ゲノム情報解析入門

Introduction to genome bioinformatics

2020.10.27　　　@W214

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ゲノム情報解析入門

1. ゲノムデータ解析のためのPython入門

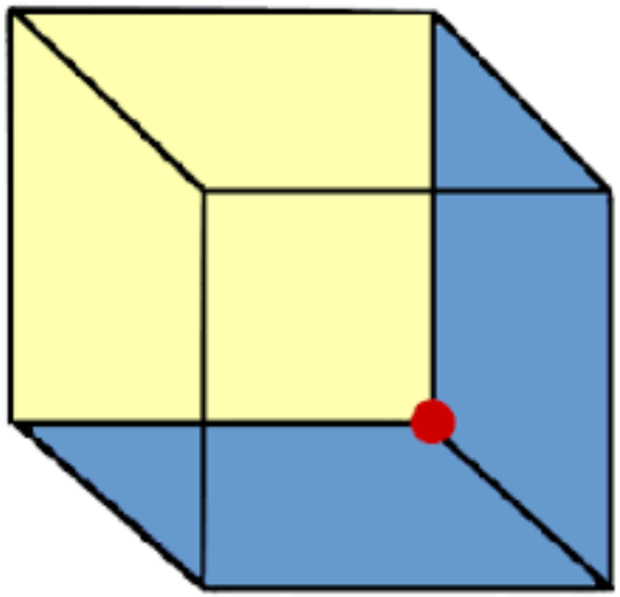
2. Bayesian inference (ベイズ推定）
3. Machine Learning （機械学習）
4. Systems Biology （システム生物学）

認識論 Epistemology

Necker Cube

Introduction: the “selfish gene”

In the preface to the second edition of his bestselling book, *The Selfish Gene,* Richard Dawkins used the metaphor of a Necker cube – a two-dimensional drawing of a three-dimensional object that can be perceived in different ways – in order to explain the intent behind his inspired metaphor: “My point is that there are two ways of looking at natural selection, the gene’s angle and that of an individual….It is a different way of seeing, not a different theory” (Dawkins 1989/1976, pp. x-xi).



Before the Concept of Evolution

Plato Idea

Essentialism（本質主義）

Aristotle Immutable essences ->

species have fixed properties

Christianity God has created species as seen now

大陸合理論 ←→ イギリス経験論

Essentialism

本質主義

本質主義（ほんしつしゅぎ、英: essentialism）とは、本質（事物の変化しない核心部分）を自立的な実体、客体的な実在物であるとみなした上で、個別の事物は必ずその本質を有し、それによってその内実を規定されている、という考えをいう。

さらに具体的に、社会科学や政治的な議論において、一定の集団やカテゴリーに、超時間的で固定的な本質を想定する立場を指していうことが多い。

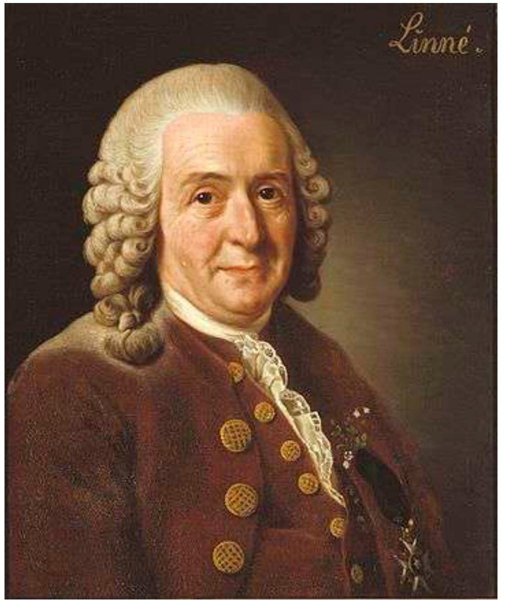
事物とその本質との関係は客観的で固定的なものであり、個物は本質の派生物、あるいは複製としての側面を持つものとみなされる。

また、すくなくとも論理的な順序としては、本質が現実存在に先立つものとされ、本質が現実存在から事後的に抽出・構成されるとは考えない。事物とその本質との関係はアプリオリなものであるから、事物が現実に存在する文脈からは独立しており、その事物がその事物である限り、その本質は同一不変であるとみなされる。

Source: Wikipedia

Carl von Linné　(1707-78)

Systema Naturae (1735)



「分類学の父」

- 動植物についての情報を整理して分類表を作り、その著書『自然の体系』(Systema Naturae、1735年)において、生物分類を体系化した。その際、それぞれの種の特徴を記述し、類似する生物との相違点を記した。これにより、近代的分類学がはじめて創始された。

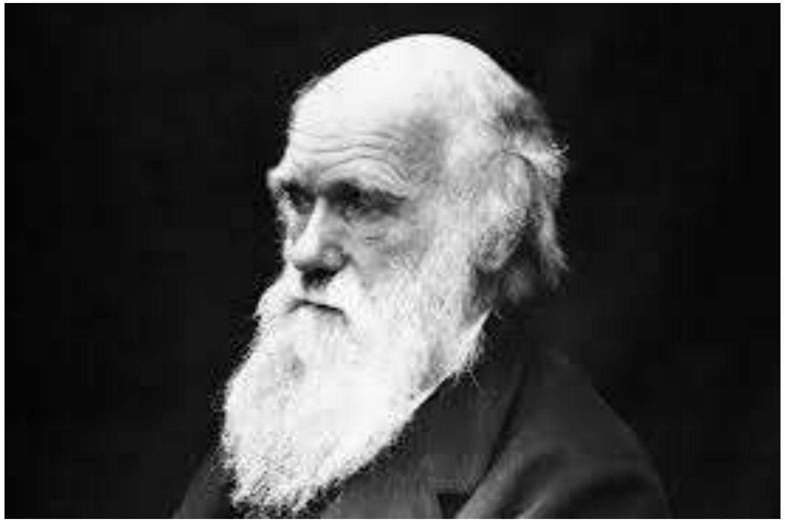
- 生物の学名を、属名と種小名の2語のラテン語で表す二名法(または二命名法)を体系づけた。ラテン語は「西洋の漢文」であり、生物の学名を2語のラテン語に制限することで、学名が体系化されるとともに、その記述が簡潔になった。現在の生物の学名は、リンネの考え方に従う形で、国際的な命名規約[2]に基づいて決定されている。

- 分類の基本単位である種のほかに、綱、目、属という上位の分類単位を設け、それらを階層的に位置づけた。後世の分類学者たちがこの分類階級をさらに発展させ、現代おこなわれているような精緻な階層構造を作り上げた。

Source: Wikipedia

神の創造によるデザインを区分することに努めた

栽培植物を含めて全ての生物は進化の結果、現在存在する



Charles Darwin
1809-1882

「種の起源」1859

「家畜と栽培植物の変異」 1868

Empiricism

David Hume

David Hume (/hjuːm/; born **David Home**; 7 May 1711 NS (26 April 1711 OS) – 25 August 1776) was a Scottish philosopher, historian, economist, and essayist, who is best known today for his highly influential system of philosophical empiricism, skepticism, and naturalism. Hume's empiricist approach to philosophy places him with John Locke, Francis Bacon and Thomas Hobbes as a British Empiricist.[3] Beginning with his *A Treatise of Human Nature* (1739), Hume strove to create a total naturalistic science of man that examined the psychological basis of human nature. Against philosophical rationalists, Hume held that passion rather than reason governs human behaviour. Hume argued against the existence of innate ideas, positing that all human knowledge is founded solely in experience; Hume thus held that genuine knowledge must either be directly traceable to objects perceived in experience, or result from abstract reasoning about relations between ideas which are derived from experience, calling the rest "nothing but sophistry and illusion",[4] a dichotomy later given the name *Hume's fork*.

David Hume	
	
Born	David Home 7 May NS [26 April OS] 1711 Edinburgh, Scotland

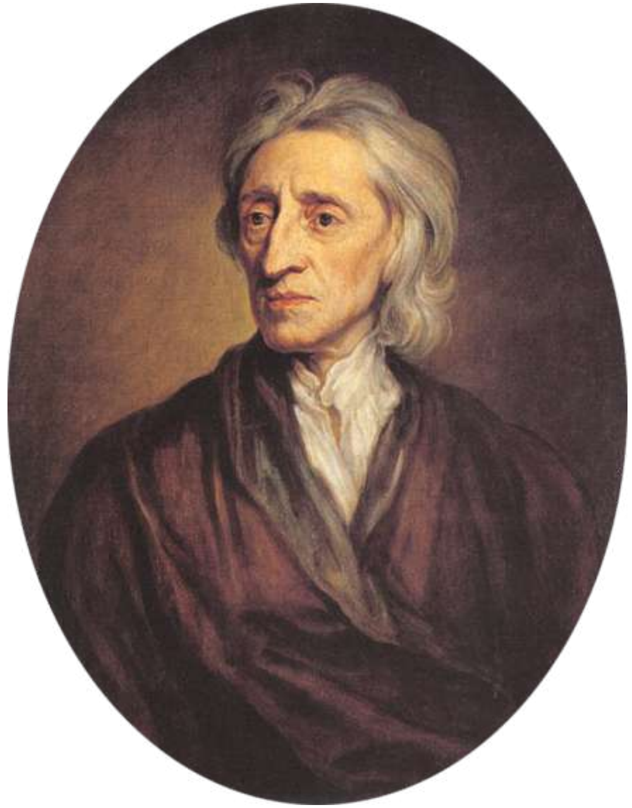
Source: Wikipedia

Empiricism

In philosophy, **empiricism** is a theory that states that knowledge comes only or primarily from sensory experience.[1] It is one of several views of epistemology, the study of human knowledge, along with rationalism and skepticism. Empiricism emphasises the role of empirical evidence in the formation of ideas, over the idea of innate ideas or traditions;[2] empiricists may argue however that traditions (or customs) arise due to relations of previous sense experiences.[3]

Empiricism in the philosophy of science emphasises evidence, especially as discovered in experiments. It is a fundamental part of the scientific method that all hypotheses and theories must be tested against observations of the natural world rather than resting solely on a priori reasoning, intuition, or revelation.

Empiricism, often used by natural scientists, says that "knowledge is based on experience" and that "knowledge is tentative and probabilistic, subject to continued revision and falsification."[4] Empirical research, including experiments and validated measurement tools, guides the scientific method.



