Emulation and History Matching
Part 2: Methodology and Implementation

5TH ANNUAL DISEASE MODELING SYMPOSIUM

Ian Vernon, Michael Goldstein (Durham University, UK),
I. Andrianakis (LSHTM),
with funding from a Medical Research Council (UK) grant
on Model Calibration (MR/J005088/1)
Overview of Part 2

- We will now demonstrate the Bayesian techniques for analysing complex models described in Part 1.
Overview of Part 2

- We will now demonstrate the **Bayesian techniques** for analysing complex models described in Part 1.

- We will apply them to two **stochastic, agent based models of HIV** (currently applying to one of Typhoid).
Overview of Part 2

- We will now demonstrate the **Bayesian techniques** for analysing complex models described in Part 1.

- We will apply them to two **stochastic, agent based models of HIV** (currently applying to one of Typhoid).

- **Mukwano**: intermediate sized model.
Overview of Part 2

- We will now demonstrate the **Bayesian techniques** for analysing complex models described in Part 1.

- We will apply them to two **stochastic, agent based models of HIV** (currently applying to one of Typhoid).

- **Mukwano**: intermediate sized model.

- **Mukwano with benefits**: Large model.
Overview of Part 2

- We will now demonstrate the Bayesian techniques for analysing complex models described in Part 1.

- We will apply them to two stochastic, agent based models of HIV (currently applying to one of Typhoid).

- Mukwano: intermediate sized model.

- Mukwano with benefits: Large model.

- We will describe the core scientific questions a modeller may wish to answer.
First major question: Is the model currently consistent with the observed measurements? To answer this we require:
Overview of Part 2

- **First major question**: Is the model currently consistent with the observed measurements? To answer this we require:
  - **Emulation** of the model (to combat the speed and dimension problem)
Overview of Part 2

- **First major question**: Is the model currently consistent with the observed measurements? To answer this we require:
  
  - **Emulation** of the model (to combat the speed and dimension problem)
  
  - **Implausibility Measures** (using observed errors and model discrepancy)
Overview of Part 2

- **First major question**: Is the model currently consistent with the observed measurements? To answer this we require:
  
  - **Emulation** of the model (to combat the speed and dimension problem)
  
  - **Implausibility Measures** (using observed errors and model discrepancy)
  
  - **Iterative history matching** (a Global parameter search).
Overview of Part 2

- **First major question**: Is the model currently consistent with the observed measurements? To answer this we require:
  - Emulation of the model (to combat the speed and dimension problem)
  - Implausibility Measures (using observed errors and model discrepancy)
  - Iterative history matching (a Global parameter search).

- **Second major question**: what is the set of all input parameters that produced model outputs consistent with known measurement.
Overview of Part 2

- **First major question**: Is the model currently consistent with the observed measurements? To answer this we require:
  - **Emulation** of the model (to combat the speed and dimension problem)
  - **Implausibility Measures** (using observed errors and model discrepancy)
  - **Iterative history matching** (a Global parameter search).

- **Second major question**: what is the set of all input parameters that produced model outputs consistent with known measurement.

- We will identify and analyse this set.
Overview of Part 2

- **First major question**: Is the model currently consistent with the observed measurements? To answer this we require:
  - Emulation of the model (to combat the speed and dimension problem)
  - Implausibility Measures (using observed errors and model discrepancy)
  - Iterative history matching (a Global parameter search).

- **Second major question**: what is the set of all input parameters that produced model outputs consistent with known measurement.

- We will identify and analyse this set.

- This can then be used to make future predictions, to analyse effects of interventions and to design future data collection.
A Bayesian Uncertainty Analysis: Mukwano

- Going to History Match an HIV disease model known as Mukwano.
A Bayesian Uncertainty Analysis: Mukwano

- Going to **History Match** an HIV disease model known as **Mukwano**.
- This involves learning about acceptable inputs $x$ to the Mukwano model, using observed data $z$. 
A Bayesian Uncertainty Analysis: Mukwano

- Going to **History Match** an HIV disease model known as **Mukwano**.
- This involves learning about acceptable inputs $x$ to the Mukwano model, using observed data $z$.
- We use **emulators** and **implausibility measures** to cut out input space iteratively.
A Bayesian Uncertainty Analysis: Mukwano

- Going to **History Match** an HIV disease model known as **Mukwano**.

- This involves learning about acceptable inputs $x$ to the Mukwano model, using observed data $z$.

- We use **emulators** and **implausibility measures** to cut out input space iteratively.

- We will discuss **relevant uncertainties**: model discrepancy, observational errors, function uncertainty etc.
A Bayesian Uncertainty Analysis: Mukwano

- Going to **History Match** an HIV disease model known as **Mukwano**.

- This involves learning about acceptable inputs $x$ to the Mukwano model, using observed data $z$.

- We use **emulators** and **implausibility measures** to cut out input space iteratively.

- We will discuss **relevant uncertainties**: model discrepancy, observational errors, function uncertainty etc.

- The **History Matching** approach described is completely general, and can be used for any model that is relatively slow to run and has lots of inputs.
A Bayesian Uncertainty Analysis: Mukwano

- Going to **History Match** an HIV disease model known as **Mukwano**.

- This involves learning about acceptable inputs \( x \) to the Mukwano model, using observed data \( z \).

- We use **emulators** and **implausibility measures** to cut out input space iteratively.

- We will discuss **relevant uncertainties**: model discrepancy, observational errors, function uncertainty etc.

- The **History Matching** approach described is completely general, and can be used for any model that is relatively slow to run and has lots of inputs.

Why History Match?

- **History Matching** is an efficient technique that seeks to identify the set $\mathcal{X}$ of all acceptable inputs $x$. 
Why History Match?

- **History Matching** is an efficient technique that seeks to identify the set $\mathcal{X}$ of all acceptable inputs $x$.

- Often $\mathcal{X}$ only occupies a tiny fraction of the original input space.
Why History Match?

- **History Matching** is an efficient technique that seeks to identify the set $\mathcal{X}$ of all acceptable inputs $x$.

- Often $\mathcal{X}$ only occupies a tiny fraction of the original input space.

- This set $\mathcal{X}$ may be empty: we do not presuppose that any such inputs exist.
Why History Match?

- **History Matching** is an efficient technique that seeks to identify the set $\mathcal{X}$ of all acceptable inputs $x$.

- Often $\mathcal{X}$ only occupies a tiny fraction of the original input space.

- This set $\mathcal{X}$ may be empty: we do not presuppose that any such inputs exist.

- This is the main difference between **History Matching** and the related technique of **Probabilistic Bayesian Calibration**.
Why History Match?

- **History Matching** is an efficient technique that seeks to identify the set $\mathcal{X}$ of all acceptable inputs $x$.
- Often $\mathcal{X}$ only occupies a tiny fraction of the original input space.
- This set $\mathcal{X}$ may be empty: we do not presuppose that any such inputs exist.

- This is the main difference between **History Matching** and the related technique of **Probabilistic Bayesian Calibration**.
- The later is a useful technique, but assumes a single ‘best input’ $x^*$ and gives its posterior distribution $\pi(x^*|z)$, via the standard Bayesian update, using e.g. MCMC.
Why History Match?

• **History Matching** is an efficient technique that seeks to identify the set \( \mathcal{X} \) of all acceptable inputs \( x \).

• Often \( \mathcal{X} \) only occupies a tiny fraction of the original input space.

• This set \( \mathcal{X} \) may be empty: we do not presuppose that any such inputs exist.

• This is the main difference between **History Matching** and the related technique of **Probabilistic Bayesian Calibration**.

• The later is a useful technique, but assumes a single ‘best input’ \( x^* \) and gives its **posterior distribution** \( \pi(x^*|z) \), via the standard Bayesian update, using e.g. MCMC.

