(xI_n - F_n) = \left(\frac{\sqrt{\beta}}{2}\right)^n H_n \left(\frac{x}{\sqrt{\beta}}\right)$$
Idea of a proof of Theorem 4

- $\lambda_1^{(n)} \leq \lambda_2^{(n)} \leq \ldots \leq \lambda_n^{(n)}$: eigenvalues of the matrix $\frac{1}{\sqrt{n}} G^{(1)}_n$
- $\xi_1^{(n)} < \ldots < \xi_n^{(n)}$: roots of the polynomial $H_n(\sqrt{n}\beta z)$
- **Weyl’s inequality**
  \[
  \sqrt{n} \max_{1 \leq j \leq n} |\lambda_j^{(n)} - \xi_j^{(n)}| \leq \|G^{(1)}_n - F_n\|_\infty = \max_{1 \leq i \leq n} \sum_{j=1}^n |(G^{(1)}_n - F_n)_{ij}|
  \]
Idea of a proof of Theorem 4

- \( \lambda_1^{(n)} \leq \lambda_2^{(n)} \leq \ldots \leq \lambda_n^{(n)} \): eigenvalues of the matrix \( \frac{1}{\sqrt{n}} G_n^{(1)} \)
- \( \xi_1^{(n)} < \cdots < \xi_n^{(n)} \): roots of the polynomial \( H_n(\sqrt{n}\beta z) \)
- **Weyl’s inequality**
  \[
  \sqrt{n} \max_{1 \leq j \leq n} |\lambda_j^{(n)} - \xi_j^{(n)}| \leq \|G_n^{(1)} - F_n\|_\infty = \max_{1 \leq i \leq n} \sum_{j=1}^n |(G_n^{(1)} - F_n)_{ij}|
  \]
- **Large deviations:**
  \[
  P\left\{ \frac{|X_{j\beta} - \sqrt{j\beta}|}{\sqrt{2}} \geq \frac{\epsilon}{3} \right\} \leq 2e^{-\epsilon^2/9}, \quad P\left\{ |N_j| \geq \frac{\epsilon}{3} \right\} \leq 2e^{-\epsilon^2/18}
  \]
  \[\implies P\left\{ \max_{1 \leq j \leq n} |\lambda_j^{(n)} - \xi_j^{(n)}| \geq \epsilon \right\} \leq 4ne^{-n\beta\epsilon^2/9} \]
Idea of a proof of Theorem 4

- $\lambda_1^{(n)} \leq \lambda_2^{(n)} \leq \ldots \leq \lambda_n^{(n)}$: eigenvalues of the matrix $\frac{1}{\sqrt{n}} G_n^{(1)}$
- $\xi_1^{(n)} < \ldots < \xi_n^{(n)}$: roots of the polynomial $H_n(\sqrt{n} \beta z)$
- Weyl’s inequality 
  \[ \sqrt{n} \max_{1 \leq j \leq n} |\lambda_j^{(n)} - \xi_j^{(n)}| \leq \|G_n^{(1)} - F_n\|_{\infty} = \max_{1 \leq i \leq n} \sum_{j=1}^{n} |(G_n^{(1)} - F_n)_{ij}| \]
- Large deviations:
  \[ P\left\{ \frac{|X_j\beta - \sqrt{j}\beta|}{\sqrt{2}} \geq \frac{\epsilon}{3} \right\} \leq 2e^{-\epsilon^2/9}, \quad P\left\{ |N_j| \geq \frac{\epsilon}{3} \right\} \leq 2e^{-\epsilon^2/18} \]
  \[ \Rightarrow \quad P\left\{ \max_{1 \leq j \leq n} |\lambda_j^{(n)} - \xi_j^{(n)}| \geq \epsilon \right\} \leq 4ne^{-n\beta\epsilon^2/9} \]
- Borel Cantelli
  \[ \max_{1 \leq j \leq n} |\lambda_j^{(n)} - \xi_j^{(n)}| = O\left(\left(\frac{\log n}{n}\right)^{1/2}\right) \quad \text{a.s.} \]
Idea of a proof of Theorem 3 ($\beta = 1$)

- The random eigenvalues of the matrix $\frac{1}{\sqrt{n}} G_n^{(1)}$ can be (uniformly, almost surely) approximated by roots of the Hermite polynomial $H_n(\sqrt{n\beta} z)$.