John Locke (1632–1704), a leading philosopher of British empiricism

Source: Wikipedia

Thomas Bayes

From Wikipedia, the free encyclopedia

Thomas Bayes (/beɪz/; c. 1701 – 7 April 1761)[2][3][note a] was an English statistician, philosopher and Presbyterian minister who is known for formulating a specific case of the theorem that bears his name: Bayes' theorem. Bayes never published what would become his most famous accomplishment; his notes were edited and published after his death by Richard Price.[4]

Thomas Bayes

Portrait purportedly of Bayes used in a 1936 book,[1] but it is doubtful whether the portrait is actually of him.[2] No earlier portrait or claimed portrait survives.

Born	c. 1701 London, England
Died	7 April 1761 (aged 59) Tunbridge Wells, Kent, England
Residence	Tunbridge Wells, Kent, England
Nationality	British
Alma mater	University of Edinburgh

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2 Bayes' theorem
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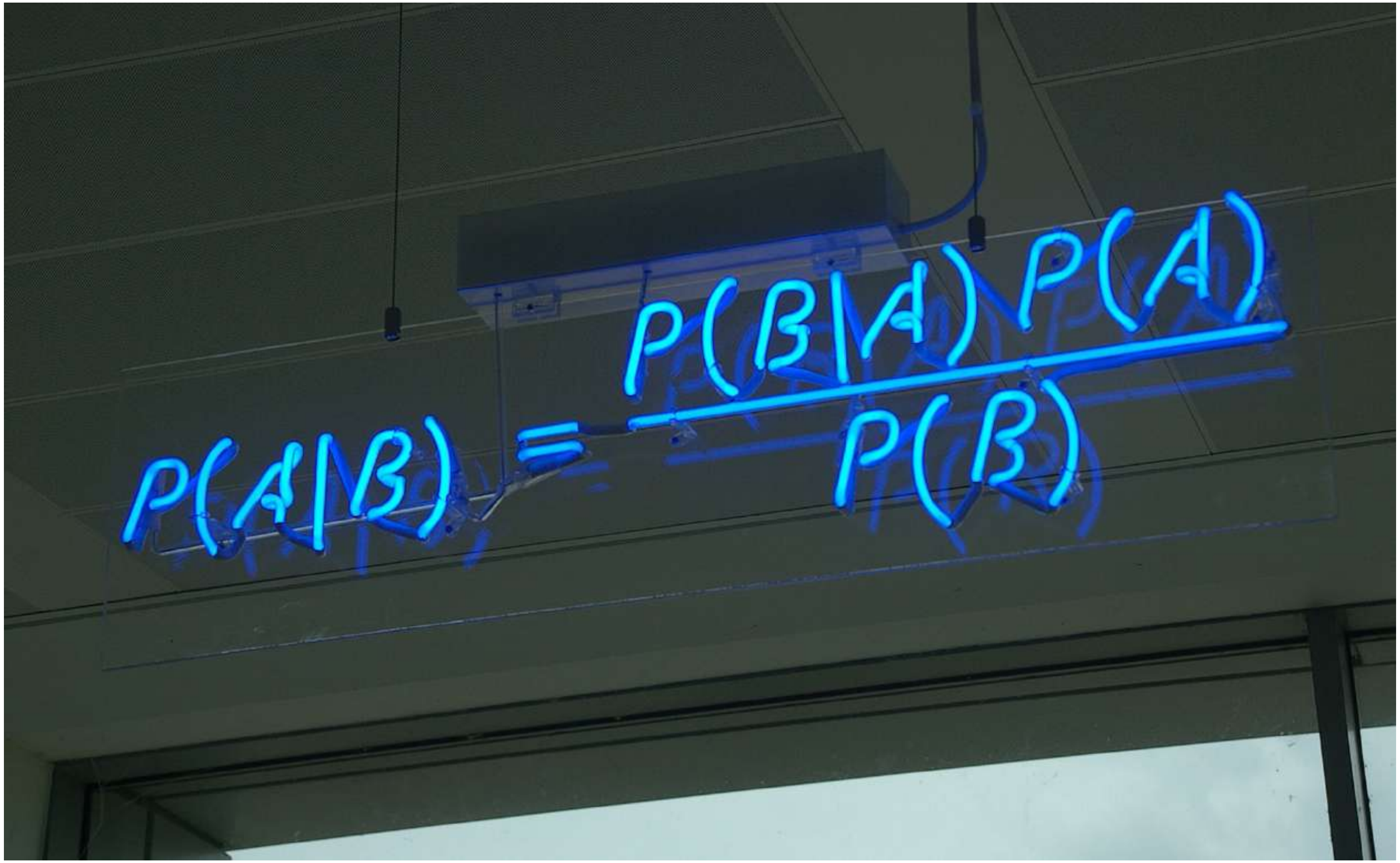
Biography [edit]

Thomas Bayes was the son of London Presbyterian minister Joshua Bayes,[5] and was possibly born in Hertfordshire.[6] He came from a prominent nonconformist family from Sheffield. In 1719, he enrolled at the University of Edinburgh to study logic and theology. On his return around 1722, he assisted his father at the latter's chapel in London before moving to Tunbridge Wells, Kent, around 1734. There he was minister of the Mount Sion chapel, until 1752.[7]

Source: Wikipedia

Bayesian inference

Bayesian inference is a method of statistical inference in which Bayes' theorem is used to update the probability for a hypothesis as more evidence or information becomes available. Bayesian inference is an important technique in statistics, and especially in mathematical statistics. Bayesian updating is particularly important in the dynamic analysis of a sequence of data. Bayesian inference has found application in a wide range of activities, including science, engineering, philosophy, medicine, sport, and law. In the philosophy of decision theory, Bayesian inference is closely related to subjective probability, often called "Bayesian probability".



Source: Wikipedia

Thomas Bayes 1701-1761

Bayesian Inference

https://www.youtube.com/watch?v=-e8wOcaascM

$$P(\theta|\text{data}) = [P(\text{data}|\theta) \times P(\theta)] / P(\text{data})$$

Pierre-Simon Laplace

From Wikipedia, the free encyclopedia

"Laplace" redirects here. For other uses, see Laplace (disambiguation).

Pierre-Simon, marquis de Laplace (/ləˈplɑːs/; French: [pjɛʁ simɔ̃ laplas]; 23 March 1749 – 5 March 1827) was a French scholar and polymath whose work was important to the development of engineering, mathematics, statistics, physics, astronomy, and philosophy. He summarized and extended the work of his predecessors in his five-volume *Mécanique Céleste* (*Celestial Mechanics*) (1799–1825). This work translated the geometric study of classical mechanics to one based on calculus, opening up a broader range of problems. In statistics, the Bayesian interpretation of probability was developed mainly by Laplace.[2]

Laplace formulated Laplace's equation, and pioneered the Laplace transform which appears in many branches of mathematical physics, a field that he took a leading role in forming. The Laplacian differential operator, widely used in mathematics, is also named after him. He restated and developed the nebular hypothesis of the origin of the Solar System and was one of the first scientists to postulate the existence of black holes and the notion of gravitational collapse.