• This involves the specification of many complex multivariate distributions related to all uncertain quantities of interest, which may or may not be warranted at this stage.
Mukwano Model description

- A dynamic, stochastic, individual based model that simulates heterosexual sexual partnerships and HIV transmission.
Mukwano Model description

- A dynamic, stochastic, individual based model that simulates heterosexual sexual partnerships and HIV transmission.

- 22 input parameters inc. contact rates, concurrency parameters, relationship duration, 2 sexual activity groups (high/low), 2 concurrency groups (high/low), 3 discrete behaviour periods.
Mukwano Model description

- A dynamic, stochastic, individual based model that simulates heterosexual sexual partnerships and HIV transmission.

- **22 input parameters** inc. contact rates, concurrency parameters, relationship duration, 2 sexual activity groups (high/low), 2 concurrency groups (high/low), 3 discrete behaviour periods.

- **18 outputs** inc. population size, HIV prevalence, prevalence of men and women in long/short duration partnerships with one or more partners.
Mukwano Model description

- A dynamic, stochastic, individual based model that simulates heterosexual sexual partnerships and HIV transmission.

- **22 input parameters** inc. contact rates, concurrency parameters, relationship duration, 2 sexual activity groups (high/low), 2 concurrency groups (high/low), 3 discrete behaviour periods.

- **18 outputs** inc. population size, HIV prevalence, prevalence of men and women in long/short duration partnerships with one or more partners.

- Run time varies from **10 mins to >3 hours** for 1 simulator run.
Mukwano Model description

- A dynamic, stochastic, individual based model that simulates heterosexual sexual partnerships and HIV transmission.

- **22 input parameters** inc. contact rates, concurrency parameters, relationship duration, 2 sexual activity groups (high/low), 2 concurrency groups (high/low), 3 discrete behaviour periods.

- **18 outputs** inc. population size, HIV prevalence, prevalence of men and women in long/short duration partnerships with one or more partners.

- Run time varies from **10 mins to >3 hours** for 1 simulator run.

- **Calibration data** provided by a general population cohort in Uganda.
## Mukwano: 22 Model input parameters

<table>
<thead>
<tr>
<th>Number</th>
<th>Input description</th>
<th>Abbr.</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Proportion of men in the high sexual activity group</td>
<td>mhag</td>
<td>0.01</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>Proportion of women in the high sexual activity group</td>
<td>whag</td>
<td>0.01</td>
<td>0.5</td>
</tr>
<tr>
<td>3</td>
<td>Mixing by activity group [c]</td>
<td>mag</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>High activity contact rate (risk behaviour 1) [partners/yr]*</td>
<td>hacr1</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>Low activity contact rate (risk behaviour 1) [partners/yr]*</td>
<td>lacr1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>Start year for risk behaviour 2</td>
<td>sy2</td>
<td>1986</td>
<td>1992</td>
</tr>
<tr>
<td>7</td>
<td>High activity contact rate (risk behaviour 2) [partners/yr]*</td>
<td>hacr2</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>8</td>
<td>Low activity contact rate (risk behaviour 2) [partners/yr]*</td>
<td>lacr2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>Start year for risk behaviour 3</td>
<td>sy3</td>
<td>1998</td>
<td>2002</td>
</tr>
<tr>
<td>10</td>
<td>High activity contact rate (risk behaviour 3) [partners/yr]*</td>
<td>hacr3</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>11</td>
<td>Low activity contact rate (risk behaviour 3) [partners/yr]*</td>
<td>lacr3</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>Mean HIV transmission probability per sex act during primary stage of infection (mean of male to female and female to male transmission probabilities)</td>
<td>atp</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>13</td>
<td>Ratio of male to female/female to male transmission probabilities</td>
<td>rtp</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>14</td>
<td>Proportion of low activity men in high concurrency group</td>
<td>lmhc</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>Proportion of low activity women in high concurrency group</td>
<td>lwhc</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>16</td>
<td>Male concurrency parameter in high concurrency group (risk behaviour 1)</td>
<td>mchc1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>17</td>
<td>Female concurrency parameter in high concurrency group (risk behaviour 1)</td>
<td>fchc1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>Male concurrency parameter in high concurrency group (risk behaviour 2)</td>
<td>mchc2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>19</td>
<td>Female concurrency parameter in high concurrency group (risk behaviour 2)</td>
<td>fchc2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>20</td>
<td>Male concurrency parameter in high concurrency group (risk behaviour 3)</td>
<td>mchc3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>21</td>
<td>Female concurrency parameter in high concurrency group (risk behaviour 3)</td>
<td>fchc3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>22</td>
<td>Duration of long-duration partnerships [years]</td>
<td>dlp</td>
<td>5</td>
<td>20</td>
</tr>
</tbody>
</table>
## Mukwano: 22 Model input parameters

<table>
<thead>
<tr>
<th>Number</th>
<th>Output description</th>
<th>Abbr.</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Population size in 2008 (male)</td>
<td>psm</td>
<td>2986</td>
<td>3650</td>
</tr>
<tr>
<td>2</td>
<td>Population size in 2008 (female)</td>
<td>psf</td>
<td>3374</td>
<td>4124</td>
</tr>
<tr>
<td>3</td>
<td>Average male partnership incidence in 2008 (partners/year)</td>
<td>ampi</td>
<td>0.4</td>
<td>0.489</td>
</tr>
<tr>
<td>4</td>
<td>HIV prevalence in 1992 (male)</td>
<td>p92m</td>
<td>0.084</td>
<td>0.112</td>
</tr>
<tr>
<td>5</td>
<td>HIV prevalence in 1992 (female)</td>
<td>p92f</td>
<td>0.096</td>
<td>0.124</td>
</tr>
<tr>
<td>6</td>
<td>HIV prevalence in 2001 (male)</td>
<td>p01m</td>
<td>0.07</td>
<td>0.09</td>
</tr>
<tr>
<td>7</td>
<td>HIV prevalence in 2001 (female)</td>
<td>p01f</td>
<td>0.083</td>
<td>0.107</td>
</tr>
<tr>
<td>8</td>
<td>HIV prevalence in 2007 (male)</td>
<td>p07m</td>
<td>0.06</td>
<td>0.084</td>
</tr>
<tr>
<td>9</td>
<td>HIV prevalence in 2007 (female)</td>
<td>p07f</td>
<td>0.093</td>
<td>0.119</td>
</tr>
<tr>
<td>10</td>
<td>Point prevalence of men with 1 long duration partnership in 2008 (%)</td>
<td>m1l</td>
<td>34.62</td>
<td>42.31</td>
</tr>
<tr>
<td>11</td>
<td>Point prevalence of men with 1 short duration partnership in 2008 (%)</td>
<td>m1s</td>
<td>10.86</td>
<td>13.27</td>
</tr>
<tr>
<td>12</td>
<td>Point prevalence of men with 1 partnership (either type) in 2008 (%)</td>
<td>m1</td>
<td>37.83</td>
<td>46.24</td>
</tr>
<tr>
<td>13</td>
<td>Point prevalence of men with 2+ long duration partnerships in 2008 (%)</td>
<td>m2l</td>
<td>3.38</td>
<td>4.13</td>
</tr>
<tr>
<td>14</td>
<td>Point prevalence of men with 2+ short duration partnerships in 2008 (%)</td>
<td>m2s</td>
<td>1.69</td>
<td>2.07</td>
</tr>
<tr>
<td>15</td>
<td>Point prevalence of men with 2+ partnerships (any combination) in 2008 (%)</td>
<td>m2</td>
<td>8.66</td>
<td>10.59</td>
</tr>
<tr>
<td>16</td>
<td>Point prevalence of women with 2+ long duration partnerships in 2008 (%)</td>
<td>w2l</td>
<td>0.85</td>
<td>1.03</td>
</tr>
<tr>
<td>17</td>
<td>Point prevalence of women with 2+ short duration partnerships in 2008 (%)</td>
<td>w2s</td>
<td>0.42</td>
<td>0.52</td>
</tr>
<tr>
<td>18</td>
<td>Point prevalence of women with 2+ partnerships (any combination) in 2008 (%)</td>
<td>w2</td>
<td>2.17</td>
<td>2.65</td>
</tr>
</tbody>
</table>
One “model run” with the input parameter $x = 0.4$.