- The uniform distribution on the roots Hermite polynomial $H_n(\sqrt{n\beta} z)$ converges weakly to Wigner’s semi-circle law.

- The empirical eigenvalue distribution of the random matrix $\frac{1}{\sqrt{n}} G_n^{(1)}$ converges weakly to Wigner’s semi-circle law (almost surely).
Random band matrices - tridiagonal \((r = 1, \beta_1 > 0)\)

\[
G_n^{(1)} = \frac{1}{\sqrt{2}} \begin{pmatrix}
\sqrt{2} N_1 & \mathcal{X}_{(n-1)\beta_1} \\
\mathcal{X}_{(n-1)\beta_1} & \sqrt{2} N_2 & \mathcal{X}_{(n-2)\beta_1} \\
\mathcal{X}_{(n-2)\beta_1} & \sqrt{2} N_3 & \mathcal{X}_{(n-3)\beta_1} & \ddots & \ddots \\
\ddots & \ddots & \ddots & \ddots & \ddots \\
\end{pmatrix}
\]

All random variables are independent!
Random 5-band matrices \((r = 2, \beta_1, \beta_2 > 0)\)

\[
G^{(2)}_n = \frac{1}{\sqrt{2}} \begin{pmatrix}
\sqrt{2} N_1 & \mathcal{X}_{(n-1)\beta_1} & \mathcal{X}_{(n-2)\beta_2} \\
\mathcal{X}_{(n-1)\beta_1} & \sqrt{2} N_2 & \mathcal{X}_{(n-2)\beta_1} & \mathcal{X}_{(n-3)\beta_2} \\
\mathcal{X}_{(n-2)\beta_2} & \mathcal{X}_{(n-2)\beta_1} & \sqrt{2} N_3 & \mathcal{X}_{(n-3)\beta_1} & \mathcal{X}_{(n-4)\beta_2} \\
\mathcal{X}_{(n-3)\beta_2} & \mathcal{X}_{(n-3)\beta_1} & \sqrt{2} N_4 & \mathcal{X}_{(n-4)\beta_1} \\
\cdots & \cdots & \cdots & \cdots & \cdots
\end{pmatrix}
\]

All random variables are independent!
Random 7-band matrices \((r = 3, \beta_1, \beta_2, \beta_3 > 0)\)

\[
G_n^{(3)} = \frac{1}{\sqrt{2}} \begin{pmatrix}
\sqrt{2} N_1 & \chi_{(n-1)\beta_1} & \chi_{(n-2)\beta_2} & \chi_{(n-3)\beta_3} \\
\chi_{(n-1)\beta_1} & \sqrt{2} N_2 & \chi_{(n-2)\beta_1} & \chi_{(n-3)\beta_2} & \chi_{(n-4)\beta_3} \\
\chi_{(n-2)\beta_2} & \chi_{(n-2)\beta_1} & \sqrt{2} N_3 & \chi_{(n-3)\beta_1} & \chi_{(n-4)\beta_2} & \chi_{(n-5)\beta_3} \\
\chi_{(n-3)\beta_3} & \chi_{(n-3)\beta_2} & \chi_{(n-3)\beta_1} & \sqrt{2} N_4 & \chi_{(n-4)\beta_1} & \chi_{(n-5)\beta_2} \\
\chi_{(n-4)\beta_3} & \chi_{(n-4)\beta_2} & \chi_{(n-4)\beta_1} & \sqrt{2} N_4 & \chi_{(n-5)\beta_1} & \ldots \\
\vdots & \vdots & \ddots & \ddots & \ddots & \ddots \\
\end{pmatrix}
\]

All random variables are independent!
Random 2\(r + 1\) band matrices \((\beta_1, \ldots, \beta_r > 0)\)