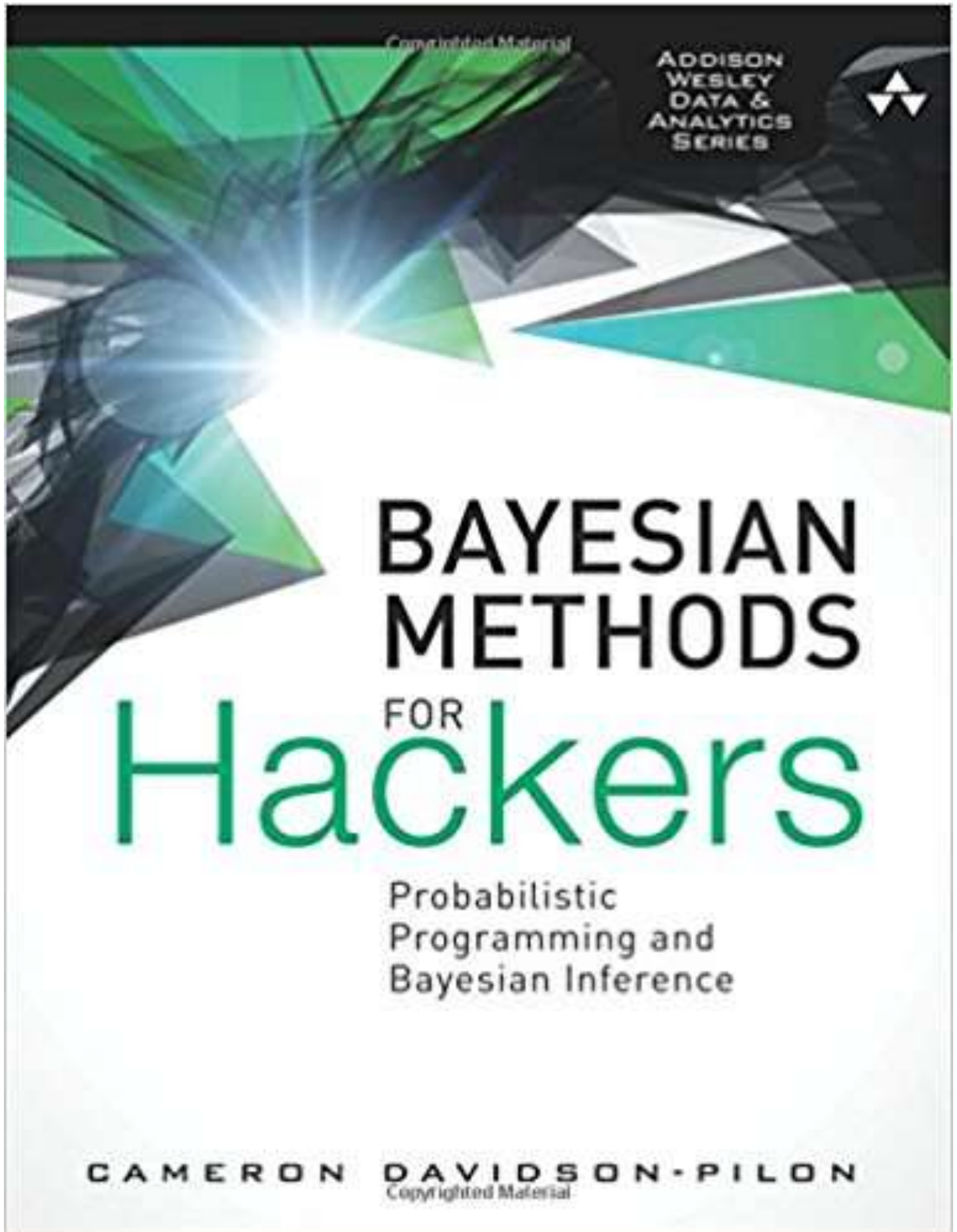
Pierre-Simon Laplace

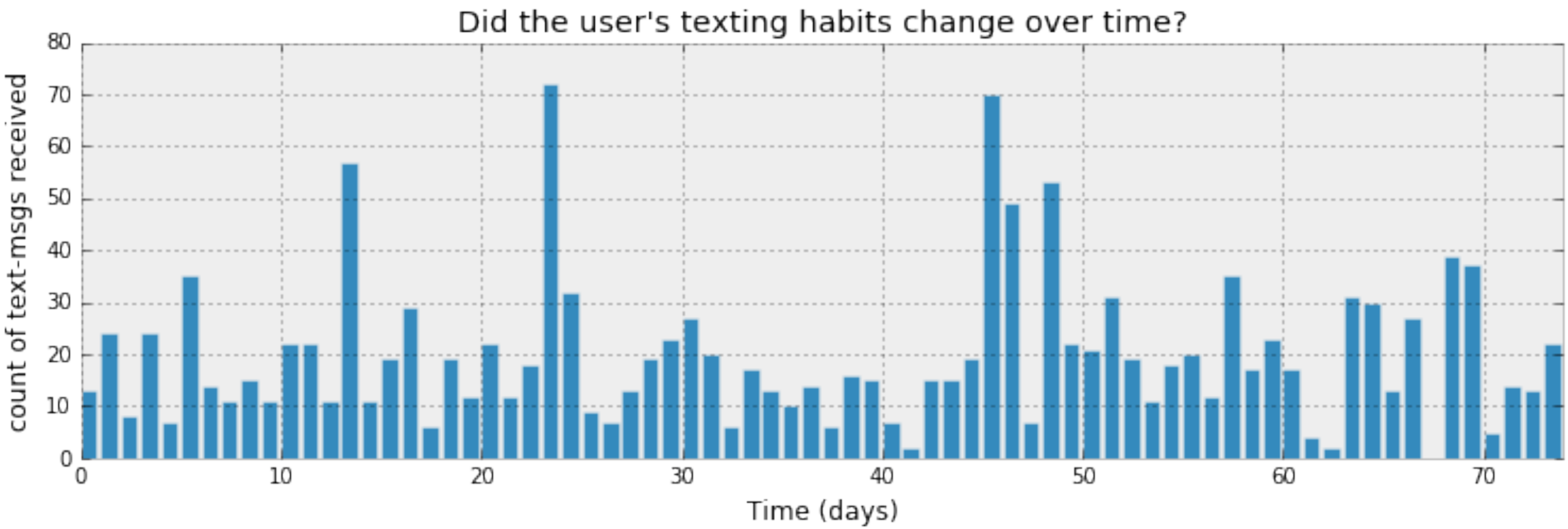
Pierre-Simon Laplace as Chancellor of the Senate under the First French Empire

Born	23 March 1749 Beaumont-en-Auge, Normandy, Kingdom of France
Died	5 March 1827 (aged 77) Paris, Kingdom of France

Source: Wikipedia

https://github.com/CamDavidsonPilon/Probabilistic-Programming-and-Bayesian-Methods-for-Hackers





Source:
https://github.com/CamDavidsonPilon/Probabilistic-Programming-and-Bayesian-Methods-for-Hackers

$$C_i \sim \text{Poisson}(\lambda)$$

$$P(Z = k) = \frac{\lambda^k e^{-\lambda}}{k!}, \quad k = 0, 1, 2, \ldots, \quad \lambda \in \mathbb{R}_{>0}$$

$$\lambda = \begin{cases} \lambda_1 & \text{if } t < \tau \\ \lambda_2 & \text{if } t \geq \tau \end{cases}$$

$$\lambda_1 \sim \text{Exp}(\alpha)$$
$$\lambda_2 \sim \text{Exp}(\alpha)$$

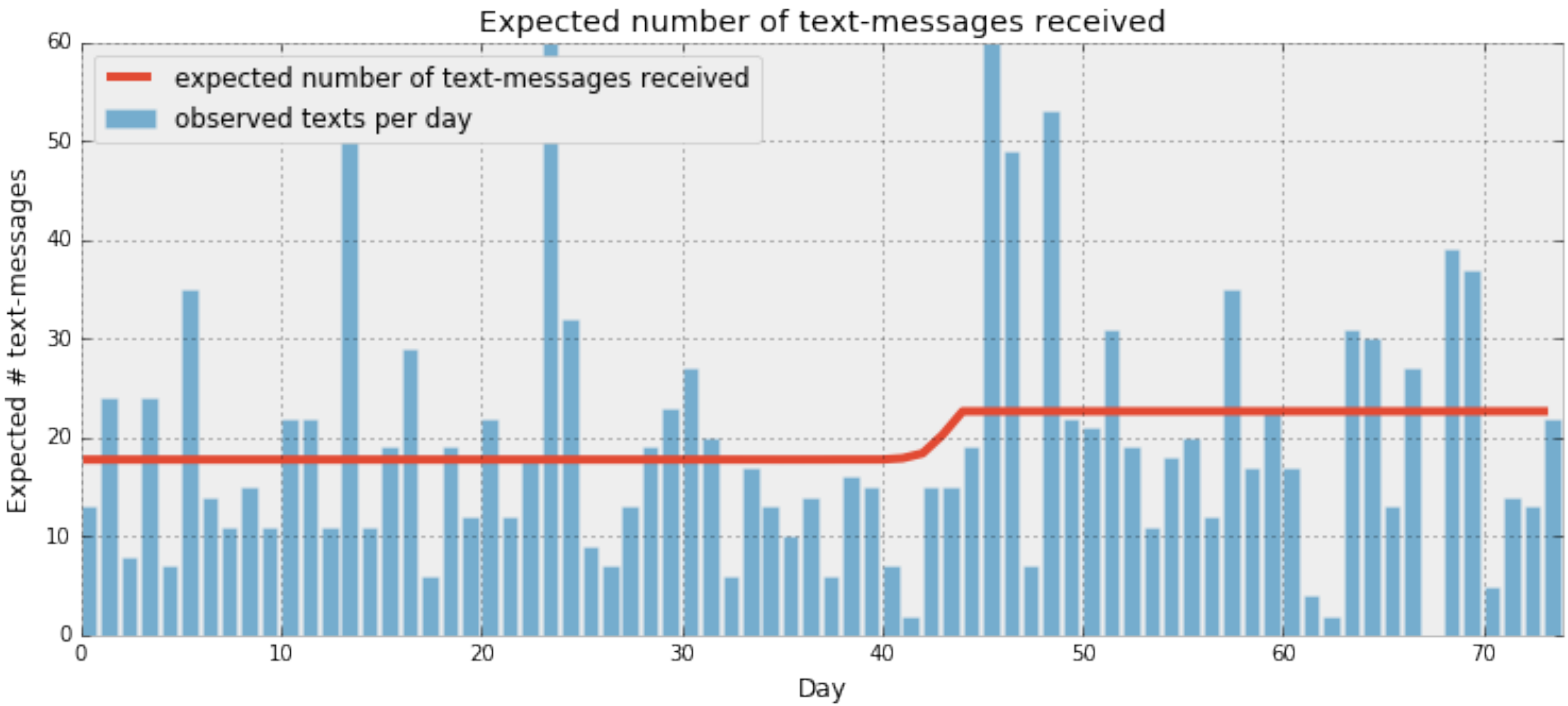
$$f_Z(z|\lambda) = \lambda e^{-\lambda z}, \quad z \geq 0$$

$$\tau \sim \text{DiscreteUniform}(1,70)$$

$$\Rightarrow P(\tau = k) = \frac{1}{70}$$

PyMC3

Source:
https://github.com/CamDavidsonPilon/Probabilistic-Programming-and-Bayesian-Methods-for-Hackers



Source:
https://github.com/CamDavidsonPilon/Probabilistic-Programming-and-Bayesian-Methods-for-Hackers

ベイズ解析

A Student Guide to Bayesian Statistics 2018 Ben Lambert SAGE
Bayesian Analysis with Python 2016 Osvaldo Martin 2016 Packt
Bayesian Methods for Hackers 2016 Cameron Davidson-Pilon Addison-Wesley

機械学習

The Hundred-Page Machine Learning Book 2019 Andriy Burkov

Python Machine Learning 2nd Edition 2017 Sebastian Raschka and Vahid Mirjalili Packt

システム生物学

A First Course in Systems Biology 2012 Eberhard O. Voit GS

Z: 確率変数 (random variables)

$P(Z)$: 確率質量関数 (probability mass function)

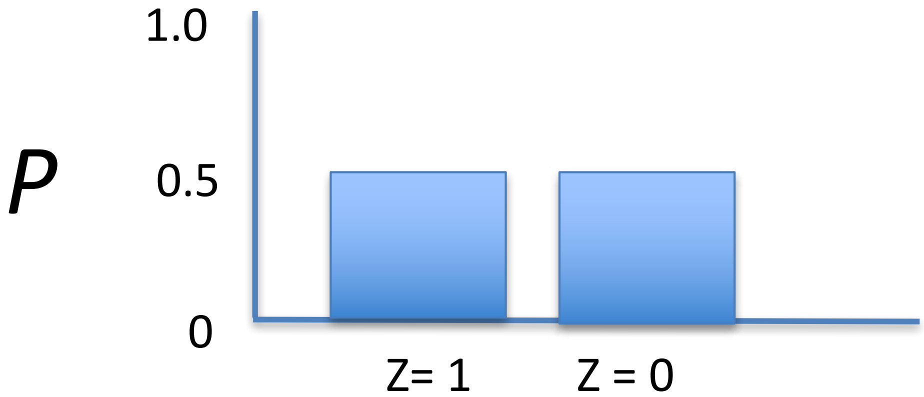
$$\sum_i P(Z_i) = 1$$

Z: 確率変数 (random variables)

$P(Z)$: 確率質量関数 (probability mass function)