If we did not know the analytic solution for $f(x, t)$ this would be generated by numerically solving the differential equation.
• Five model runs with the input parameter varying from $x = 0.1$ to $x = 0.5$
Observed data: 1D example

- Five model runs with the input parameter varying from $x = 0.1$ to $x = 0.5$
- We are going to measure $f(x, t)$ at $t = 3.5$
Observed data: 1D example

- Five model runs with the input parameter varying from $x = 0.1$ to $x = 0.5$
- We are going to measure $f(x, t)$ at $t = 3.5$
Five model runs with the input parameter varying from $x = 0.1$ to $x = 0.5$

- We are going to measure $f(x, t)$ at $t = 3.5$
- The measurement is not a point but comes with measurement error.
Mukwano Output: Male HIV Prevalence (3 Runs)
Mukwano Output: Male HIV Prevalence (10 Runs)
Mukwano Output: Male HIV Prevalence (250 Runs)
• **Design:** Construct a batch of runs of the model using a *space filling* maximin Latin Hypercube design:
Design: Latin Hypercubes

- **Design**: Construct a batch of runs of the model using a space filling maximin Latin Hypercube design:

- These designs are both space filling and approximately orthogonal, both desirable features for fitting emulators.
Design: Latin Hypercubes

- **Design**: Construct a batch of runs of the model using a space filling maximin Latin Hypercube design:

  - These designs are both space filling and approximately orthogonal, both desirable features for fitting emulators.

- We evaluated 250 runs of the model for the first Wave.
Observed data: 1D example

- Five model runs with the input parameter varying from $x = 0.1$ to $x = 0.5$
- We are going to measure $f(x, t)$ at $t = 3.5$
Five model runs with the input parameter varying from $x = 0.1$ to $x = 0.5$

We are going to measure $f(x, t)$ at $t = 3.5$
Observed data: 1D example

- Five model runs with the input parameter varying from $x = 0.1$ to $x = 0.5$
- We are going to measure $f(x, t)$ at $t = 3.5$
- The measurement is not a point but comes with measurement error.
Major question: which values of $x$ ensure the output $f(x, t = 3.5)$ is consistent with the observations?
Major question: which values of $x$ ensure the output $f(x, t = 3.5)$ is consistent with the observations?

It would seem that $x$ has to be at least between 0.3 and 0.4.
To answer this, we can now discard other values of $f(x, t)$ and think of $f(x, t = 3.5)$ as a function of $x$ only.
To answer this, we can now discard other values of $f(x, t)$ and think of $f(x, t = 3.5)$ as a function of $x$ only.

That is take $f(x) \equiv f(x, t = 3.5)$
We can now plot the concentration \( f(x,t) \) as a function of the input parameter \( x \).
We can now plot the concentration $f(x)$ as a function of the input parameter $x$.

- Black horizontal line: the observed measurement of $Y$
We can now plot the concentration $f(x)$ as a function of the input parameter $x$.

- Black horizontal line: the observed measurement of $Y$
- Dashed horizontal lines: the measurement errors
If we know the analytical expression for $Y(k) = \exp(3.5k)$, then we can identify the values of $x$ of interest.
If we know the analytical expression for $Y(k) = \exp(3.5k)$, then we can identify the values of $x$ of interest.

Ignoring the measurement error would lead to a single value for $x$ but this is incorrect: we have to include the errors.
If we know the analytical expression for $Y(k) = \exp(3.5k)$, then we can identify the values of $x$ of interest.

Ignoring the measurement error would lead to a single value for $x$ but this is incorrect: we have to include the errors.
If we know the analytical expression for \( Y(k) = \exp(3.5k) \), then we can identify the values of \( x \) of interest.

Ignoring the measurement error would lead to a single value for \( x \) but this is incorrect: we have to include the errors.
Observed errors and Model Discrepancy: 1D example

- Uncertainty in the measurement of $f(x, t)$ leads to uncertainty in the inferred values of $x$. 
Observed errors and Model Discrepancy: 1D example

- Uncertainty in the measurement of $f(x, t)$ leads to uncertainty in the inferred values of $x$.
- Hence we see a range (green/yellow) of possible values of $x$ consistent with the measurements, with all the implausible values of $x$ in red.
Another important form of uncertainty is that of model discrepancy related to how accurate we believe the model to be.
Another important form of uncertainty is that of model discrepancy related to how accurate we believe the model to be. This uncertainty arises from many issues: is the form of model appropriate, is the model a simplified description of a more complex system etc?
Model discrepancy is represented as uncertainty around the model output $f(x)$ itself: here the purple dashed lines.
• Model discrepancy is represented as uncertainty around the model output $f(x)$ itself: here the purple dashed lines.

• This results in more uncertainty in $x$, and hence a larger range of $x$ values.
We represent the model as a function, which maps the vector of 22 inputs $x$ to the vector of 18 outputs $f(x)$. 
Linking Model to Reality

- We represent the model as a function, which maps the vector of 22 inputs $x$ to the vector of 18 outputs $f(x)$.

- We use the “Best Input Approach” to link the model $f(x)$ to the real system $y$ (i.e. the real Uganda) via:

$$y = f(x^*) + \epsilon$$

where we define $\epsilon$ to be the model discrepancy and assume that $\epsilon$ is independent of $f$ and $x^*$. 
Linking Model to Reality

- We represent the model as a function, which maps the vector of 22 inputs $x$ to the vector of 18 outputs $f(x)$.

- We use the “Best Input Approach” to link the model $f(x)$ to the real system $y$ (i.e. the real Uganda) via:

  $$ y = f(x^*) + \epsilon $$

  where we define $\epsilon$ to be the model discrepancy and assume that $\epsilon$ is independent of $f$ and $x^*$.

- Finally, we relate the true system $y$ to the observational data $z$ by,

  $$ z = y + e $$

  where $e$ represent the observational errors.
Linking Model to Reality

- We represent the model as a function, which maps the vector of 22 inputs $x$ to the vector of 18 outputs $f(x)$.

- We use the “Best Input Approach” to link the model $f(x)$ to the real system $y$ (i.e. the real Uganda) via:

$$y = f(x^*) + \epsilon$$

where we define $\epsilon$ to be the model discrepancy and assume that $\epsilon$ is independent of $f$ and $x^*$.

- Finally, we relate the true system $y$ to the observational data $z$ by,

$$z = y + e$$

where $e$ represent the observational errors.

- We will use the Bayes Linear methodology, which only involves expectations, variances and covariances.
Linking Model to Reality

- It is vital to include both the observed errors $e$ and the model discrepancy $\epsilon$ within the analysis.
Linking Model to Reality

- It is vital to include both the observed errors $e$ and the model discrepancy $\epsilon$ within the analysis.
- For example, not including $\epsilon$ assumes that the model is perfect.
Linking Model to Reality

- It is vital to include both the observed errors $e$ and the model discrepancy $\epsilon$ within the analysis.
- For example, not including $\epsilon$ assumes that the model is perfect.
- Various levels of effort can be put into assessing say $\mathbb{E}[e]$, $\mathbb{E}[\epsilon]$, $\text{Var}(e)$ and $\text{Var}(\epsilon)$, for example, a common assessment is that $\mathbb{E}[e] = 0$ and $\mathbb{E}[\epsilon] = 0$. 
Linking Model to Reality

- It is vital to include both the observed errors $e$ and the model discrepancy $\epsilon$ within the analysis.
- For example, not including $\epsilon$ assumes that the model is perfect.
- Various levels of effort can be put into assessing say $\mathbb{E}[e]$, $\mathbb{E}[\epsilon]$, $\text{Var}(e)$ and $\text{Var}(\epsilon)$, for example, a common assessment is that $\mathbb{E}[e] = 0$ and $\mathbb{E}[\epsilon] = 0$.
- In our first paper on Mukwano the modellers gave the simple assessment that $3\sqrt{\text{Var}(\epsilon)}$ corresponds to approximately 10% of model output.
Linking Model to Reality