\[
\sqrt{2} G_n^{(r)} = \\
\begin{pmatrix}
\sqrt{2} N_1 & \chi_{(n-1)\beta_1} & \cdots & \chi_{(n-r)\beta_r} \\
\chi_{(n-1)\beta_1} & \sqrt{2} N_2 & \cdots & \chi_{(n-r)\beta_{r-1}} & \chi_{(n-r-1)\beta_r} \\
\chi_{(n-2)\beta_2} & \chi_{(n-2)\beta_1} & \ddots & \vdots & \ddots & \ddots \\
\vdots & \vdots & \ddots & \ddots & \ddots & \ddots \\
\chi_{(n-r)\beta_r} & \chi_{(n-r)\beta_{r-1}} & \cdots & \ddots & \ddots & \ddots \\
\chi_{(n-r-1)\beta_r} & \chi_{(n-r-1)\beta_{r-1}} & \cdots & \ddots & \ddots & \ddots \\
\chi_{(n-r-1)\beta_{r-1}} & \chi_{(n-r-1)\beta_{r-2}} & \cdots & \cdots & \ddots & \ddots \\
\vdots & \vdots & \ddots & \ddots & \ddots & \ddots \\
\chi_{2\beta_1} & \chi_{\beta_2} & \cdots & \cdots & \ddots & \ddots \\
\chi_{\beta_1} & \sqrt{2} N_{n-1} & \chi_{\beta_1} & \cdots & \cdots & \ddots \\
\chi_{\beta_1} & \chi_{\beta_1} & \sqrt{2} N_n \\
\end{pmatrix}
\]

All random variables are independent!
5-band and tridiagonal block matrices (2 × 2 blocks)

\[ G^{(2)}_n = \]

\[
\frac{1}{\sqrt{2}} \begin{pmatrix}
\sqrt{2} N_1 & x_{(n-1)\beta_1} & x_{(n-2)\beta_2} & 0 \\
x_{(n-1)\beta_1} & \sqrt{2} N_2 & x_{(n-2)\beta_1} & x_{(n-3)\beta_2} \\
x_{(n-2)\beta_2} & x_{(n-2)\beta_1} & \sqrt{2} N_3 & x_{(n-3)\beta_1} \\
0 & x_{(n-3)\beta_2} & x_{(n-3)\beta_1} & \sqrt{2} N_4 \\
& & & \ddots \\
& & & \ddots \\
& & & \ddots \\
& & & \ddots \\
& & & \ddots \\
\end{pmatrix}
\]
7-band and tridiagonal block matrices (3 × 3 blocks)

\[ G_n^{(3)} = \begin{pmatrix}
\sqrt{2} N_1 & x_{(n-1)\beta_1} & x_{(n-2)\beta_2} & x_{(n-3)\beta_3} & 0 & 0 \\
 x_{(n-1)\beta_1} & \sqrt{2} N_2 & x_{(n-2)\beta_1} & x_{(n-3)\beta_2} & x_{(n-4)\beta_3} & 0 \\
 x_{(n-2)\beta_2} & x_{(n-2)\beta_1} & \sqrt{2} N_3 & x_{(n-3)\beta_1} & x_{(n-4)\beta_2} & x_{(n-5)\beta_3} \\
 x_{(n-3)\beta_3} & x_{(n-3)\beta_2} & x_{(n-3)\beta_1} & \sqrt{2} N_4 & x_{(n-4)\beta_1} & x_{(n-5)\beta_2} \\
 0 & x_{(n-4)\beta_3} & x_{(n-4)\beta_2} & x_{(n-4)\beta_1} & \sqrt{2} N_5 & x_{(n-5)\beta_1} \\
 0 & 0 & x_{(n-5)\beta_3} & x_{(n-5)\beta_2} & x_{(n-5)\beta_1} & \sqrt{2} N_6 \\
\end{pmatrix} \]
2\(r + 1\)-band and tridiagonal block matrices (\(r \times r\) blocks)

\[
G_n^{(r)} = \begin{pmatrix}
    B_0 & A_1 & \cdots & \cdots & A_{m-2} & B_{m-2} & A_{m-1} \\
    A_1^T & B_1 & A_2 & \cdots & \cdots & \cdots & \cdots \\
    \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\
    A_{m-2}^T & B_{m-2} & A_{m-1} & \cdots & \cdots & \cdots & \cdots \\
    A_{m-1}^T & B_{m-1} & \cdots & \cdots & \cdots & \cdots & \cdots \\
\end{pmatrix} \in \mathbb{R}^{n \times n}
\]

where

- \(n = mr\)
- \(B_i\) are symmetric random matrices
- \(A_i\) are lower random triangular matrices