コイン投げ (Coin throw)　Z = おもて: 1 or うら: 0

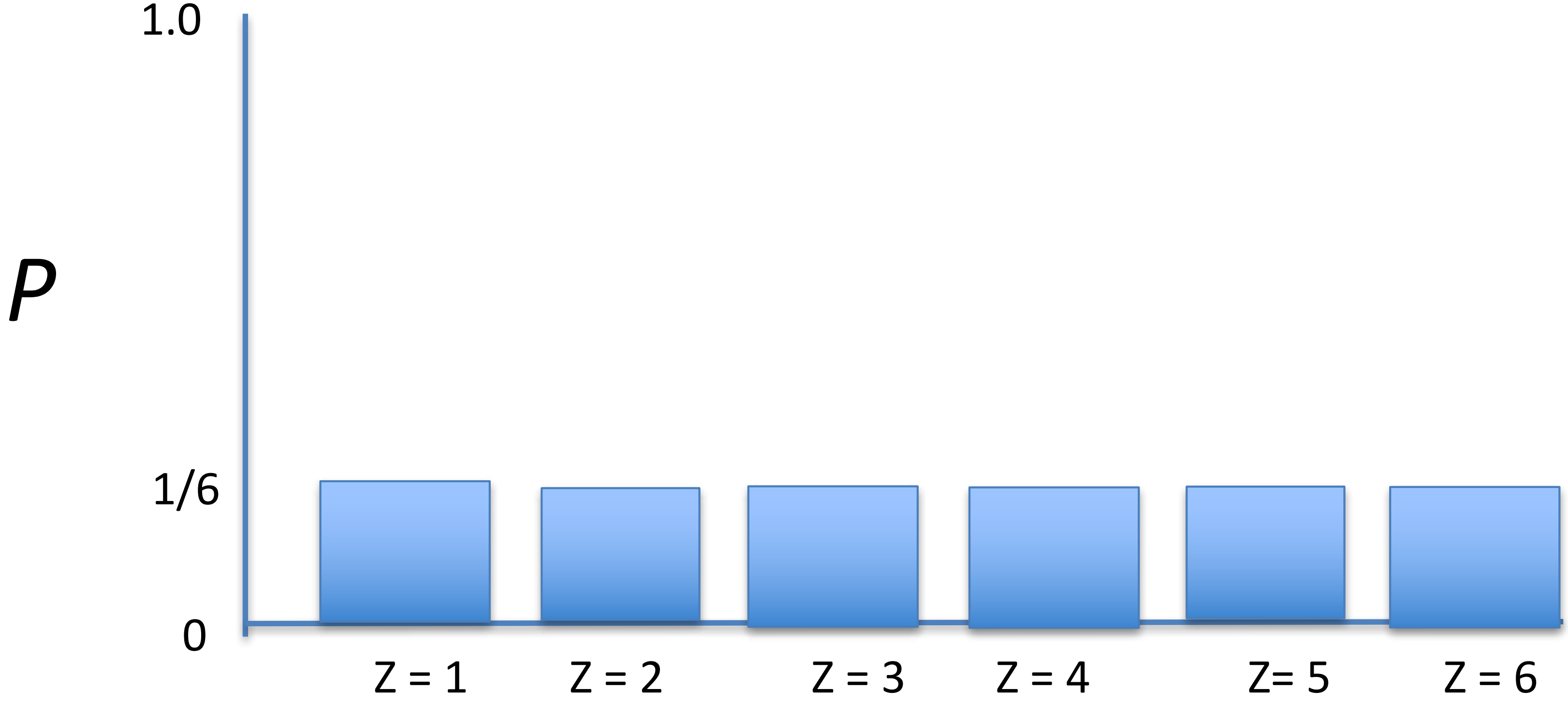
$P(1) = 0.5$, $P(0) = 0.5$



$P(Z=1) + P(Z=0) = 1$

サイコロ投げ（Dice throw)　Z = 1, 2, 3, 4, 5, 6

$P(1) = 1/6$, $P(2) = 1/6$, $P(3) = 1/6$, $P(5) = 1/6$, $P(5) = 1/6$, $P(6) = 1/6$,

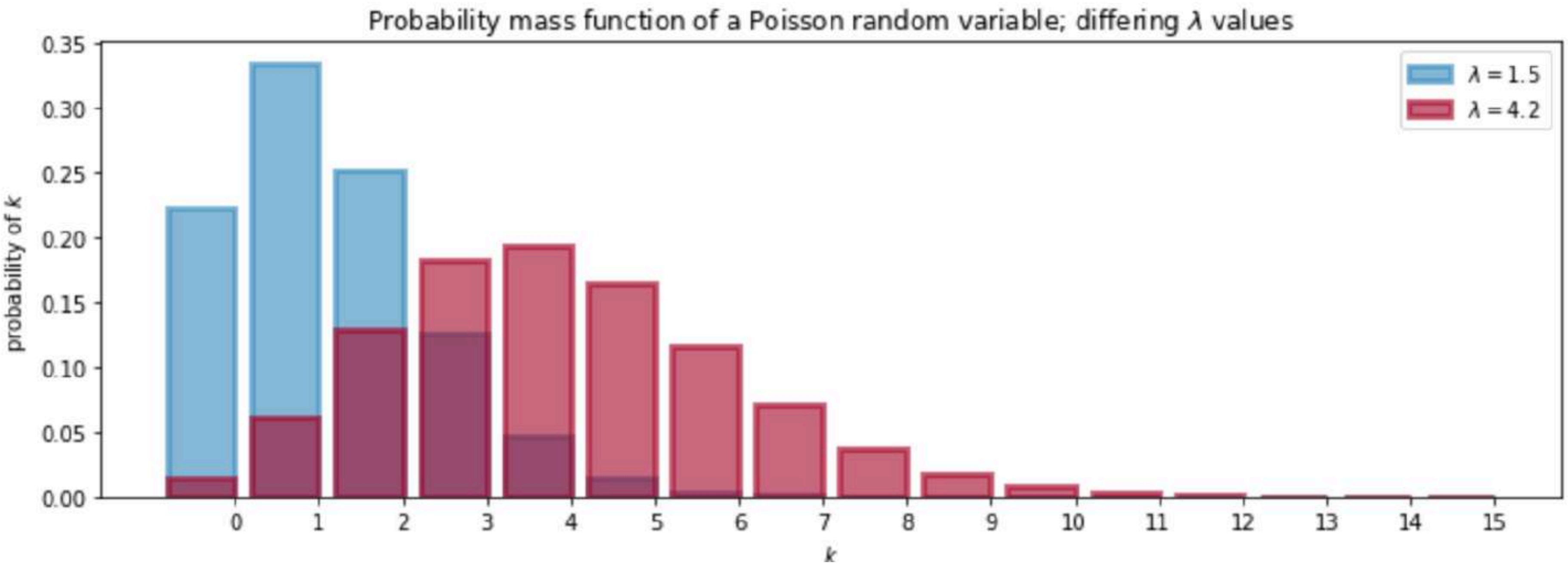


$$P(Z=1) + P(Z=2) + P(Z=3) + P(Z=4) + P(Z=5) + P(Z=6) = \sum_i P(Z = i) = 1$$

ポアソン分布 (Poisson Distribution)

10Kgのパン生地に400粒のレーズンをいれてこねた後、0.1Kgずつのパンに分けて焼いた時、パン一個あたりのレーズンの数の分布は？　　$\lambda = 4$

$$P(Z=k) = \frac{\lambda^k e^{-\lambda}}{k!},\ \ k = 0, 1, 2, \ldots,\ \ \lambda \in \mathbb{R}_{>0}$$



競馬の例 （Horse Race) :　馬A と 馬B の勝敗の割合

馬A

馬B

	0 負 (lose)	1 勝 (win)
0 負 (lose)	30/100	10/100
1 勝 (win)	10/100	50/100

$$\sum_{i=0}^{1}\sum_{j=0}^{1} P(Z_A = i, Z_B = j) = 30/100 + 10/100 + 10/100 + 50/100 = 1$$

Lambert, B. A Student’s Guide to Bayesian Statistics, 2018より引用

競馬の例 （Horse Race）: 周辺分布 (Marginal Distribution)

		A		
		0 負 (lose)	1 勝 (win)	$P(Z_B)$
B	0 負 (lose)	30/100	10/100	40/100
	1 勝 (win)	10/100	50/100	60/100
	$P(Z_A)$	40/100	60/100	

周辺確率

$P(Z_A=0) = P(Z_A=0, Z_B=0) + P(Z_A=0, Z_B=1) = 30/100+10/100 = 40/100$

条件付き確率（Conditional Probability)

P(X|Y）＝P(X,Y)/P(Y)