- It is vital to include both the observed errors $e$ and the model discrepancy $\epsilon$ within the analysis.
- For example, not including $\epsilon$ assumes that the model is perfect.
- Various levels of effort can be put into assessing say $E[e]$, $E[\epsilon]$, $\text{Var}(e)$ and $\text{Var}(\epsilon)$, for example, a common assessment is that $E[e] = 0$ and $E[\epsilon] = 0$.
- In our first paper on Mukwano the modellers gave the simple assessment that $3\sqrt{\text{Var}(\epsilon)}$ corresponds to approximately 10% of model output.
- In subsequent work we performed far more detailed assessments of internal and external discrepancy by considering model deficiencies and possible model improvements. In prep, but for a list of simple assessment techniques see:

Consider the graph of $f(x,t)$: in general we do not have the analytic solution of $f(x)$, here given by the dashed line.
Consider the graph of $f(x)$: in general we do not have the analytic solution of $f(x)$, here given by the dashed line.
Emulation: 1D example

Consider the graph of \( f(x) \): in general we do not have the analytic solution of \( f(x) \), here given by the dashed line.

Instead we only have a finite number of runs of the model, in this case five.
The emulator can be used to represent our beliefs about the behaviour of the model at untested values of $x$, and is fast to evaluate.
Emulation: 1D example

- The emulator can be used to represent our beliefs about the behaviour of the model at untested values of $x$, and is fast to evaluate.
- Gives the expected value of $f(x)$ (blue line) along with a credible interval for $f(x)$ (red lines) representing the uncertainty about the model’s behaviour.
Mukwano: Emulation

- For each of the 18 outputs we pick active variables $x^A$ then emulate univariately (at first) using:

$$f_i(x) = \sum_j \beta_{ij} g_{ij}(x^A) + u_i(x^A) + \delta_i(x)$$
For each of the 18 outputs we pick active variables $x^A$ then emulate univariately (at first) using:

$$f_i(x) = \sum_j \beta_{ij} g_{ij}(x^A) + u_i(x^A) + \delta_i(x)$$

The $\sum_j \beta_{ij} g_{ij}(x^A)$ is a 3rd order polynomial in the active inputs.
For each of the 18 outputs we pick active variables $x^A$ then emulate univariately (at first) using:

$$f_i(x) = \sum_j \beta_{ij} g_{ij}(x^A) + u_i(x^A) + \delta_i(x)$$

- The $\sum_j \beta_{ij} g_{ij}(x^A)$ is a 3rd order polynomial in the active inputs.
- $u_i(x^A)$ is a Gaussian process.
Mukwano: Emulation

- For each of the 18 outputs we pick active variables $x^A$ then emulate univariately (at first) using:

$$f_i(x) = \sum_j \beta_{ij} g_{ij}(x^A) + u_i(x^A) + \delta_i(x)$$

- The $\sum_j \beta_{ij} g_{ij}(x^A)$ is a 3rd order polynomial in the active inputs.
- $u_i(x^A)$ is a Gaussian process.
- The nugget $\delta_i(x)$ models the effects of inactive variables as random noise.
Mukwano: Emulation

- For each of the 18 outputs we pick active variables $x^A$ then emulate univariately (at first) using:

$$f_i(x) = \sum_j \beta_{ij} g_{ij}(x^A) + u_i(x^A) + \delta_i(x)$$

- The $\sum_j \beta_{ij} g_{ij}(x^A)$ is a 3rd order polynomial in the active inputs.
- $u_i(x^A)$ is a Gaussian process.
- The nugget $\delta_i(x)$ models the effects of inactive variables as random noise.
- The $u_i(x^A)$ have covariance structure given by:

$$\text{Cov}(u_i(x_1^A), u_i(x_2^A)) = \sigma_i^2 \exp[-|x_1^A - x_2^A|^2/\theta_i^2]$$
For each of the 18 outputs we pick active variables $x^A$ then emulate univariately (at first) using:

$$f_i(x) = \sum_j \beta_{ij} g_{ij}(x^A) + u_i(x^A) + \delta_i(x)$$

- The $\sum_j \beta_{ij} g_{ij}(x^A)$ is a 3rd order polynomial in the active inputs.
- $u_i(x^A)$ is a Gaussian process.
- The nugget $\delta_i(x)$ models the effects of inactive variables as random noise.
- The $u_i(x^A)$ have covariance structure given by:

$$\text{Cov}(u_i(x_1^A), u_i(x_2^A)) = \sigma_i^2 \exp[-|x_1^A - x_2^A|^2/\theta_i^2]$$

- The Emulators give the expectation $\mathbb{E}[f_i(x)]$ and variance $\text{Var}[f_i(x)]$ at point $x$ for each output given by $i = 1, \ldots, 20$, and are fast to evaluate.
We perform an initial wave 1 set of \( n \) runs at input locations \( x^{(1)}, x^{(2)}, \ldots, x^{(n)} \), using a Latin hypercube design, giving a column vector of model output values

\[
D_i = (f_i(x^{(1)}), f_i(x^{(2)}), \ldots, f_i(x^{(n)}))^T
\]
Emulation Theory: Bayes Theorem

- We perform an initial wave 1 set of $n$ runs at input locations $x^{(1)}, x^{(2)}, \ldots, x^{(n)}$, using a Latin hypercube design, giving a column vector of model output values

$$D_i = (f_i(x^{(1)}), f_i(x^{(2)}), \ldots, f_i(x^{(n)}))^T$$

- If we had provided prior distributions for each part of the emulator we could use Bayes Theorem to update our beliefs $\pi(f_i(x))$ about $f(x)$:

$$\pi(f_i(x)|D_i) = \frac{\pi(D_i|f_i(x))\pi(f_i(x))}{\pi(D_i)}$$

where $\pi(f_i(x))$ and $\pi(f_i(x)|D)$ are the prior and posterior pdfs for $f_i(x)$. 
We perform an initial wave 1 set of \( n \) runs at input locations \( x^{(1)}, x^{(2)}, \ldots, x^{(n)} \), using a Latin hypercube design, giving a column vector of model output values

\[
D_i = (f_i(x^{(1)}), f_i(x^{(2)}), \ldots, f_i(x^{(n)}))^T
\]

If we had provided prior distributions for each part of the emulator we could use Bayes Theorem to update our beliefs \( \pi(f_i(x)) \) about \( f(x) \):

\[
\pi(f_i(x) | D_i) = \frac{\pi(D_i | f_i(x)) \pi(f_i(x))}{\pi(D_i)}
\]

where \( \pi(f_i(x)) \) and \( \pi(f_i(x) | D) \) are the prior and posterior pdfs for \( f_i(x) \).

This follows the standard Bayesian statistics paradigm, however this involves a detailed, full specification of the joint prior distribution: a complex and difficult task, and is hard to calculate.
Emulation Theory: Bayes Linear Methods

- There is a better way: if we are instead prepared to specify just the expectations, variances and covariances of the parts of the emulator, we can use Bayes Linear methodology.
Emulation Theory: Bayes Linear Methods

- There is a better way: if we are instead prepared to specify just the expectations, variances and covariances of the parts of the emulator, we can use Bayes Linear methodology.

- This is an alternative version of Bayesian statistics that is easier to specify and far easier to calculate with.
Emulation Theory: Bayes Linear Methods

- There is a better way: if we are instead prepared to specify just the expectations, variances and covariances of the parts of the emulator, we can use Bayes Linear methodology.

- This is an alternative version of Bayesian statistics that is easier to specify and far easier to calculate with.

