The human sex odds at birth in France: a **provisional** geo-spatial-temporal approach in the vicinity of nuclear facilities

- Centre de Stockage (CdS) de l'Aube (Champagne-Ardenne)
- Institute Laue-Langevin (ILL) de Grenoble
- Commissariat à l'Énergie Atomique (CEA) de Saclay/Paris

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HELENA Workshop: **Organism and Ecosystem Functioning**, 25./26. 6. 2013 Monastery Scheyern, Germany
Content

- Preliminary Note
- Background and Motivation
- Data and Statistical Methods
- Results
  - TBL Gorleben, Germany
  - CdS l’Aube
  - ILL Grenoble
  - CEA Saclay
    - Control region Bure (rock laboratory for final HAW storage)
- Conclusion
- Outlook
Preliminary note

➢ Mankind as a “biologic and social system” has an important stabilizing function, which is not well understood: mankind sustains a nearly constant gender proportion at birth equivalent to **105 : 100** (male : female)

<table>
<thead>
<tr>
<th>Example* USA + Europe combined 1975 – 2007</th>
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<tbody>
<tr>
<td>• births 392 932 591</td>
</tr>
<tr>
<td>• male 201 748 551</td>
</tr>
<tr>
<td>• female 191 184 040</td>
</tr>
<tr>
<td>• Sex Odds SO 1.0553</td>
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<tr>
<td>• StdErr[ log(SO) ] 0.0001</td>
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<tr>
<td>• 95%-CI [1.0551, 1.0555]</td>
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</tbody>
</table>

➢ Changes of the biological parameter SO may be a sign of genetic damage

➢ We study spatial-temporal determinants of the sex odds at the municipality level

Preliminary note

- Side effect of our presentation

Illustration of the bio-statistical and epidemiological “tool box”

- Hypothesis
- Distribution (theoretical vs. empirical, underdispersion vs. overdispersion)
- Test
- Confidence Limits
- p-value
- Logistic Regression
- Poisson Regression
- Nonlinear Regression
- Statistical Modeling
- Modeling Strategies
- Variable Selection
- Change-Point Analysis
- Exploratory Analysis
- Data Mining
- Coping with large Data Sets
Background and Motivation  Bomb Tests – Accidents – Reactors – etc.

Cumulative Emissions of Radio Nuclides – Increasing Pollution of the Biosphere
Background and Motivation  Radiation induced genetic effects

Muller
X-ray mutagenesis in 1927

In 1946 Muller was awarded the Nobel Prize in Physiology or Medicine, "for the discovery that mutations can be induced by X-rays".

Pauling
1954 Nobel Prize in Chemistry
1962 Nobel Peace Prize

In 1958, Pauling and his wife presented the United Nations with the petition signed by more than 11,000 scientists calling for an end to nuclear-weapon testing.

Neel

“Ionizing radiation can and undoubtedly does produce lethal mutations associated with the X chromosome, and under the simplest of circumstances these mutations may lead to an altered sex ratio among progeny born subsequent to exposure” (1966).
Background and Motivation   Sex determining mechanism

Female

Male

X chromosome
Y chromosome

Sex chromosomes
Background and Motivation  Sex Ratio or Sex Odds - terminology

- **Sex Ratio (SR)** is the pertinent term for the number of newborn boys divided by the number of newborn girls

  \[ SR = \frac{\text{boys}}{\text{girls}} = \frac{m}{f} \]

- The **male probability**

  \[ p_{\text{male}} = \frac{\text{boys}}{\text{girls} + \text{boys}} = \frac{m}{m+f} \]

  leads to the more appropriate **Sex Odds (SO)**

  \[ SO = \frac{p_{\text{male}}}{1 - p_{\text{male}}} = \frac{\text{boys}}{\text{girls}} = SR \]

- Comparing two **SO** leads to the obvious and natural measure **Sex Odds Ratio**

  \[ \text{SOR} = \frac{SO_{\text{exposed}}}{SO_{\text{nonexposed}}} \]

- The **inconvenient term** **Sex Ratio Ratio** is avoided

  (in German: Geschlechtsverhältnisverhältnis vs. Geschlechtschancenverhältnis)
Background and Motivation  
Radiation induced genetic effects

Genetic theory for the human sex odds at birth

Irradiated parents and offspring gender sex odds

- Fathers only => sex odds ↑
- Mothers only => sex odds ↓
- Both parents => ???