条件付確率　= 同時確率/周辺確率

Conditional Probability　simultaneous (joint) probability / marginal probability

Aが勝った場合に、Bも勝つ確率

$$\mathbf{P(Z_B=1|Z_A=1)} = P(Z_A=1, Z_B=1) / P(Z_A=1)$$

$$= P(Z_A=1, Z_B=1) / P(Z_A=1, Z_B=0) + P(Z_A=1, Z_B=1)$$

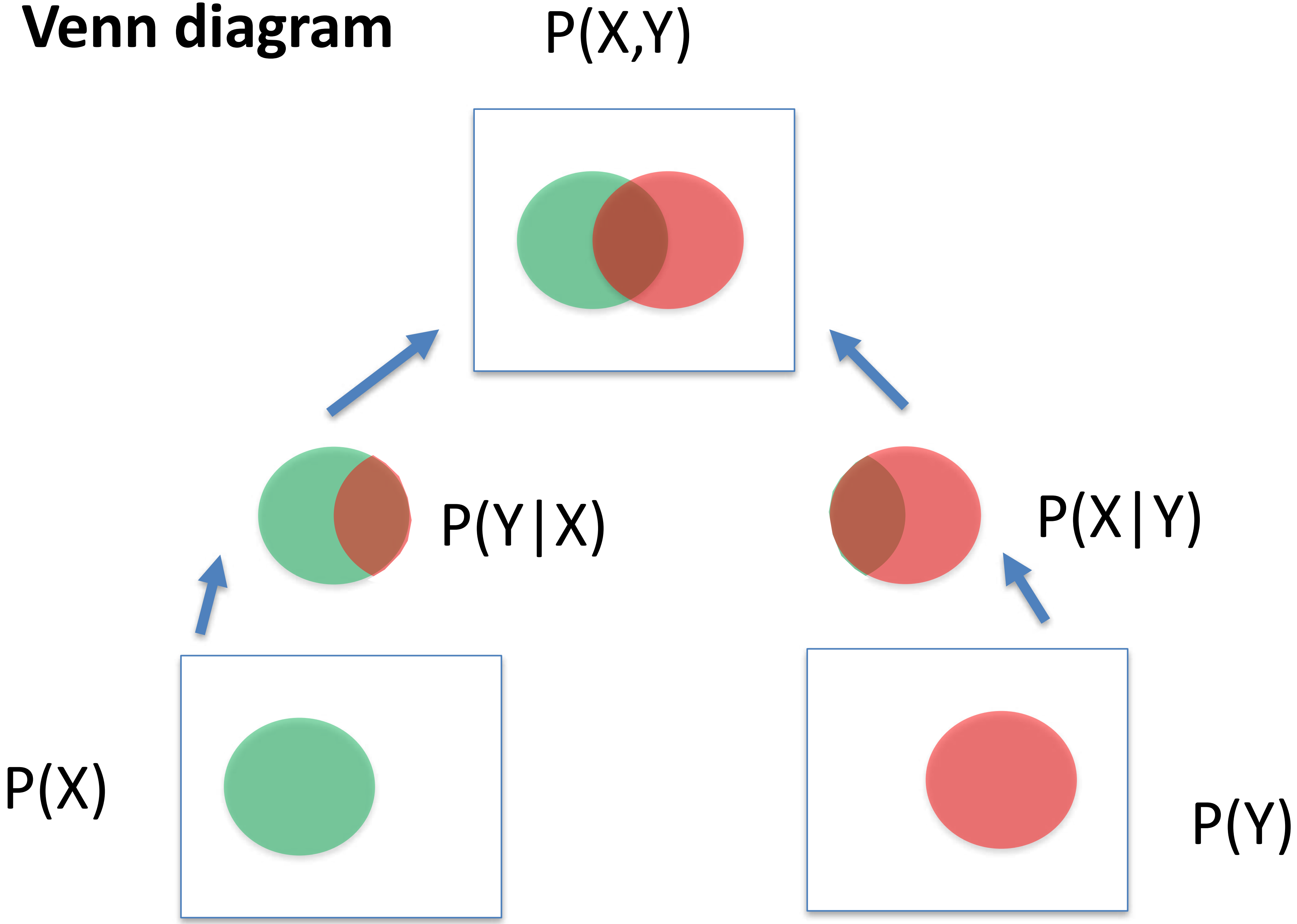
$$= (50/100) / [(10/100) + (50/100)] = 5/6$$

B \ A	0 負 (lose)	1 勝 (win)
0 負 (lose)	30/100	10/100
1 勝 (win)	10/100	50/100

—>

Bが勝った場合に
Aが勝つ確率は？

Venn diagram



Baysean Inference

https://www.youtube.com/watch?v=-e8wOcaascM

Thomas Bayes 1701-1761

$$P(\theta|\text{data}) = [P(\text{data}|\theta) \times P(\theta)] / P(\text{data})$$

ベイズの定理　(Bayes's rule)

$$\mathbf{P(X|Y) = [P(Y|X) \times P(X)] / P(Y)}$$

1/ $P(X|Y) = P(X,Y)/P(Y)$

2/ $P(Y|X) = P(X,Y)/P(X)$

3/ $P(X|Y) \times P(Y) = P(X,Y) = P(Y|X) \times P(X)$

$\rightarrow$ $P(X|Y) = [P(Y|X) \times P(X)] / P(Y)$

$$P(X|Y) \times P(Y) = P(X,Y) = P(Y|X) \times P(X)$$

$$\rightarrow \quad P(X|Y) = [P(Y|X) \times P(X)] \,/\, P(Y)$$

Use of Bayes theorem (modified from Lambert, 2018)

Example of Colon Cancer

1. Out of all men aged 40, 1% have colon cancer
2. Screen of colon cancer: 80% of men with colon cancer show positive
3. 10% of men without colon cancer show screen positive

Question: What is the percentage of colon cancer if screen result is positive?

P(cancer) = 0.01
P(Sc+|cancer) = 0.8
P(Sc+|no cancer) = 0.1 Question: **P(cancer|Sc+)**

P(cancer|Sc+) x P(Sc+) = P(cancer, Sc+) = P(Sc+|cancer) x P(cancer)

P(cancer|Sc+) = [P(Sc+|cancer) x P(cancer)] / P(Sc+)

= (0.8 x 0.01) /0.11 = 0.08

P(Sc+) = P(Sc+, cancer) + P(Sc+, no cancer)

= P(Sc+|cancer) x P(cancer) + P(Sc+|no cancer) x P(no cancer)

= 0.8 x 0.01 + 0.1 x 0.99 = 0.11

Thomas Bayes 1701-1761

Baysean Inference

https://www.youtube.com/watch?v=-e8wOcaascM

$$P(\theta|\text{data}) = [P(\text{data}|\theta) \times P(\theta)] / P(\text{data})$$

Posterior = Likelihood x Prior / P(data)

事後確率 尤度 事前確率

Likelihood (尤度)

Head (表）　　Tail (裏）

Coin throw (コイン投げ）

$P(\mathrm{H}) = \theta = 0.5$

Throw coin twice (２回コイン投げをする時の結果）

1st throw １回目

2nd throw 2回目

$P(\mathrm{H}, \mathrm{H}) = \theta^2 = 0.5 \times 0.5 = 0.25$

Coin throw: x 2 (2回のコイン投げ)

H H

H T

T T

T H

= θ^2 = 0.5 x 0.5
= 0.25

= $(1-\theta)^2$ = 0.5 x 0.5
= 0.25

=2 x θ x $(1-\theta)$ = 2 x 0.5 x 0.5
= 0.5

Binomial distribution (二項分布）

n: trial number (試行回数）
k: number of success (成功回数）

$P(X=k|\theta) = {}_nC_k\, \theta^k(1-\theta)^{n-k}$

$P(X=0) = \theta^0(1-\theta)^2 = (1-0.5)^2 = 0.25$
$P(X=1) = 2\text{x}\ \theta\ \text{x}\ (1-\theta) = 2\text{x}(0.5)\text{x}(1-0.5) = 0.5$
$P(X=2) = \theta^2(1-\theta)^0 = (0.5)^2 = 0.25$

尤度 （Likelihood)

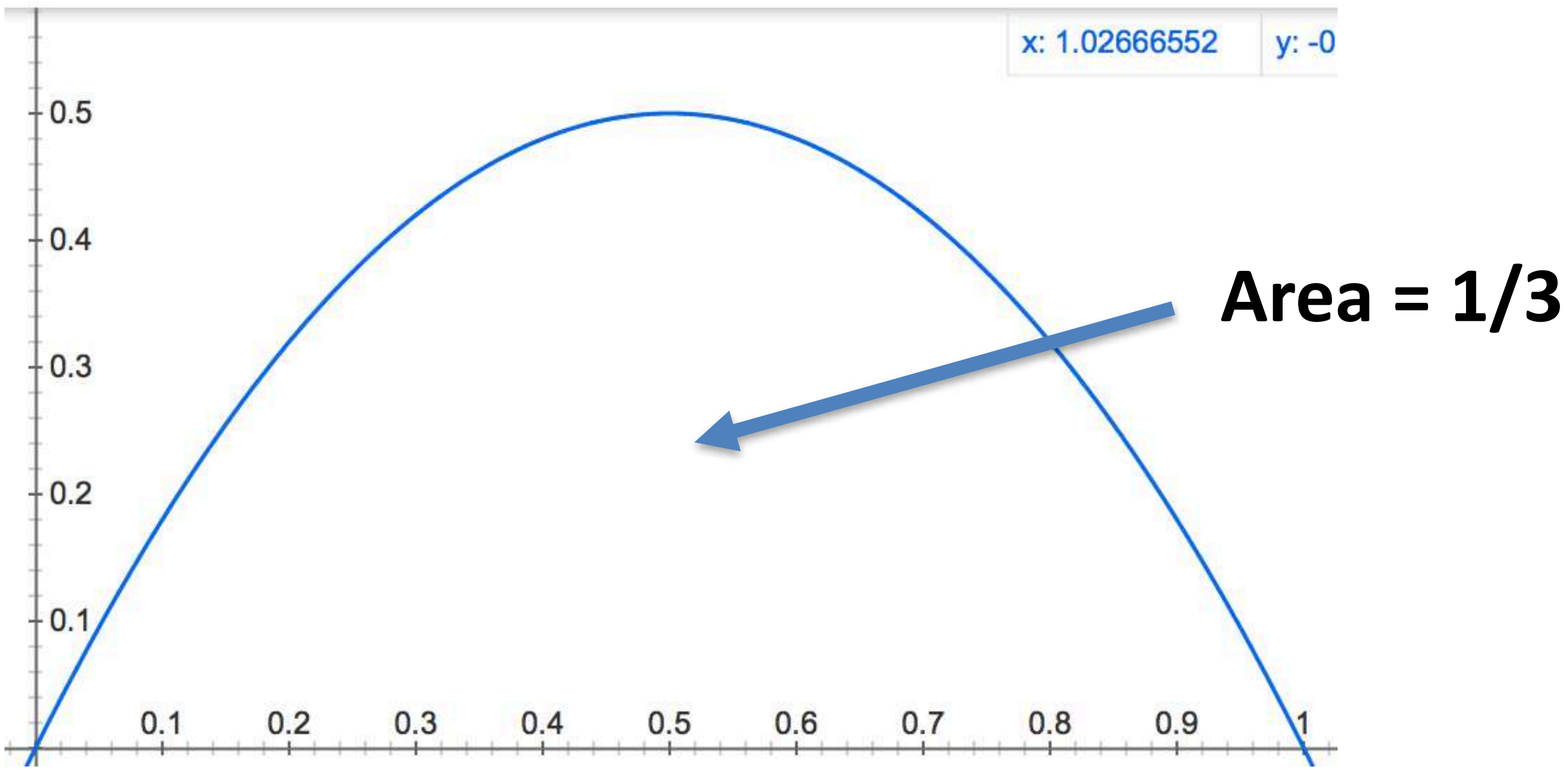
$$L(\theta|\text{data}) = P(\text{data}|\theta)$$