- Instead of Bayes Theorem we use the Bayes linear update:

\[
\begin{align*}
E_D(f_i(x)) &= E(f_i(x)) + \text{Cov}(f_i(x), D_i) \text{Var}(D_i)^{-1}(D_i - E(D_i)) \\
\text{Var}_D(f_i(x)) &= \text{Var}(f_i(x)) - \text{Cov}(f_i(x), D_i) \text{Var}(D_i)^{-1} \text{Cov}(D_i, f_i(x))
\end{align*}
\]

where \(E_D(f_i(x))\) and \(\text{Var}_D(f_i(x))\) are the Bayes Linear adjusted expectation and variance for \(f_i(x)\) at new input point \(x\).
Emulation Theory: Bayes Linear Methods

- There is a better way: if we are instead prepared to specify just the expectations, variances and covariances of the parts of the emulator, we can use Bayes Linear methodology.

- This is an alternative version of Bayesian statistics that is easier to specify and far easier to calculate with.

- Instead of Bayes Theorem we use the Bayes linear update:

$$E_{D_i}(f_i(x)) = E(f_i(x)) + \text{Cov}(f_i(x), D_i)\text{Var}(D_i)^{-1}(D_i - E(D_i))$$

$$\text{Var}_{D_i}(f_i(x)) = \text{Var}(f_i(x)) - \text{Cov}(f_i(x), D_i)\text{Var}(D_i)^{-1}\text{Cov}(D_i, f_i(x))$$

where $E_{D_i}(f_i(x))$ and $\text{Var}_{D_i}(f_i(x))$ are the Bayes Linear adjusted expectation and variance for $f_i(x)$ at new input point $x$.

- For a step by step guide to emulation see the tutorial paper:

Emulating stochastic models

- For a **stochastic model**, whereby $K$ repeated runs of the model at the same input location $x$ gives different output realisations $f^{(k)}(x)$, there are choices over what to emulate.
Emulating stochastic models

- For a stochastic model, whereby $K$ repeated runs of the model at the same input location $x$ gives different output realisations $f^{(k)}(x)$, there are choices over what to emulate.

- A simple choice is to emulate the mean of $f^{(k)}(x)$ in detail, and treat the variance of $f^{(k)}(x)$ as a constant, see:
Emulating stochastic models

- For a stochastic model, whereby $K$ repeated runs of the model at the same input location $x$ gives different output realisations $f^{(k)}(x)$, there are choices over what to emulate.

- A simple choice is to emulate the mean of $f^{(k)}(x)$ in detail, and treat the variance of $f^{(k)}(x)$ as a constant, see:

Emulating stochastic models

- For a **stochastic model**, whereby $K$ repeated runs of the model at the same input location $x$ gives different output realisations $f^{(k)}(x)$, there are choices over what to emulate.

- A simple choice is to emulate the **mean** of $f^{(k)}(x)$ in detail, and treat the **variance** of $f^{(k)}(x)$ as a constant, see:


- Or we can emulate both the **mean** of $f^{(k)}(x)$ and the **(log)-variance** of $f^{(k)}(x)$ in detail, see:
Emulating stochastic models

- For a stochastic model, whereby $K$ repeated runs of the model at the same input location $x$ gives different output realisations $f^{(k)}(x)$, there are choices over what to emulate.

- A simple choice is to emulate the mean of $f^{(k)}(x)$ in detail, and treat the variance of $f^{(k)}(x)$ as a constant, see:


- Or we can emulate both the mean of $f^{(k)}(x)$ and the (log)-variance of $f^{(k)}(x)$ in detail, see:

Emulating stochastic models

- For a **stochastic model**, whereby \( K \) repeated runs of the model at the same input location \( x \) gives different output realisations \( f^{(k)}(x) \), there are choices over what to emulate.

- A simple choice is to emulate the **mean** of \( f^{(k)}(x) \) in detail, and treat the **variance** of \( f^{(k)}(x) \) as a constant, see:


- Or we can emulate both the **mean** of \( f^{(k)}(x) \) and the **(log)-variance** of \( f^{(k)}(x) \) in detail, see:


- We can (try to) emulate any feature of interest of the distribution of \( f(x) \).
Emulating stochastic models
Emulating stochastic models

Female HIV prevalence (1992) vs Design point index
Emulating stochastic models
Comparing the emulator to the observed measurement we again identify the set of $x$ values currently consistent with this data (the observed errors here have been reduced for clarity).
Comparing the emulator to the observed measurement we again identify the set of \( x \) values currently consistent with this data (the observed errors here have been reduced for clarity).

Note: uncertainty on \( x \) now includes uncertainty coming from the emulator.
Implausibility Measures (Univariate)

We can now calculate the Implausibility $I_{(i)}(x)$ at any input parameter point $x$ for each of the $i = 1, \ldots, 11$ outputs. This is given by:

$$I_{(i)}^2(x) = \frac{|E_{D_i}(f_i(x)) - z_i|^2}{(\text{Var}_{D_i}(f_i(x)) + \text{Var}[\epsilon_i] + \text{Var}[\epsilon_i])}$$
Implausibility Measures (Univariate)

We can now calculate the Implausibility $I_{(i)}(x)$ at any input parameter point $x$ for each of the $i = 1, \ldots, 11$ outputs. This is given by:

$$I_{(i)}^2(x) = \frac{|E_{D_i}(f_i(x)) - z_i|^2}{(\text{Var}_{D_i}(f_i(x)) + \text{Var}[\epsilon_i] + \text{Var}[\epsilon_i])}$$

- $E_{D_i}(f_i(x))$ and $\text{Var}_{D_i}(f_i(x))$ are the emulator expectation and variance.
Implausibility Measures (Univariate)

We can now calculate the Implausibility $I_{(i)}(x)$ at any input parameter point $x$ for each of the $i = 1, \ldots, 11$ outputs. This is given by:

$$I_{(i)}^2(x) = \frac{|E_{D_i}(f_i(x)) - z_i|^2}{(\text{Var}_{D_i}(f_i(x)) + \text{Var}[\epsilon_i] + \text{Var}[e_i])}$$

- $E_{D_i}(f_i(x))$ and $\text{Var}_{D_i}(f_i(x))$ are the emulator expectation and variance.
- $z_i$ are the observed data and $\text{Var}[\epsilon_i]$ and $\text{Var}[e_i]$ are the (univariate) Model Discrepancy and Observational Error variances.
Implausibility Measures (Univariate)

We can now calculate the Implausibility \( I(i)(x) \) at any input parameter point \( x \) for each of the \( i = 1, \ldots, 11 \) outputs. This is given by:

\[
I^2_{(i)}(x) = \frac{|E_{D_i}(f_i(x)) - z_i|^2}{(\text{Var}_{D_i}(f_i(x)) + \text{Var}[^{\epsilon_i}] + \text{Var}[^{e_i}])}
\]

- \( E_{D_i}(f_i(x)) \) and \( \text{Var}_{D_i}(f_i(x)) \) are the emulator expectation and variance.
- \( z_i \) are the observed data and \( \text{Var}[^{\epsilon_i}] \) and \( \text{Var}[^{e_i}] \) are the (univariate) Model Discrepancy and Observational Error variances.
- **Large values** of \( I(i)(x) \) imply that we are highly unlikely to obtain acceptable matches between model output and observed data at input \( x \).
Implausibility Measures (Univariate)

We can now calculate the Implausibility $I_{(i)}(x)$ at any input parameter point $x$ for each of the $i = 1, \ldots, 11$ outputs. This is given by:

$$I_{(i)}^2(x) = \frac{|E_{D_i}(f_i(x)) - z_i|^2}{(\text{Var}_{D_i}(f_i(x)) + \text{Var}[\epsilon_i] + \text{Var}[e_i])}$$

- $E_{D_i}(f_i(x))$ and $\text{Var}_{D_i}(f_i(x))$ are the emulator expectation and variance.
- $z_i$ are the observed data and $\text{Var}[\epsilon_i]$ and $\text{Var}[e_i]$ are the (univariate) Model Discrepancy and Observational Error variances.
- **Large values** of $I_{(i)}(x)$ imply that we are highly unlikely to obtain acceptable matches between model output and observed data at input $x$.
- **Small values** of $I_{(i)}(x)$ do not imply that $x$ is good!
Implausibility Measures (Univariate)