**Background and Motivation**  

**Chernobyl: Sex Odds in Europe**

### 39 European countries 1975 – 2007; USA 1975 – 2002

![Graph showing live births sex odds over time for Europe and USA, with a Chernobyl gender gap highlighted.](image)

### Criterion

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>DF</th>
<th>Value/DF</th>
<th>Pr &gt; ChiSq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deviance</td>
<td>56.92</td>
<td>54</td>
<td>1.054</td>
<td>0.367</td>
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<tr>
<td>Pearson</td>
<td>56.92</td>
<td>54</td>
<td>1.054</td>
<td>0.367</td>
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</table>

(N= 393 million births)

### Analysis of Maximum Likelihood Estimates

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Error</th>
<th>Chi-Square</th>
<th>Pr &gt; ChiSq</th>
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<tr>
<td>Intercept</td>
<td>0.0533</td>
<td>0.000401</td>
<td>17635.6787</td>
<td>&lt;.0001</td>
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<td>-0.00224</td>
<td>0.000251</td>
<td>79.5937</td>
<td>&lt;.0001</td>
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<td>-0.00247</td>
<td>0.000543</td>
<td>20.7330</td>
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<td>d87</td>
<td>0.00200</td>
<td>0.000523</td>
<td>14.5855</td>
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<td>t87</td>
<td>0.00419</td>
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<td>36.8871</td>
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<td>dusa</td>
<td>-0.00423</td>
<td>0.000451</td>
<td>88.1824</td>
<td>&lt;.0001</td>
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**Excellent compliance with the binomial assumption**
As learned from the Atomic Bomb Tests and from Chernobyl, the human secondary sex odds (SO) at birth (male : female) is a simple and sensitive genetic health indicator. As childhood cancer is elevated near nuclear power plants, we looked after the sex odds at the municipality level in Germany and Switzerland and found increased sex odds within 5 – 40 km circular discs around nuclear facilities (NF).


Is the human sex odds at birth distorted in the vicinity of nuclear facilities (NF)? A preliminary geo-spatial-temporal approach, EnviroInfo 2010, Proceedings of the, 24th International Conference on Informatics for Environmental Protection, Cologne / Bonn, Germany

Scherb H, Voigt K.

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Is the human sex odds at birth distorted in the vicinity of nuclear facilities in France?
Data and Statistical Methods  France convenient – centralist country

36 561 municipalities, 1968 – 2007
1 281 729 municipality years
30 018 962 total live births
15 386 928 male live births
14 632 034 female live births
SO 1.0516

Source: Etat civil INSEE [producteur], Centre Maurice Halbwachs (CMH) [diffuseur]
Secular downward trend and logistic regression line

France municipality level data: SOR/10 years = \(-0.125\%\), p-value 0.0002

Source: Etat civil INSEE [producteur], Centre Maurice Halbwachs (CMH) [diffuseur]
Logistic regression for modeling and significance testing of determinants of the outcome of a binomial variable, e.g. boys among newborn children

Sample SAS code for logistic regression and nonlinear regression of log odds data

Simple jump function – time trend

*Comment: m=male, f=female;

data a; set a;
d35=0;
if km < 35 then d35=1;
run;

proc logistic data=a;
model m/(m+f) = d35/scale=d;
run;

Rayleigh function – spatial trend

*Comment: m=male, f=female;

data nlin; set nlin;
x=km;
so=m/f;
z=log(so);
var=1/m+1/f;
w=1/var;
run;

proc nlin data=nlin;
parms a=.00 b=.05 c=20;
model z = a + b*(x/c)*exp(-((x/c)**2-1)/2);
der.a=1;
der.b=(x/c)*exp(-((x/c)**2-1)/2);
der.c= -b*(x/c**2)*exp(-((x/c)**2-1)/2) + b*(x**3/c**4)*exp(-((x/c)**2-1)/2);
_weight_=w;
run;
Results  TBL Gorleben, CdS l’Aube, CEA Saclay, and ILL Grenoble

- **Transportbehälterlager (TBL) Gorleben, Germany**
  Gorleben is a radioactive waste disposal site, currently used as an intermediate storage facility planned to serve as a future deep final repository for waste from nuclear reactors.

- **Centre de stockage (CdS) de l'Aube, France**
  Disposal facility for intermediate and low level short lived waste. Disposal of waste resulting from processing of the spent fuel ????

- **Commissariat à l'Énergie Atomique (CEA) de Saclay/Paris**
  The Saclay Nuclear Research Centre is one of 9 laboratories belonging to the CEA.

- **ILL Grenoble, France**
  The Institut Laue–Langevin, founded in 1967 and honoring the physicists Max von Laue and Paul Langevin, provides one of the most intense neutron sources in the world.
### Results

Local data for Gorleben, l’Aube, Saclay, and Grenoble

<table>
<thead>
<tr>
<th>Year</th>
<th>Births within 30 km from the TBL Gorleben</th>
<th>Births within 30 km from the CdS de l’Aube</th>
<th>Births within 5 km from the CEA Saclay</th>
<th>Births within 80 km from the ILL Grenoble</th>
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<tbody>
<tr>
<td></td>
<td>total</td>
<td>male</td>
<td>female</td>
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<td>1968</td>
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<td>2011</td>
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</tbody>
</table>

Total: 27584 14163 13421 31501 16076 15425 47805 24654 23151 1027170 527809 499361
Results  Time trend for Gorleben area – 1996 HAW from la Hague

30 km from TBL Gorleben; jump 1998 SOR 1.148; p-value = 0.0011
Results  Spatial trend for TBL Gorleben

SOR from 1996 to 2011 vs. from 1981 to 1995; F-test p-value = 0.0091
Results  Sensitivity and Specificity of the effect

- **Preliminary analysis, data not yet complete**
  (e.g. Saxony & Thuringia not included – German reunification!)