$$P(X=k|\theta) = {}_nC_k\, \theta^k(1-\theta)^{n-k}$$

$$n = 2$$

$$L(\theta \mid X = 1) = P(X = 1|\theta) = 2\theta \times (1-\theta)$$

Likelihood



θ

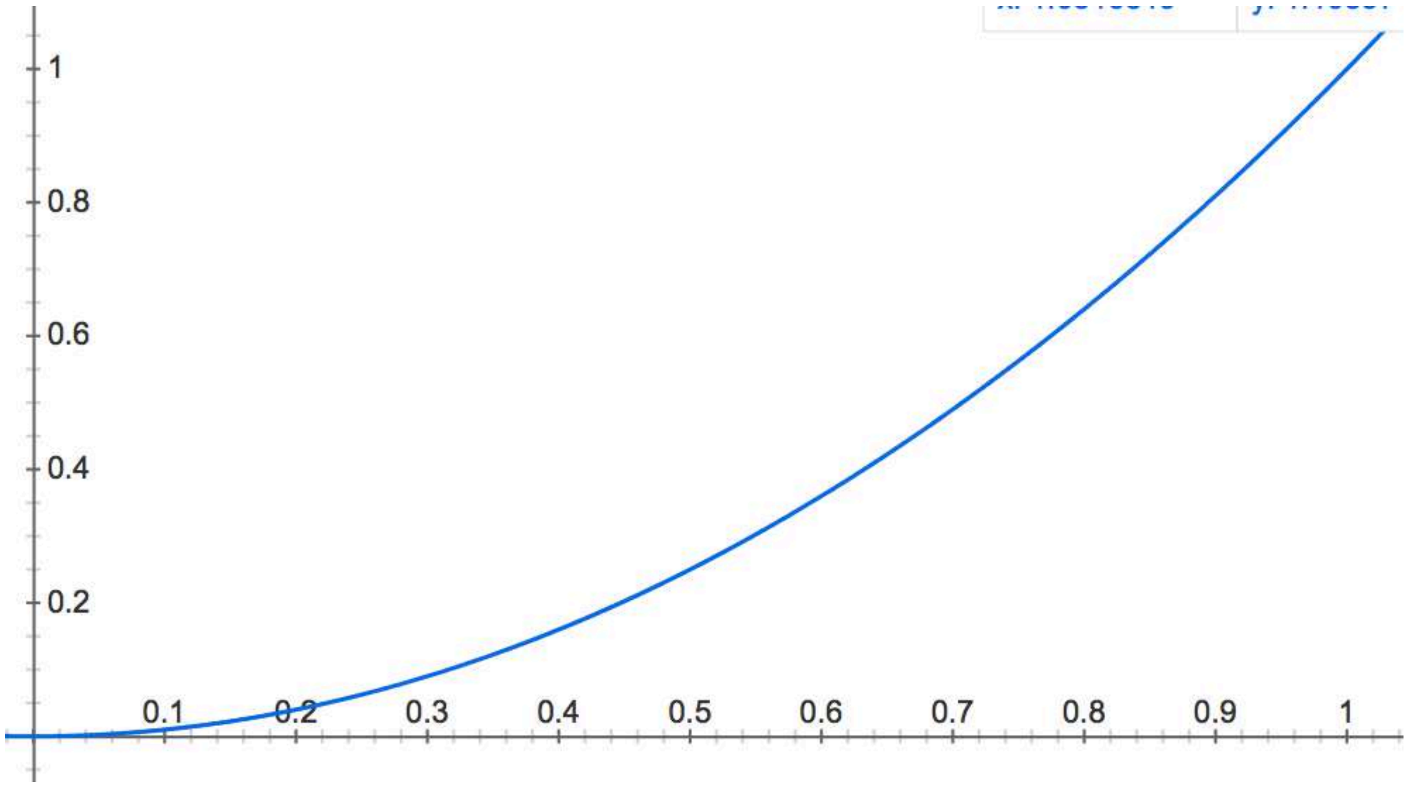
Maximum Likelihood (最尤推定値)

$$P(X=k|\theta) = {}_nC_k\, \theta^k(1-\theta)^{n-k}$$

$$n = 2$$

$$L(\theta \mid X = 2) = P(X = 2 | \theta) = \theta^2$$

Likelihood



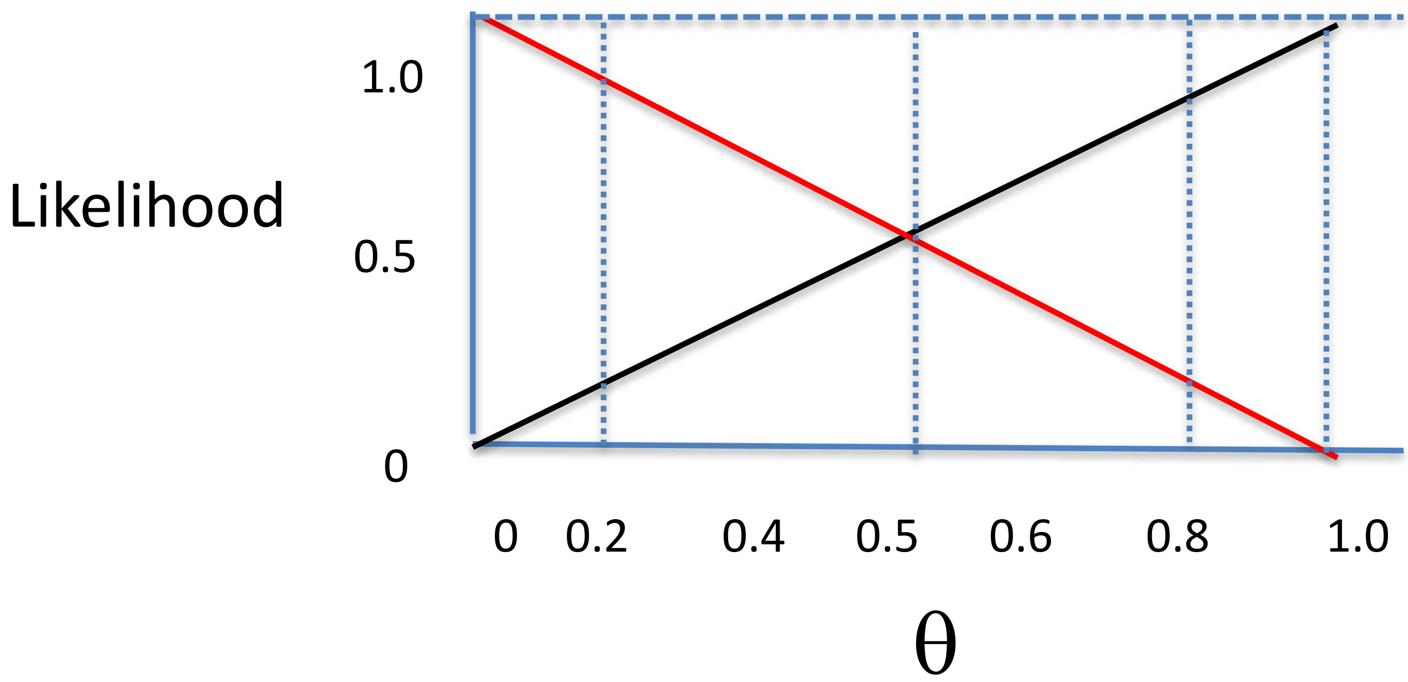
θ

Likelihood (尤度)

X = 0   No Disease
X = 1   Disease

Goal: estimate the probability θ that a randomly chosen person has a disease

$$L(\theta | X=0) = 1 - \theta$$
$$L(\theta | X=1) = \theta$$



進化の研究者

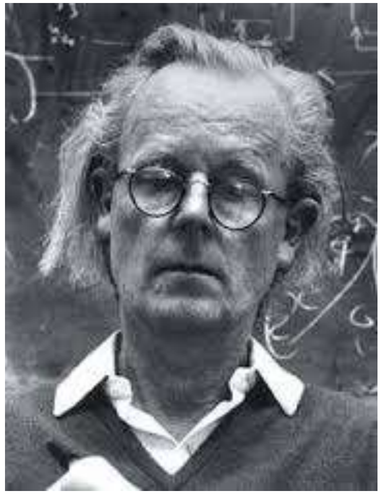
R. A. Fisher
(1890-1962)

Maximum Likelihood
Estimation

Motoo Kimura
(1924-1994)

J.B.S. Haldane
(1892-1964)

Maynard Smith
(1920-2004)



Sewell Wright
(1889-1988)

Richard Dawkins
(1941-)

Rothamsted Experimental Station, 1919–1933 [edit]

In 1919, he began working at the Rothamsted Experimental Station in Hertfordshire, where he would remain for 14 years.[10] He had been offered a position at the Galton Laboratory in University College London led by Karl Pearson, but instead accepted a temporary role at Rothamsted to investigate the possibility of analysing the vast amount of crop data accumulated since 1842 from the "Classical Field Experiments". He analysed the data recorded over many years, and in 1921 published *Studies in Crop Variation*, and his first application of the analysis of variance (ANOVA).[22] In 1928, Joseph Oscar Irwin began a three-year stint at Rothamsted and became one of the first people to master Fisher's innovations. Between 1912 and 1922 Fisher recommended, analyzed (with heuristic proofs) and vastly popularized the maximum likelihood estimation method.[23]