We can now calculate the **Implausibility** $I_{(i)}(x)$ at any input parameter point $x$ for each of the $i = 1, \ldots, 11$ outputs. This is given by:

$$I_{(i)}^2(x) = \frac{|E_{D_i}(f_i(x)) - z_i|^2}{(\text{Var}_{D_i}(f_i(x)) + \text{Var}[\xi_i] + \text{Var}[\epsilon_i] + \text{Var}[e_i])}$$

- $E_{D_i}(f_i(x))$ and $\text{Var}_{D_i}(f_i(x))$ are the emulator expectation and variance.
- $z_i$ are the observed data and $\text{Var}[\epsilon_i]$ and $\text{Var}[e_i]$ are the (univariate) Model Discrepancy and Observational Error variances.
- **Large values** of $I_{(i)}(x)$ imply that we are **highly unlikely to obtain acceptable matches between model output and observed data at input $x$**.
- **Small values** of $I_{(i)}(x)$ do not imply that $x$ is good!
Implausibility Measures (Univariate)

We can now calculate the Implausibility $I_{(i)}(x)$ at any input parameter point $x$ for each of the $i = 1, \ldots, 11$ outputs. This is given by:

$$I_{(i)}^2(x) = \frac{|E_{D_i}(f_i(x)) - z_i|^2}{(\text{Var}_{D_i}(f_i(x)) + \text{Var}[\xi_i(x)] + \text{Var}[\epsilon_i] + \text{Var}[\epsilon_i])}$$

- $E_{D_i}(f_i(x))$ and $\text{Var}_{D_i}(f_i(x))$ are the emulator expectation and variance.
- $z_i$ are the observed data and $\text{Var}[\epsilon_i]$ and $\text{Var}[\epsilon_i]$ are the (univariate) Model Discrepancy and Observational Error variances.
- **Large values** of $I_{(i)}(x)$ imply that we are highly unlikely to obtain acceptable matches between model output and observed data at input $x$.
- **Small values** of $I_{(i)}(x)$ do not imply that $x$ is good!
Implausibility Measures (Univariate)

- We can combine the univariate implausibilities across the 11 outputs by maximizing over the current outputs:

\[ I_M(x) = \max_{i \in Q} I_{(i)}(x) \]
Implausibility Measures (Univariate)

- We can combine the univariate implausibilities across the 11 outputs by maximizing over the current outputs:

\[ I_M(x) = \max_{i \in Q} I_{(i)}(x) \]

- We can then impose a cutoff

\[ I_M(x) < c_M \]

in order to discard regions of input parameter space \( x \) that we now deem to be implausible.
Implausibility Measures (Univariate)

• We can combine the univariate implausibilities across the 11 outputs by maximizing over the current outputs:

\[ I_M(x) = \max_{i \in Q} I_{(i)}(x) \]

• We can then impose a cutoff

\[ I_M(x) < c_M \]

in order to discard regions of input parameter space \( x \) that we now deem to be implausible.

• The choice of cutoff \( c_M \) is often motivated by Pukelsheim’s 3-sigma rule, which does not require precise distributions.
Implausibility Measures (Univariate)

- We can combine the univariate implausibilities across the 11 outputs by maximizing over the current outputs:

\[ I_M(x) = \max_{i \in Q} I_i(x) \]

- We can then impose a cutoff

\[ I_M(x) < c_M \]

in order to discard regions of input parameter space \( x \) that we now deem to be implausible.

- The choice of cutoff \( c_M \) is often motivated by Pukelsheim’s 3-sigma rule, which does not require precise distributions.

- We may simultaneously employ other choices of implausibility measure: e.g. multivariate, second maximum etc.
### Multivariate Implausibility Measure

- As we have constructed a multivariate model discrepancy, we can define a **multivariate Implausibility measure**:

\[
I^2(x) = (E[f(x)] - z)^T \text{Var}[f(x) - z]^{-1} (E[f(x)] - z),
\]

which becomes:

\[
I^2(x) = (E[f(x)] - z)^T (\text{Var}[f(x)] + \text{Var}[\epsilon] + \text{Var}[e])^{-1} (E[f(x)] - z)
\]

- where \( \text{Var}[f(x)] \), \( \text{Var}[\epsilon] \) and \( \text{Var}[e] \) are now the multivariate emulator variance, multivariate model discrepancy and multivariate observational errors respectively (all \( 18 \times 18 \) matrices).

- We now have two implausibility measures \( I_M(x) \) and \( I(x) \) that we can use to reduce the input space.

- We impose suitable cutoffs on each measure to define a smaller set of non-implausible inputs.
Comparing the emulator to the observed measurement we again identify the set of values currently consistent with this data (the observed errors here have been reduced for clarity).

- Note: uncertainty on $x$ now includes uncertainty coming from the emulator.
2D Minimised Implausibility Projections: Wave 1

- **Minimised Implausibility Projections**: at each 2D grid point, **minimise** the implausibility $I_M(x)$ over a large 20D hypercube.
2D Minimised Implausibility Projections: Wave 1

- Minimised Implausibility Projections: at each 2D grid point, minimise the implausibility $I_M(x)$ over a large 20D hypercube.
- If a point on these plots is implausible (coloured red), then it will be implausible for any choice of the 15 other inputs.
Minimised Implausibility Projections: at each 2D grid point, minimise the implausibility $I_M(x)$ over a large 20D hypercube.

If a point on these plots is implausible (coloured red), then it will be implausible for any choice of the 15 other inputs.

If a point is green, it may or may not prove to be an acceptable input.
• **Optical Depth Plots**: at each 2D grid point plot the proportion of a large 20D latin hypercube set of points that survive the cutoff $I_M(x) < c_M$. 
• **Optical Depth Plots**: at each 2D grid point plot the proportion of a large 20D latin hypercube set of points that survive the cutoff $I_M(x) < c_M$.

• These plots show the ‘depth’ of the non-implausible volume $\mathcal{X}_j$ for wave $j$, at each grid point.
2D Optical Depth Plots: Wave 2

- **Optical Depth Plots**: at each 2D grid point plot the proportion of a large 20D latin hypercube set of points that survive the cutoff $I_M(x) < c_M$.

- These plots show the ‘depth’ of the non-implausible volume $\chi_j$ for wave $j$, at each grid point.

- Shows where the majority of non-implausible points can be found, but not necessarily where the best matches are.
Minimised Implausibility and Depth Plots (NEEDED?)
Iterative Input Space Reduction: 1D example

- Comparing the emulator to the observed measurement we again identify the set of $x$ values currently consistent with this data (the observed errors here have been reduced for clarity).
- Note: uncertainty on $x$ now includes uncertainty coming from the emulator.
We perform a 2nd iteration or wave of runs to improve emulator accuracy.
We perform a 2nd iteration or wave of runs to improve emulator accuracy. The runs are located only at non-implausible (green/yellow) points.
We perform a 2nd iteration or wave of runs to improve emulator accuracy.

The runs are located only at non-implausible (green/yellow) points.

Now the emulator is more accurate than the observations, and we can identify the set of all $x$ values of interest.
Iterative Input Space Reduction: Mukwano Model Wave 1
Iterative Input Space Reduction: Mukwano Model Wave 4
Iterative Input Space Reduction: Mukwano Model Wave 7
Iterative Input Space Reduction: Mukwano Model Wave 9
Iterative History Matching for Reducing Input Space.

We use an iterative strategy to reduce the input parameter space. Denoting the current non-implausible volume by $\mathcal{X}_j$, at each stage or wave we:
Iterative History Matching for Reducing Input Space.

We use an iterative strategy to reduce the input parameter space. Denoting the current non-implausible volume by $\mathcal{X}_j$, at each stage or wave we:

1. Design and perform a set of runs over the non-implausible input region $\mathcal{X}_j$. 
Iterative History Matching for Reducing Input Space.