Problem: location of the eigenvalues?
Excursion: matrix orthogonal polynomials


\[ P_n(x) = D_n x^n + D_{n-1} x^{n-1} + \ldots + D_1 x + D_0 \]

where \( D_0, \ldots, D_n \) are \( r \times r \) matrices with real entries

- Example:

\[ P_3(x) = \begin{pmatrix} x^3 + x - 1 & 2x + 1 \\ x - 1 & 3x^2 \end{pmatrix} \]
Excursion: matrix orthogonal polynomials


\[ P_n(x) = D_n x^n + D_{n-1} x^{n-1} + \ldots + D_1 x + D_0 \]

where \( D_0, \ldots, D_n \) are \( r \times r \) matrices with real entries

- Example:

\[ P_3(x) = \begin{pmatrix} x^3 + x - 1 & 2x + 1 \\ x - 1 & 3x^2 \end{pmatrix} \]

- Roots of a matrix polynomial are defined by \( \det P_n(x) = 0 \)

- Matrix measure \( \psi \) is a matrix of signed Borel measures on the real line such for any Borel set \( A \) the matrix \( \psi(A) \) is nonnegative definite (spectral measure of multivariate stationary processes)

- "Inner product" with respect to the matrix measure \( \psi \)

\[ \langle P_n, P_m \rangle := \int_{\mathbb{R}} P_n(x) d\psi(x) P_m^T(x) \in \mathbb{R}^{r \times r} \]
Excursion: matrix orthogonal polynomials

- Matrix polynomials are called orthonormal if and only if

\[ \langle P_n, P_m \rangle = \delta_{n,m} I_r \in \mathbb{R}^{r \times r} \]

- Some properties of the scalar case are still valid
  - All roots of orthogonal matrix polynomials are real
  - **Favard’s Theorem:** \( \{P_n\}_{n \in \mathbb{N}} \) defines a sequence of matrix orthonormal polynomials if and only if

\[ xP_n(x) = A_{n+1}P_{n+1}(x) + B_nP_n(x) + A_n^TP_{n-1}(x), \quad n \geq 0, \]

for symmetric matrices \( B_n \) and arbitrary non singular matrices \( A_n \)

[D. and Studden (2002)]
Excursion: matrix orthogonal polynomials

- Matrix multiplication is not commutative
- Orthonormal matrix polynomials are not uniquely determined
- The roots of matrix orthogonal polynomials are not interlacing
- Characterization of the boundary of the moment space corresponding to matrix measures?
- There exists no example of matrix orthogonal polynomials, which has been completely understood
Excursion: matrix orthogonal polynomials

- Matrix multiplication is not commutative
- Orthonormal matrix polynomials are **not** uniquely determined
- The roots of matrix orthogonal polynomials are **not** interlacing
- Characterization of the boundary of the moment space corresponding to matrix measures?
- There exists no example of matrix orthogonal polynomials, which has been completely understood
  - **Example:** Scalar Chebyshev polynomials (first kind)

\[
T_{-1}(x) = 0, \quad T_0(x) = 1, \quad T_{n+1}(x) = 2xT_n(x) - T_{n-1}(x)
\]

- Trigonometric representation: \( T_n(x) = \cos(n \arccos x) \)
- Measure of orthogonality: arcsine distribution with density

\[
\frac{1}{\pi} \frac{1}{\sqrt{1 - x^2}} I_{[-1,1]}(x)
\]
Excursion: matrix Chebyshev polynomials

- $A \in \mathbb{R}^{r \times r}$ non singular; $B \in \mathbb{R}^{r \times r}$ symmetric
- Recurrence relation $T_{0}^{A,B}(x) = I_{p}$

\[ T_{1}^{A,B}(x) = (\sqrt{2}A)^{-1}(xI_{p} - B) \]

\[ xT_{1}^{A,B}(x) = AT_{2}^{A,B}(x) + BT_{1}^{A,B}(x) + \sqrt{2}A^{T}T_{0}^{A,B}(x) \]

\[ xT_{n}^{A,B}(x) = AT_{n+1}^{A,B}(x) + BT_{n}^{A,B}(x) + A^{T}T_{n-1}^{A,B}(x), \quad n \geq 2, \]

- If $r = 1$ the measure of orthogonality is given by a linear transformation of the arcsine distribution with density

\[ \frac{1}{\pi} \frac{1}{\sqrt{1 - x^2}} I_{[-1,1]}(x) \]