Rothamsted Research

From Wikipedia, the free encyclopedia

Coordinates: 51°48′33″N 0°21′19″W

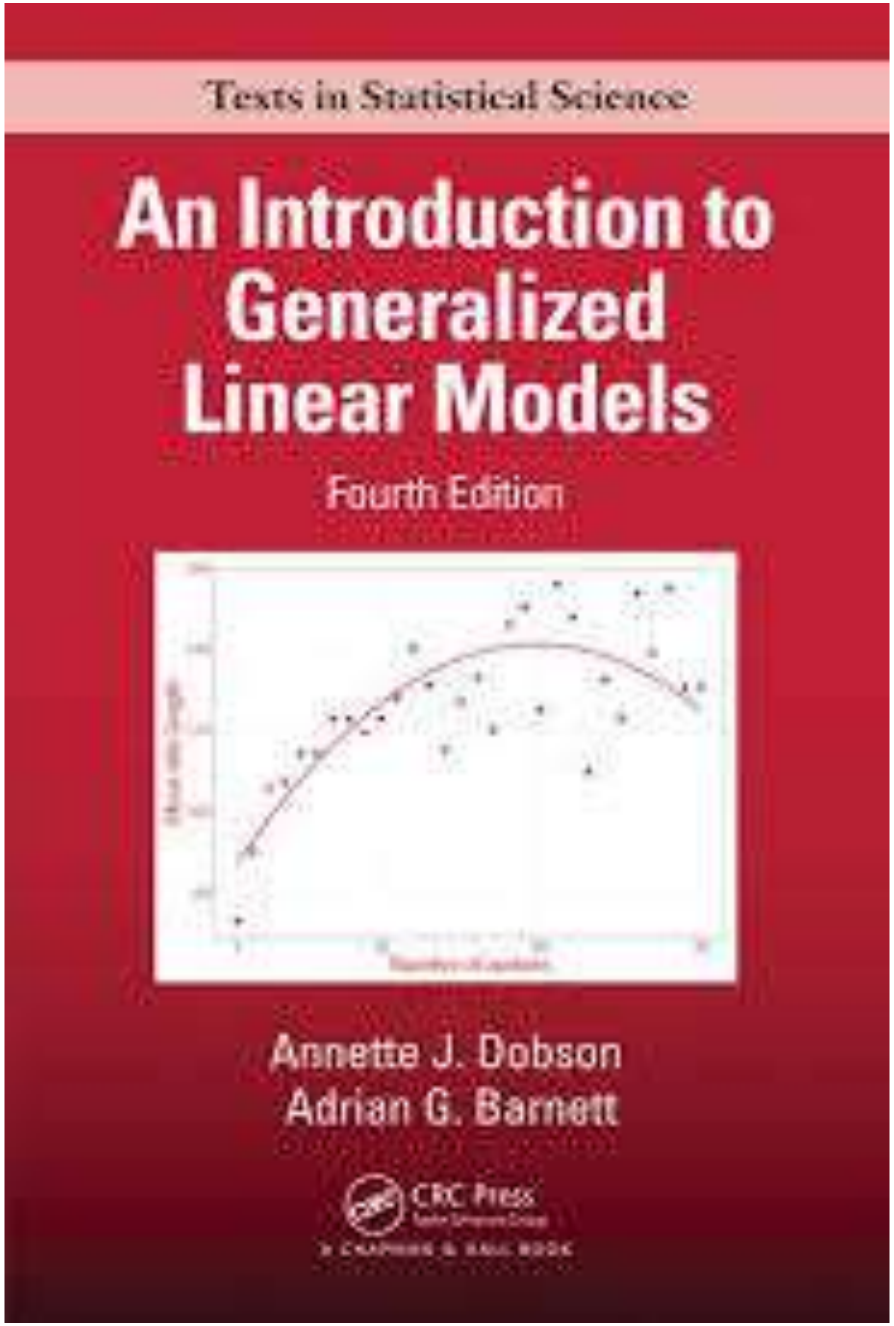
Rothamsted Research, previously known as the **Rothamsted Experimental Station** and then the **Institute of Arable Crops Research**, is one of the oldest agricultural research institutions in the world, having been founded in 1843. It is located at Harpenden in the English county of Hertfordshire and is a registered charity under English law.[1]

Panorama of Rothamsted Research

One of the station's best known and longest-running experiments is the Park Grass Experiment, a biological study that started in 1856 and has been continuously monitored ever since.[2]

Source: Wikipedia

An Introduction to Generalized Linear Models, Third Edition (Chapman & Hall/CRC Texts in Statistical Science) 2008/6/6
[Annette J. Dobson](), [Adrian G. Barnett]()



Thomas Bayes 1701-1761

Baysean Inference

https://www.youtube.com/watch?v=-e8wOcaascM

$$P(\theta|data) = [P(data|\theta) \times P(\theta)] / P(data)$$

Posterior = Likelihood x Prior / P(data)

Example of Bayes Inference (from Ben Lambert 2018)

θ *:* Disease rate (= probability of one person with a disease
= frequency of people with disease)

Observation:

1/ After observing 10 people, 3 had disease.

Premise:

$P(y=3|\theta) = {}_{10}C_3 \times \theta^3 \times (1-\theta)^7$

Prior: Uniform distribution

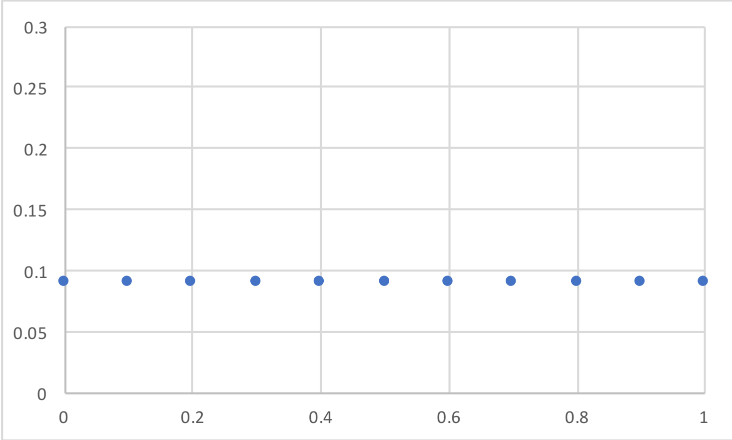
Example of Bayes Inference (from Ben Lambert 2018)

Bayes' Box

$P(\theta|y) = [P(y|\theta) \times P(\theta)] / P(y), \; P(y) = \Sigma [P(y|\theta) \times P(\theta)]$

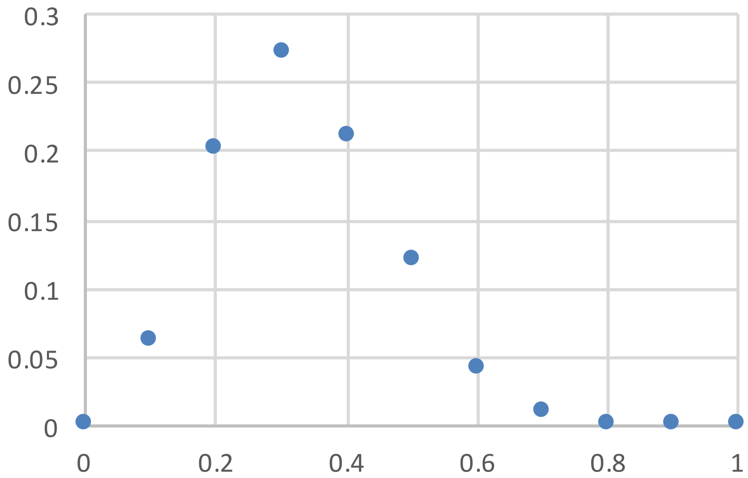
θ	$P(\theta)$ Prior	$P(y\|\theta)$ Likelihood	$P(y\|\theta)$x $P(\theta)$	$P(\theta\|y)$ Posterior
0.0	0.09	0.00	0.00	0.00
0.1	0.09	0.06	0.01	0.07
0.2	0.09	0.20	0.02	0.22
0.3	0.09	0.27	0.02	0.30
0.4	0.09	0.21	0.01	0.23
0.5	0.09	0.12	0.00	0.13
0.6	0.09	0.04	0.00	0.04
0.7	0.09	0.01	0.00	0.01
0.8	0.09	0.00	0.00	0.00
0.9	0.09	0.00	0.00	0.00
1.0	0.09	0.00	0.00	0.00
Sum	1.0	0.91	0.08	1.00

Prior P(θ)



P(θ) = c
Uniform prior
= Uninformative prior

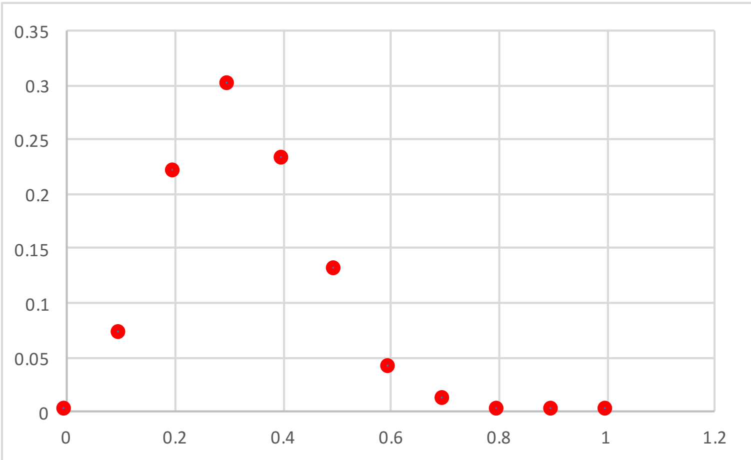
Likelihood P(y|θ)



Bayes' theorem

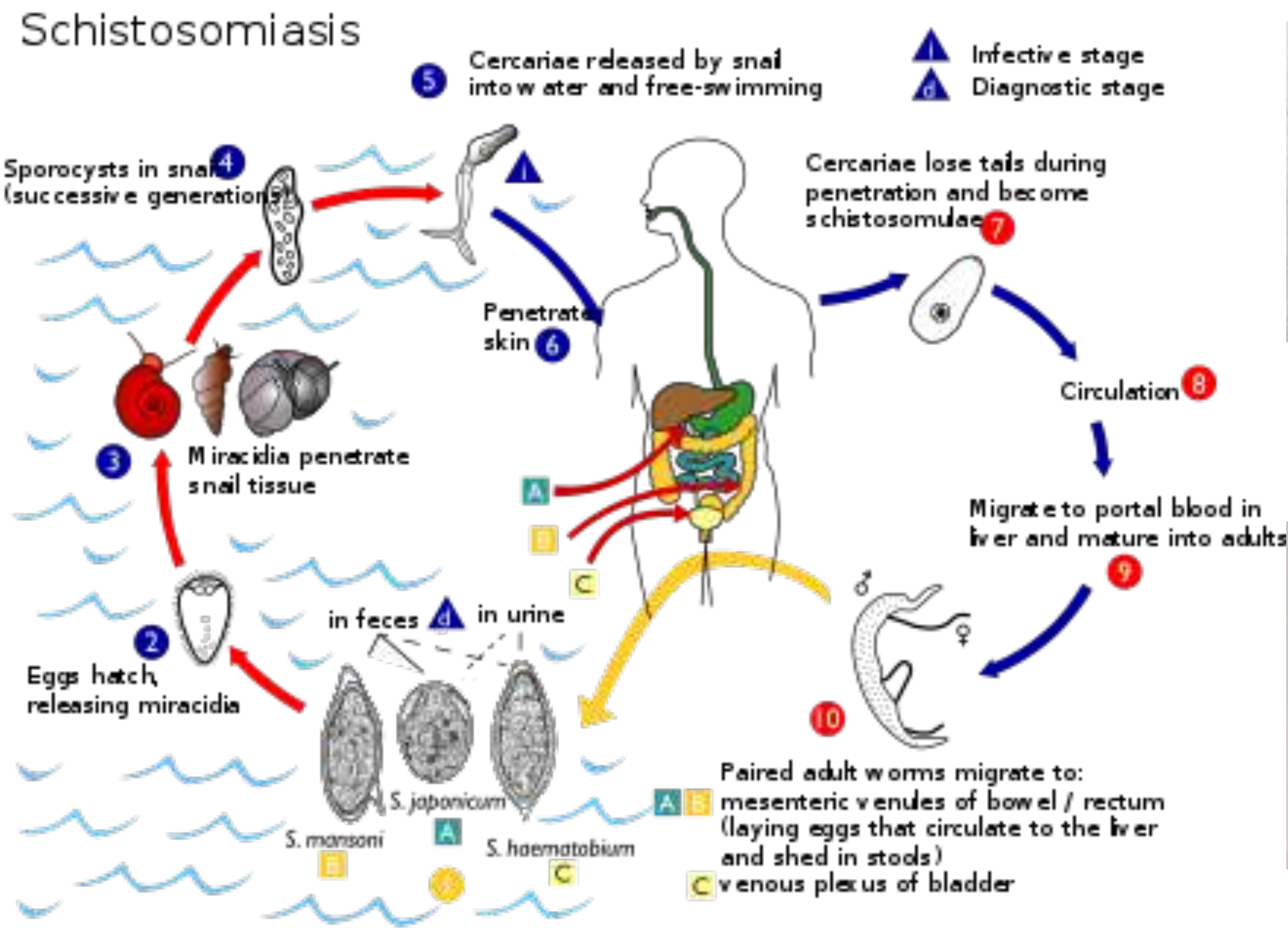
P(θ|y) = [P(y|θ) x P(θ)] / P(y)