We use an iterative strategy to reduce the input parameter space. Denoting the current non-implausible volume by $\mathcal{X}_j$, at each stage or wave we:

1. Design and perform a set of runs over the non-implausible input region $\mathcal{X}_j$
2. Identify the set $Q_{j+1}$ of informative outputs that we can emulate easily
Iterative History Matching for Reducing Input Space.

We use an iterative strategy to reduce the input parameter space. Denoting the current non-implausible volume by $\mathcal{X}_j$, at each stage or wave we:

1. Design and perform a set of runs over the non-implausible input region $\mathcal{X}_j$
2. Identify the set $Q_{j+1}$ of informative outputs that we can emulate easily
3. Construct new emulators for $f_i(x)$, where $i \in Q_{j+1}$ defined only over $\mathcal{X}_j$
Iterative History Matching for Reducing Input Space.

We use an iterative strategy to reduce the input parameter space. Denoting the current non-implausible volume by $\mathcal{X}_j$, at each stage or wave we:

1. Design and perform a set of runs over the non-implausible input region $\mathcal{X}_j$
2. Identify the set $Q_{j+1}$ of informative outputs that we can emulate easily
3. Construct new emulators for $f_i(x)$, where $i \in Q_{j+1}$ defined only over $\mathcal{X}_j$
4. Evaluate the new implausibility functions $I_i(x)$, $i \in Q_{j+1}$ only over $\mathcal{X}_j$
Iterative History Matching for Reducing Input Space.

We use an iterative strategy to reduce the input parameter space. Denoting the current non-implausible volume by $\mathcal{X}_j$, at each stage or wave we:

1. Design and perform a set of runs over the non-implausible input region $\mathcal{X}_j$
2. Identify the set $Q_{j+1}$ of informative outputs that we can emulate easily
3. Construct new emulators for $f_i(x)$, where $i \in Q_{j+1}$ defined only over $\mathcal{X}_j$
4. Evaluate the new implausibility functions $I_i(x) \; i \in Q_{j+1}$ only over $\mathcal{X}_j$
5. Define a new (reduced) non-implausible region $\mathcal{X}_{j+1}$, by $I_M(x) < c_M$, which should satisfy $\mathcal{X} \subset \mathcal{X}_{j+1} \subset \mathcal{X}_j$
Iterative History Matching for Reducing Input Space.

We use an *iterative strategy* to reduce the input parameter space. Denoting the current non-implausible volume by $X_j$, at each stage or *wave* we:

1. Design and perform a set of runs over the non-implausible input region $X_j$
2. Identify the set $Q_{j+1}$ of informative outputs that we can emulate easily
3. Construct new emulators for $f_i(x)$, where $i \in Q_{j+1}$ defined only over $X_j$
4. Evaluate the new implausibility functions $I_i(x), i \in Q_{j+1}$ only over $X_j$
5. Define a new (reduced) non-implausible region $X_{j+1}$, by $I_M(x) < c_M$, which should satisfy $X \subset X_{j+1} \subset X_j$
6. Unless (a) the emulator variances are now small in comparison to the other sources of uncertainty (model discrepancy and observation errors) or (b) computational resources are exhausted or (c) all the input space is deemed implausible, return to step 1
Iterative History Matching for Reducing Input Space.

We use an iterative strategy to reduce the input parameter space. Denoting the current non-implausible volume by $X_j$, at each stage or wave we:

1. Design and perform a set of runs over the non-implausible input region $X_j$
2. Identify the set $Q_{j+1}$ of informative outputs that we can emulate easily
3. Construct new emulators for $f_i(x)$, where $i \in Q_{j+1}$ defined only over $X_j$
4. Evaluate the new implausibility functions $I_i(x)$, $i \in Q_{j+1}$ only over $X_j$
5. Define a new (reduced) non-implausible region $X_{j+1}$, by $I_M(x) < c_M$, which should satisfy $X \subset X_{j+1} \subset X_j$

6. Unless (a) the emulator variances are now small in comparison to the other sources of uncertainty (model discrepancy and observation errors) or (b) computational resources are exhausted or (c) all the input space is deemed implausible, return to step 1

7. If 6(a) true, generate a large number of acceptable runs from the final non-implausible volume $X$, with appropriate sampling.
Why Does Iterative Refocussing Work?

Why do we reduce space in waves? Why not attempt to do it all at once?
Why Does Iterative Refocussing Work?

Why do we reduce space in waves? Why not attempt to do it all at once? Because this requires an accurate emulator valid over whole input space.

• In contrast, the iterative approach is far more efficient, as at each wave the emulators are found to be significantly more accurate. This is expected as:

1. We have ‘zoomed in’ on a smaller part of the function $f(x)$, it will be smoother and most likely easier to fit with low order polynomials.
Why Does Iterative Refocussing Work?

Why do we reduce space in waves? Why not attempt to do it all at once? Because this requires an accurate emulator valid over whole input space.

- In contrast, the iterative approach is far more efficient, as at each wave the emulators are found to be significantly more accurate. This is expected as:

1. We have ‘zoomed in’ on a smaller part of the function $f(x)$, it will be smoother and most likely easier to fit with low order polynomials.
2. We have a much higher density of runs in the new volume, and hence the Gaussian process part of the emulator will do more work.
Why Does Iterative Refocussing Work?

Why do we reduce space in waves? Why not attempt to do it all at once?
Because this requires an accurate emulator valid over whole input space.

- In contrast, the iterative approach is far more efficient, as at each wave the emulators are found to be significantly more accurate. This is expected as:

1. We have ‘zoomed in’ on a smaller part of the function \( f(x) \), it will be smoother and most likely easier to fit with low order polynomials.
2. We have a much higher density of runs in the new volume, and hence the Gaussian process part of the emulator will do more work.
3. We can identify more active variables, leading to more detailed polynomial and Gaussian process parts of the emulator, as previously dominant variables are now somewhat suppressed.
Why Does Iterative Refocussing Work?

Why do we reduce space in waves? Why not attempt to do it all at once? Because this requires an accurate emulator valid over whole input space.

- In contrast, the iterative approach is far more efficient, as at each wave the emulators are found to be significantly more accurate. This is expected as:

1. We have ‘zoomed in’ on a smaller part of the function \( f(x) \), it will be smoother and most likely easier to fit with low order polynomials.

2. We have a much higher density of runs in the new volume, and hence the Gaussian process part of the emulator will do more work.

3. We can identify more active variables, leading to more detailed polynomial and Gaussian process parts of the emulator, as previously dominant variables are now somewhat suppressed.

4. We can hence add more outputs to the set of informative and easy to emulate outputs \( Q_k \).
Why Does Iterative Refocussing Work?

Why do we reduce space in waves? Why not attempt to do it all at once? Because this requires an accurate emulator valid over whole input space.

- In contrast, the iterative approach is far more efficient, as at each wave the emulators are found to be significantly more accurate. This is expected as:

  1. We have ‘zoomed in’ on a smaller part of the function $f(x)$, it will be smoother and most likely easier to fit with low order polynomials.
  2. We have a much higher density of runs in the new volume, and hence the Gaussian process part of the emulator will do more work.
  3. We can identify more active variables, leading to more detailed polynomial and Gaussian process parts of the emulator, as previously dominant variables are now somewhat suppressed.
  4. We can hence add more outputs to the set of informative and easy to emulate outputs $Q_k$.
  5. In the stochastic case we can increase the repetitions.
Why Does Iterative Refocussing Work?

Why do we reduce space in waves? Why not attempt to do it all at once? Because this requires an accurate emulator valid over whole input space.

- In contrast, the iterative approach is far more efficient, as at each wave the emulators are found to be significantly more accurate. This is expected as:

1. We have ‘zoomed in’ on a smaller part of the function $f(x)$, it will be smoother and most likely easier to fit with low order polynomials.

2. We have a much higher density of runs in the new volume, and hence the Gaussian process part of the emulator will do more work.