- **Open problem:** The matrix measure $X_{A,B}$ of orthogonality in the case $r > 1$ ?
Limiting spectrum of random band matrices

Return to random of block matrices

We are interested in the eigenvalues of the matrix

\[ G_n^{(r)} = \begin{pmatrix} B_0 & A_1 & & & \\ A_1^T & B_1 & A_2 & & \\ & \ddots & \ddots & \ddots & \\ & & A_{m-2}^T & B_{m-2} & A_{m-1} \\ & & & A_{m-1}^T & B_{m-1} \end{pmatrix} \in \mathbb{R}^{n \times n} \]

where

- \( n = mr \)
- \( B_i \) are symmetric random matrices
- \( A_i \) are lower random triangular matrices

**Problem:** location of the eigenvalues?
The structure of the blocks \((r \times r)\)

\[
B_i = \frac{1}{\sqrt{2}} \begin{pmatrix} \sqrt{2}N_{ir+1} & \mathcal{X}_{(n-ir-1)\beta_1} & \cdots & \mathcal{X}_{(n-(i+1)r+1)\beta_{r-1}} \\ \mathcal{X}_{(n-ir-1)\beta_1} & \sqrt{2}N_{ir+2} & \cdots & \mathcal{X}_{(n-(i+1)r+1)\beta_{r-2}} \\ \vdots & \vdots & \ddots & \vdots \\ \mathcal{X}_{(n-(i+1)r+1)\beta_{r-1}} & \cdots & \mathcal{X}_{(n-(i+1)r+1)\beta_1} & \sqrt{2}N_{(i+1)r} \end{pmatrix},
\]

\[
A_i = \frac{1}{\sqrt{2}} \begin{pmatrix} \mathcal{X}_{(n-ir)\beta_r} & 0 & 0 & \cdots & 0 \\ \mathcal{X}_{(n-ir)\beta_{r-1}} & \mathcal{X}_{(n-ir-1)\beta_r} & 0 & \cdots & 0 \\ \vdots & \vdots & \ddots & \ddots & \vdots \\ \mathcal{X}_{(n-ir)\beta_1} & \mathcal{X}_{(n-ir-1)\beta_{r-1}} & \cdots & \cdots & \mathcal{X}_{(n-(i+1)r+1)\beta_r} \end{pmatrix},
\]
The structure of the blocks in the case $r = 3$:

$$B_i = \frac{1}{\sqrt{2}} \begin{pmatrix} \sqrt{2} N_{3i+1} & \chi_{(n-3i-1)\beta_1} & \chi_{(n-3i-2)\beta_2} \\ \chi_{(n-3i-1)\beta_1} & \sqrt{2} N_{3i+2} & \chi_{(n-3i-2)\beta_1} \\ \chi_{(n-3i-2)\beta_2} & \chi_{(n-3i-2)\beta_1} & \sqrt{2} N_{3i+3} \end{pmatrix}$$

$$A_i = \frac{1}{\sqrt{2}} \begin{pmatrix} \chi_{(n-3i)\beta_3} & 0 & 0 \\ \chi_{(n-3i)\beta_2} & \chi_{(n-3i-1)\beta_3} & 0 \\ \chi_{(n-3i)\beta_1} & \chi_{(n-3i-1)\beta_2} & \chi_{(n-3i-2)\beta_3} \end{pmatrix}$$
The structure of the blocks in the case $r = 3$:

$$B_i = \frac{1}{\sqrt{2}} \begin{pmatrix} \sqrt{2} N_{3i+1} & x_{(n-3i-1)\beta_1} & x_{(n-3i-2)\beta_2} \\ x_{(n-3i-1)\beta_1} & \sqrt{2} N_{3i+2} & x_{(n-3i-2)\beta_1} \\ x_{(n-3i-2)\beta_2} & x_{(n-3i-2)\beta_1} & \sqrt{2} N_{3i+3} \end{pmatrix}$$

$$A_i = \frac{1}{\sqrt{2}} \begin{pmatrix} x_{(n-3i)\beta_3} & 0 & 0 \\ x_{(n-3i)\beta_2} & x_{(n-3i-1)\beta_3} & 0 \\ x_{(n-3i)\beta_1} & x_{(n-3i-1)\beta_2} & x_{(n-3i-2)\beta_3} \end{pmatrix}$$

Note: in the following discussion we will explain the structure always in the case $r = 3$!
Eigenvalues of block matrices and roots of polynomials