- Paneling of Germany by 70 x 70 km\(^2\) squares
  (≈ 40 km radius circular discs)
  grid centered precisely at TBL Gorleben

- 1\(^{st}\) Castor transported to Gorleben April 1995

- Testing the uniform, parsimonious, one-sided null hypotheses in all 70 x 70 km\(^2\) squares:
  “No Sex Odds upward jump from 1996 onward”

- **Conclusions**

Gorleben is unique in Germany with a one-sided p-value of 0.0012 < 0.0020, see:
http://www.nlga.niedersachsen.de/download/60794

Next to Gorleben is Ellweiler (p=0.0121), which is a “closed” nuclear processing and storage site
with possible radioactive releases in January 1995: damage of coverings and erosion of the waste dump
after strong rainfall, see:
http://dip21.bundestag.de/dip21/btd/13/006/1300610.asc
Results  Time trend for l’Aube area – any incidents around 2000 ?! *

30 km from CdS de l’Aube; jump 2000 SOR 1.178; p – value <  0.0001

Results \hspace{1cm} Local absolute births for l’Aube – synoptic Poisson model

30 km CdS de l’Aube; synoptic Poisson model with 3.4 % overdispersion and \( p \)-value 0.4145

Deficit: 394 girls, \( p \)-value < 0.0001
Results  Time trend for Saclay – Accident in July 1979

5 km from Saclay; jump 1979 SOR 1.060; p-value = 0.0144

Live Births (LB) Sex Odds (SO)

CEA Saclay Accident July 1979
Results  Time trends for Grenoble 80 km area

80 km from ILL Grenoble; SOR 1.005 vs. rest of France (brk. line); p-value = 0.0166
Results  Spatial analysis only: ILL Grenoble

Spatial trend of the live births sex odds in 10 km distance categories around the Institut Laue-Langevin (ILL) at Grenoble 1968 - 2007

Rayleigh function for SO around ILL Grenoble; F-test p-value = 0.0482
Results  **Spatial-temporal analyses: control region Bure**

Control region **Bure**, rock laboratory for studying long-time HAW disposal techniques, first boring in 1994

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![Graph showing live births (LB) sex odds (SO) from 1966 to 2014 with a constant SO of 1.0570 and 95% CI of [1.0385, 1.0758]](image-url)
Results  **Spatial-temporal analyses: control region Bure**

Control region **Bure**, rock laboratory for studying long-time HAW disposal techniques, first boring in 1994, no significant “after-vs.-before–effect”

*SOR from 1994 to 2007 vs. from 1968 to 1993; F-test p-value = 0.2708*
Results Possible consequences

- Within 30 km from l’Aube or Gorleben there is a theoretical **deficit of 720 girls** in the combined period*region up to 8 years from 2000 onward (l’Aube) and from 1998 onward (Gorleben), respectively

- Within 80 km from the ILL Grenoble there is a theoretical **deficit of 2994 girls** from 1968 to 2007 compared to the remainder of France

- Under the somewhat speculative assumption of a sex odds of 3:10 among the “missing children”, we obtain approximately twice the figures for missing girls as missing children, i.e. $\approx 1400$ and $6000$ missing children for l’Aube/Gorleben and ILL Grenoble, respectively; see our publications

- There is no corresponding spatial and/or temporal effect at the Control Site Rock Laboratory Bure, France
“Low-dose” ionizing radiation increases the secondary sex odds in humans. The preliminary long term sex odds ratio is in the range of 1.01 to 1.02 per mSv/year.

Our results disprove the prevailing believe (e.g. by UNSCEAR) that radiation-induced genetic effects have yet to be detected in human populations.

For fundamental criticism concerning the basis of radiation safety standards see The Lesvos Declaration, 6 May 2009 or the book Fukushima and Health: What to Expect (Documents of the ECRR).

The culprit of the many effects observed and reported may be incorporated radionuclides inadequately assessed by the radiological sciences.
Outlook (own research)

- Continuation of Studies concerning low dose ionizing radiation and Sex Odds
- Germany (old Bundesländer – former GDR)
- France (large number of nuclear facilities not yet considered)
- Next publications: Nuclear Facilities international, Sex Odds in Cuba
  Storage sites like Jülich, Ahaus, Lubmin in Germany
- Collaboration with other scientific disciplines, e.g. Epidemiology Genetics
Outlook (general)

- Important data on underestimated environmental and health topics exist.
- However, often there is no (optimal) utilization of the existing data bases.
- Thus, greater input from mathematics, statistics, and computer science is needed to scrutinize those data.
- To achieve this goal, the full spectrum of different data analysis approaches should be considered and applied appropriately.
- Improved interdisciplinary skills are needed at all stages of environmental health research.
Outlook (general)  Russia vs. Cuba: Publication under Review
The human sex odds at birth in France in the vicinity of nuclear facilities

Thank you for your attention

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