3. We can identify more active variables, leading to more detailed polynomial and Gaussian process parts of the emulator, as previously dominant variables are now somewhat suppressed.

4. We can hence add more outputs to the set of informative and easy to emulate outputs $Q_k$.

5. In the stochastic case we can increase the repetitions.

- This is a major strength of the History Matching approach.
Mukwano Output: Male HIV Prevalence
Mukwano Output: Male HIV Prevalence (1 Run)
Mukwano Output: Male HIV Prevalence (2 Runs)
Mukwano Output: Male HIV Prevalence (3 Runs)
Mukwano Output: Male HIV Prevalence (10 Runs)
Mukwano Output: Male HIV Prevalence
Mukwano Output: Male HIV Prevalence

Final non-implausible volume: $1.3 \times 10^{-11}$ of the original.
Final non-implausible volume: $1.3 \times 10^{-11}$ of the original.
• Final non-implausible volume: $1.3 \times 10^{-11}$ of the original.

• We can perform a sensitivity analysis on the volume of the non-implausible region, by decreasing the size of each of the four main uncertainty contributions.
- Final non-implausible volume: $1.3 \times 10^{-11}$ of the original.

- We can perform a sensitivity analysis on the volume of the non-implausible region, by decreasing the size of each of the four main uncertainty contributions.

<table>
<thead>
<tr>
<th>Decrease</th>
<th>Observation Error</th>
<th>Emulator Uncertainty</th>
<th>Model Discrepancy</th>
<th>Stochastic Variability</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>19.8</td>
<td>11.8</td>
<td>10.7</td>
<td>54.8</td>
</tr>
<tr>
<td>90%</td>
<td>45.4</td>
<td>24.9</td>
<td>21.9</td>
<td>91.4</td>
</tr>
</tbody>
</table>
Mukwano 2.0

- Our epidemiologists came up with a larger version of Mukwano (96 inputs, 50 outputs)
Mukwano 2.0

- Our epidemiologists came up with a larger version of Mukwano (96 inputs, 50 outputs)
- Simulates HIV transmission under various ART treatment strategies.
Mukwano 2.0

- Our epidemiologists came up with a larger version of Mukwano (96 inputs, 50 outputs)

- Simulates HIV transmission under various ART treatment strategies.

- Predicts the effects of ART on mortality and transmission over the next 15-20 years.
Mukwano 2.0

- Our epidemiologists came up with a larger version of Mukwano (96 inputs, 50 outputs).
- Simulates HIV transmission under various ART treatment strategies.
- Predicts the effects of ART on mortality and transmission over the next 15-20 years.
- A simplified version of history matching was applied.
Mukwano 2.0

- Our epidemiologists came up with a larger version of Mukwano (96 inputs, 50 outputs)
- Simulates HIV transmission under various ART treatment strategies.
- Predicts the effects of ART on mortality and transmission over the next 15-20 years.
- A simplified version of history matching was applied.
- History matching was carried out using emulators based on linear regression.
Mukwano 2.0

- Our epidemiologists came up with a larger version of Mukwano (96 inputs, 50 outputs)
- Simulates HIV transmission under various ART treatment strategies.
- Predicts the effects of ART on mortality and transmission over the next 15-20 years.
- A simplified version of history matching was applied.
- History matching was carried out using emulators based on linear regression.
Proportion starting ART with CD4 250 cells / µl
Optical Depth Plots

Final non-implausible volume: \(2.4 \times 10^{-45}\) of the original.
Minimised Implausibility and Depth Plots

- Male low risk contact rate
  - Baseline transmission
  - Male high concurrency (period 3)
  - Prop. low risk men high conc. 70
History matching provided hundreds of input points that match all the outputs simultaneously.
Mukwano 2.0

- History matching provided hundreds of input points that match all the outputs simultaneously.

- These inputs are used to run the simulator into the future and predict the effect of different ART interventions to mortality, HIV prevalence etc.
• History matching provided hundreds of input points that match all the outputs simultaneously.

• These inputs are used to run the simulator into the future and predict the effect of different ART interventions to mortality, HIV prevalence etc.

• It allows incorporating in the predictions the uncertainty about the values of the input parameters, model discrepancy, observations etc.
History matching provided hundreds of input points that match all the outputs simultaneously.

These inputs are used to run the simulator into the future and predict the effect of different ART interventions to mortality, HIV prevalence etc.

It allows incorporating in the predictions the uncertainty about the values of the input parameters, model discrepancy, observations etc.

The results feed into a number of other research projects that quantify the effect of different ART deployment strategies, costs, etc.
History matching provided hundreds of input points that match all the outputs simultaneously.

These inputs are used to run the simulator into the future and predict the effect of different ART interventions to mortality, HIV prevalence etc.

It allows incorporating in the predictions the uncertainty about the values of the input parameters, model discrepancy, observations etc.

The results feed into a number of other research projects that quantify the effect of different ART deployment strategies, costs, etc.

We can hence use the above approach to make decisions about the most effective intervention, but also to design the most efficient data collection campaign.
• Using the emulator we can choose several values of $x$ consistent with the measurement of $f(x, t)$ at $t = 3.5$, and perform corresponding runs of the model.
Designing new experiment: 1D example

- Using the emulator we can choose several values of $x$ consistent with the measurement of $f(x, t)$ at $t = 3.5$, and perform corresponding runs of the model.
Designing new experiment: 1D example

- Using the emulator we can choose several values of $x$ consistent with the measurement of $f(x, t)$ at $t = 3.5$, and perform corresponding runs of the model.
- We can check the predictions made by these runs for $Y(t = 2)$. 
Designing new experiment: 1D example

- Using the emulator we can choose several values of \( x \) consistent with the measurement of \( f(x, t) \) at \( t = 3.5 \), and perform corresponding runs of the model.
- We can check the predictions made by these runs for \( Y(t = 2) \).
Designing new experiment: 1D example

- The predictions imply that any measurement of $Y(t = 2)$ is highly unlikely to be informative for $x$.
- This is due to the measurement errors swamping the signal from the model output $Y(t = 2)$. 
The predictions for $Y(t = 5)$ show a different conclusion.
The predictions for $Y(t = 5)$ show a different conclusion.
The predictions for $Y(t = 5)$ show a different conclusion.

For each possible measurement of $Y(t = 5)$ it is highly likely that we will be able to rule out several more values of $x$ as implausible.
For one possible measurement, see that non-implausible values of $x$ would lie between 0.344 and 0.354, ruling out 70% of the possible values of $x$. 
Designing new experiment: 1D example

- For one possible measurement, see that non-implausible values of \( x \) would lie between 0.344 and 0.354, ruling out 70% of the possible values of \( x \).
- This high expected space reduction in \( x \) implies that Experiment B, measuring \( f(x, t) \) at \( t = 5 \), is clearly the best choice.
Final Concluding Comments

- We have a broad methodology for performing full uncertainty analyses on such complex models of disease.
Final Concluding Comments

- We have a broad methodology for performing full uncertainty analyses on such complex models of disease.

- The correct treatment of uncertainty is vital: without this, any analysis will be problematic and untrustworthy.
Final Concluding Comments

- We have a broad methodology for performing full uncertainty analyses on such complex models of disease.

- The correct treatment of uncertainty is vital: without this, any analysis will be problematic and untrustworthy.

- The emulation methods we describe can be used to exhaustively explore model features (helpful when developing models).
Final Concluding Comments

- We have a broad methodology for performing full uncertainty analyses on such complex models of disease.

- The correct treatment of uncertainty is vital: without this, any analysis will be problematic and untrustworthy.

- The emulation methods we describe can be used to exhaustively explore model features (helpful when developing models).

- Due to the need to synthesis many sources of uncertainty within one coherent calculation, a Bayesian approach is ideal.
References

References


References


References

Vernon, I.; Goldstein, M.; Bower, R. G.; Galaxy Formation: “Bayesian History Matching for the Observable Universe”.


References


References


References


References