Theorem 5: [D., Reuther, 2010] Let
\[ \lambda_1^{(n)} \leq \lambda_2^{(n)} \leq \ldots \leq \lambda_n^{(n)} \]
denote the eigenvalues of the random block matrix
\[ \frac{1}{\sqrt{n}} G_n^{(r)} , \]
then as \( n \to \infty \):
\[ \max_{1 \leq j \leq n} |\lambda_j^{(n)} - \xi_j^{(n)}| = O\left(\left(\frac{\log n}{n}\right)^{1/2}\right) \quad a.s. \]
where
\[ \xi_1^{(n)} \leq \xi_2^{(n)} \leq \ldots \leq \xi_n^{(n)} \]
are the roots of the \( m = (n/r) \)th matrix orthonormal polynomial \( R_{m,n}(x) \) defined by \( R_{-1,n}(x) = 0, \ R_{0,n}(x) = I_r \)
\[ xR_{k,n}(x) = A_{k+1,n}R_{k+1,n}(x) + B_{k,n}R_{k,n}(x) + A_{k,n}^T R_{k-1,n}(x); \quad k \geq 0, \]
Coefficients in the recurrence relation (here for $r = 3$):

$$A_{k,n} = \frac{1}{\sqrt{2n}} \begin{pmatrix} \sqrt{(3k-2)\beta_3} & 0 & 0 \\ \sqrt{(3k-1)\beta_2} & \sqrt{(3k-1)\beta_3} & 0 \\ \sqrt{3k\beta_1} & \sqrt{3k\beta_2} & \sqrt{3k\beta_3} \end{pmatrix}$$

$$B_{k,n} = \frac{1}{\sqrt{2n}} \begin{pmatrix} 0 & \sqrt{(3k+1)\beta_1} & \sqrt{(3k+1)\beta_2} \\ \sqrt{(3k+1)\beta_1} & 0 & \sqrt{(3k+2)\beta_1} \\ \sqrt{(3k+1)\beta_2} & \sqrt{3k+2\beta_1} & 0 \end{pmatrix}$$
Coefficients in the recurrence relation (here for $r = 3$):

**Note:** If $n \to \infty$ and $\frac{k}{n} \to u \in (0, 1)$, then

\[
A_{k,n} = \frac{1}{\sqrt{2n}} \begin{pmatrix}
\sqrt{(3k-2)\beta_3} & 0 & 0 \\
\sqrt{(3k-1)\beta_2} & \sqrt{(3k-1)\beta_3} & 0 \\
\sqrt{3k\beta_1} & \sqrt{3k\beta_2} & \sqrt{3k\beta_3}
\end{pmatrix}
\]

\[\to A(u) := \sqrt{\frac{3u}{2}} \begin{pmatrix}
\sqrt{\beta_3} & 0 & 0 \\
\sqrt{\beta_2} & \sqrt{\beta_3} & 0 \\
\sqrt{\beta_1} & \sqrt{\beta_2} & \sqrt{\beta_3}
\end{pmatrix}
\]

\[
B_{k,n} = \frac{1}{\sqrt{2n}} \begin{pmatrix}
0 & \sqrt{(3k+1)\beta_1} & \sqrt{(3k+1)\beta_2} \\
\sqrt{(3k+1)\beta_1} & 0 & \sqrt{(3k+2)\beta_1} \\
\sqrt{3k+2\beta_1} & \sqrt{3k+2\beta_1} & 0
\end{pmatrix}
\]

\[\to B(u) := \sqrt{\frac{3u}{2}} \begin{pmatrix}
0 & \sqrt{\beta_1} & \sqrt{\beta_2} \\
\sqrt{\beta_1} & 0 & \sqrt{\beta_1} \\
\sqrt{\beta_2} & \sqrt{\beta_1} & 0
\end{pmatrix}
\]
Matrix orthogonal polynomials with \textit{varying coefficients}

\textbf{Problem:} For \( n \in \mathbb{N} \) let \( \{ R_{k,n}(x) \} \) denote a sequence of matrix orthonormal polynomials defined by \( R_{-1,n}(x) = 0_r, \ R_{0,n}(x) = I_r \)

\[ xR_{k,n}(x) = A_{k+1,n}R_{k+1,n}(x) + B_{k,n}R_{k,n}(x) + A_{k,n}^T R_{k-1,n}(x); \quad k \geq 0, \]

where

\[ \lim_{k \to u} B_{k,n} = B(u), \quad \lim_{k \to u} A_{k,n} = A(u) \]

whenever \( u \in (0, 1) \). What is the behavior of the roots of the polynomials

\[ Q_{k,n}(x) \]

if \( n \to \infty \)?
Matrix orthogonal polynomials with varying coefficients

Problem: For $n \in \mathbb{N}$ let $\{R_{k,n}(x)\}_{k \in \mathbb{N}_0}$ denote a sequence of matrix orthonormal polynomials defined by $R_{-1,n}(x) = 0_r$, $R_{0,n}(x) = I_r$

$$xR_{k,n}(x) = A_{k+1,n}R_{k+1,n}(x) + B_{k,n}R_{k,n}(x) + A_{k,n}^T R_{k-1,n}(x); \quad k \geq 0,$$

where

$$\lim_{k \to n \to u} B_{k,n} = B(u), \quad \lim_{k \to n \to u} A_{k,n} = A(u)$$

whenever $u \in (0, 1)$. What is the behavior of the roots of the polynomials $Q_{k,n}(x)$ if $n \to \infty$?

Note: By Theorem 5 we expect that the eigenvalues of the random band matrix have similar properties ($k = m; n = mr \to u = 1/r$)!
An algebraic equation (Widom, 1974)

Define the equation \((x, z \in \mathbb{C})\)

\[
0 = f_u(z, x) := \det(A(u)^Tz + B(u) + A(u)z^{-1} - xl_r)
\] (3)

Note:

- For fixed \(x \in \mathbb{C}\) there exist \(2r\) roots \(z_1(x, u), \ldots z_{2r}(x, u)\) of equation (3), which can ordered according to

\[
|z_1(x, u)| \leq |z_2(x, u)| \ldots \leq |z_{2r}(x, u)|
\]

- For any \(u \in (0, 1)\)

\[
\Gamma_0(u) = \{x \in \mathbb{C} \mid |z_r(x, u)| = |z_{r+1}(x, u)|\} \subset \mathbb{R}
\]

is a union of at most \(r\) disjoint intervals.
Weak asymptotics for matrix orthonormal polynomials

**Theorem 6** [Delvaux, D., 2011] Let

\[ \nu_n = \frac{1}{n} \sum_{j=1}^{n} \delta_{\xi_j(n)} \]

denote empirical distribution function of the roots of the polynomial \( R_{k,n}(x) \) defined by

\[ xR_{k,n}(x) = A_{k+1,n}R_{k+1,n}(x) + B_{k,n}R_{k,n}(x) + A_{k,n}^T R_{k-1,n}(x); \quad k \geq 0, \]

where

\[ \lim_{k \to u} B_{k,n} = B(u), \quad \lim_{k \to u} A_{k,n} = A(u). \]

Then \( \nu_n \) converges weakly to a measure \( \mu_{0,u} \), with logarithmic potential

\[ \frac{1}{ru} \int_0^u \log |z_1(x, t) \ldots z_r(x, t)| \, dt + C_u, \quad x \in \mathbb{C} \setminus \bigcup_{0 \leq t \leq u} \Gamma_0(t), \]

(here \( C_u \) is some constant).
Identification of the limit distribution

**Theorem 7** [Delvaux, D. 2011] The measure $\mu_{0,u}$ with logarithmic potential

$$
\frac{1}{ru} \int_0^u \log |z_1(x, t) \ldots z_r(x, t)| \, dt + C_u, \quad x \in \mathbb{C} \setminus \bigcup_{0 \leq t \leq u} \Gamma_0(t),
$$

is absolute continuous with density given by

$$
\frac{d\mu_{0,u}(x)}{dx} = \frac{1}{2\pi ur} \int_0^u \sum_{k: |z_k(x, s)|=1} \left| \frac{\partial}{\partial x} \frac{z_k(x, s)}{z_k(x, s)} \right| \, ds
$$
Application to random block matrices

- By Theorem 5 it can be shown that the eigenvalue distribution has the same asymptotic properties as the distribution of the roots of matrix orthogonal polynomials $Q_{m,n}(x)$, where $m = n/r$
- This means
  \[
  \lim_{n \to \infty} \frac{m}{n} = \frac{1}{r}
  \]
- Theorem 7 yields for the limiting distribution
  \[
  \frac{d\mu_{0,1/r}(x)}{dx} = \frac{1}{2\pi} \int_0^{1/r} \frac{1}{\sqrt{s}} \sum_{k : |z_k(x/\sqrt{s})| = 1} \left| \frac{z_k'(x/\sqrt{s})}{z_k(x/\sqrt{s})} \right| ds
  \]
  where $z_1(x), z_2(x), \ldots, z_{2r}(x)$ are the (ordered) roots of the equation
  \[
  0 = f(z, x) := \det(A^T(1)z + B(1) + A(1)z^{-1} - xI_r)
  \]
Application to random block matrices

\[
\begin{align*}
A(1) & := \sqrt{\frac{r}{2}} \begin{pmatrix}
\sqrt{\beta_1} & 0 & 0 & \cdots & 0 \\
0 & \sqrt{\beta_r} & 0 & \cdots & 0 \\
\sqrt{\beta_1} & \sqrt{\beta_2} & \sqrt{\beta_1} & \cdots & \sqrt{\beta_1} \\
\sqrt{\beta_1} & \sqrt{\beta_2} & \sqrt{\beta_1} & \cdots & \sqrt{\beta_1} \\
\cdot & \cdot & \cdot & \cdots & \cdot \\
\end{pmatrix} \\
& \in \mathbb{R}^{r \times r},
\end{align*}
\]

\[
B(1) := \sqrt{\frac{r}{2}} \begin{pmatrix}
0 & \sqrt{\beta_1} & \sqrt{\beta_2} & \cdots & \sqrt{\beta_{r-1}} \\
\sqrt{\beta_1} & 0 & \sqrt{\beta_1} & \cdots & \sqrt{\beta_{r-2}} \\
\sqrt{\beta_1} & \sqrt{\beta_1} & 0 & \cdots & \sqrt{\beta_{r-2}} \\
\sqrt{\beta_1} & \sqrt{\beta_1} & \sqrt{\beta_1} & \cdots & 0 \\
\cdot & \cdot & \cdot & \cdots & \cdot \\
\end{pmatrix} \\
& \in \mathbb{R}^{r \times r},
\]
Limiting spectrum of random band matrices

Eigenvalues of a $5000 \times 5000$ matrix ($\beta_1 = \beta_2 = 1$)

Figure: Left panel: histogram of the simulated eigenvalues  
Right panel: asymptotic distribution
Eigenvalues of a $5000 \times 5000$ matrix ($\beta_1 = 5; \beta_2 = 1$)

Figure: Left panel: histogram of the simulated eigenvalues
Right panel: asymptotic distribution
Eigenvalues of a $5000 \times 5000$ matrix

**Figure:**  *Left panel: histogram and density ($\beta_1 = 1; \beta_2 = 1$)*  
*Right panel: histogram and density ($\beta_1 = 5; \beta_2 = 1$)*
Conclusions and further research

- Optimal designs - (matrix) orthogonal polynomials - random matrices
- I did **not** present a solution of the design problem for the dose finding trial (it is too complicated)!

Possible future research:
- Measure of orthogonality for matrix Chebyshev polynomials?
- Wigner block matrices (there seem to exist relations to free probability)?
- Distribution of the eigenvalues of the band matrices considered here?
- Use matrix orthogonal polynomials for solving optimal design problems?
- Matrix measures and stationary processes?
Conclusions and further research

- Optimal designs - (matrix) orthogonal polynomials - random matrices

- I did not present a solution of the design problem for the dose finding trial (it is too complicated)!

Possible future research:

- Measure of orthogonality for matrix Chebyshev polynomials?
- Wigner block matrices (there seem to exist relations to free probability)?
- Distribution of the eigenvalues of the band matrices considered here?
- Use matrix orthogonal polynomials for solving optimal design problems?
- Matrix measures and stationary processes?
Limiting spectrum of random band matrices

Some selected references

- **Optimal design**

- **β-ensembles**

- **Matrix polynomials**
  H. Dette and W.J. Studden. *Matrix measures, moment spaces and Favard’s theorem for the interval [0, 1] and [0, ∞]*. Linear Algebra Appl. 345 (2002), 169-193.

- **(Random) block matrices**