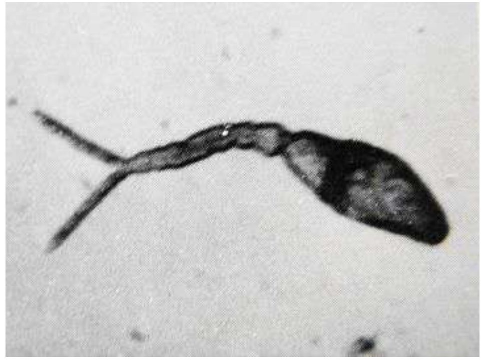
Posterior P(θ|y)



Example of Bayes Inference (from Dobson and Barnett, 2008)

Infection by *Schistosoma japonicum* (日本住血吸虫)





Cercaria

Male/Female

カワニナ x → ミヤイリ貝○

Example of Bayes Inference (from Dobson and Barnett, 2008)

Infection by *Schistosoma japonicum*

θ *:* Infection rate (= probability of one person infected
= frequency of infected person)

H0: Infection is not endemic ($\theta <= 0.5$)
H1: Infection is endemic ($\theta > 0.5$)

Observations:

1/ After a visit to a village, the investigator thinks he is 80% sure that infection is endemic.

2/ Sampling stool from 10 individuals of the village 7 had *S. japonicum*

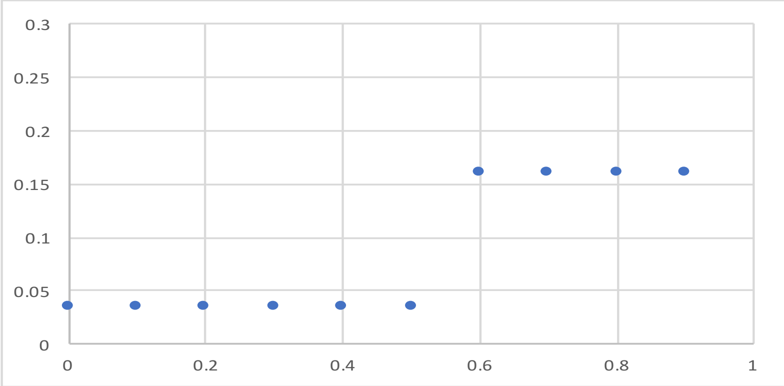
$$P(y|\theta) = Bin(10, \theta) = {}_{10}C_7 \times \theta^7 \times (1-\theta)^3$$

Bayes' Box

$P(\theta|y) = [P(y|\theta) \times P(\theta)] / P(y), \quad P(y) = \Sigma\, [P(y|\theta) \times P(\theta)]$

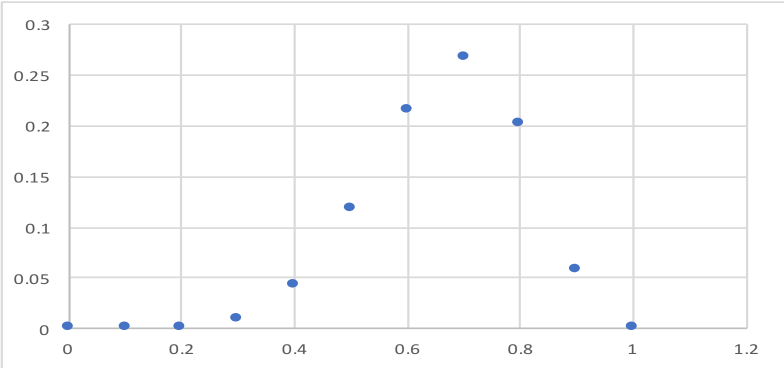
θ	Hypothesis	$P(\theta)$ Prior	$P(y\|\theta)$ Likelihood	$P(y\|\theta) \times P(\theta)$	$P(\theta\|y)$ Posterior
0.0	H_0	0.0333	0.000	0.000	0.000
0.1	H_0	0.0333	0.000	0.000	0.000
0.2	H_0	0.0333	0.001	0.000	0.000
0.3	H_0	0.0333	0.009	0.000	0.002
0.4	H_0	0.0333	0.043	0.001	0.011
0.5	H_0	0.0333	0.117	0.004	0.032
Sum		0.2			0.046
0.6	H_1	0.16	0.215	0.034	0.277
0.7	H_1	0.16	0.267	0.043	0.344
0.8	H_1	0.16	0.201	0.032	0.260
0.9	H_1	0.16	0.057	0.009	0.074
1.0	H_1	0.16	0.000	0.000	0.000
Sum		0.8		0.124	0.954

Prior $P(\theta)$



Informative prior

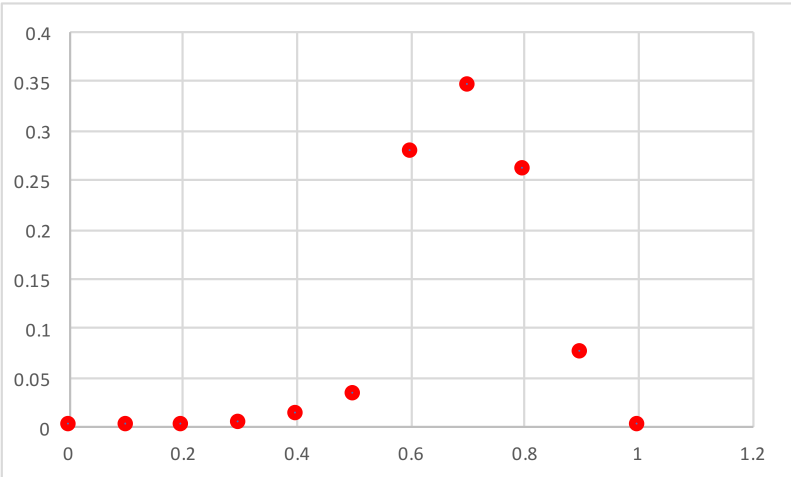
Likelihood $P(y|\theta)$



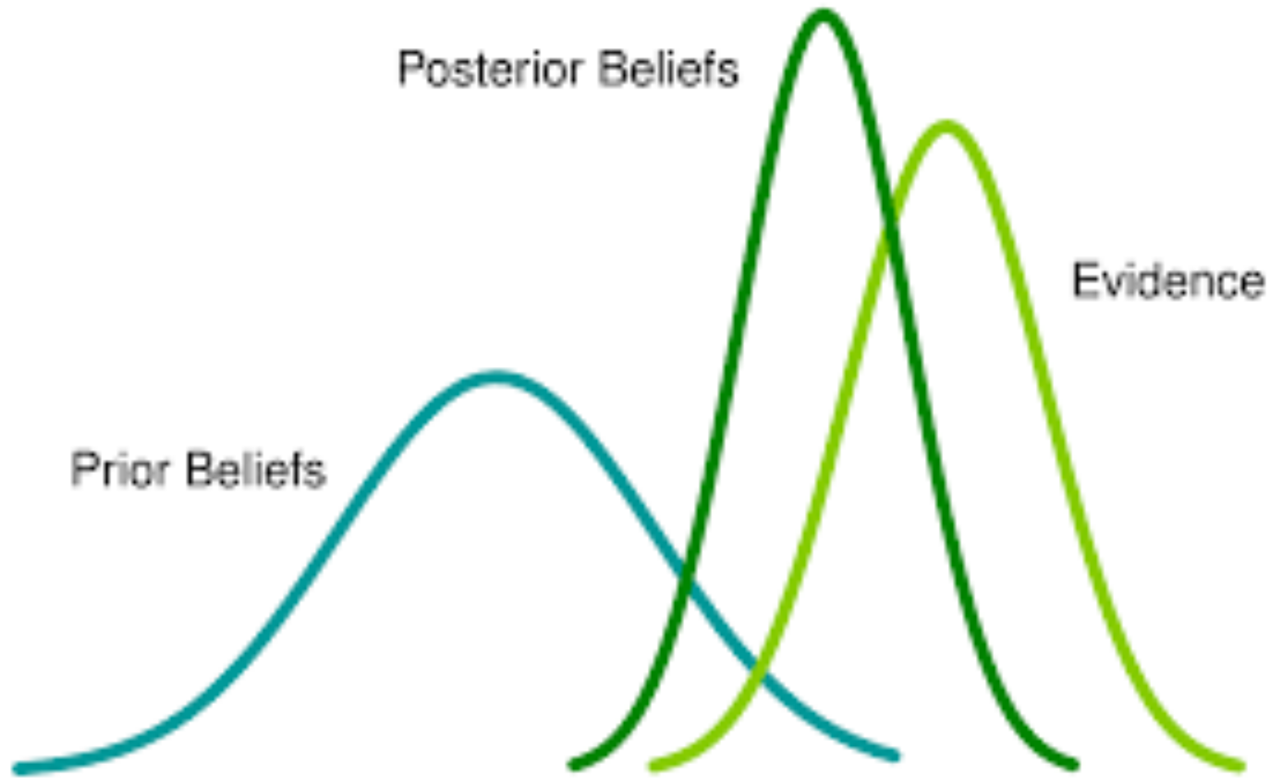
Bayes' theorem

$P(\theta|y) = [P(y|\theta) \times P(\theta)] / P(y)$

Posterior $P(\theta|y)$



- remember θ is continuous
- calculation increases

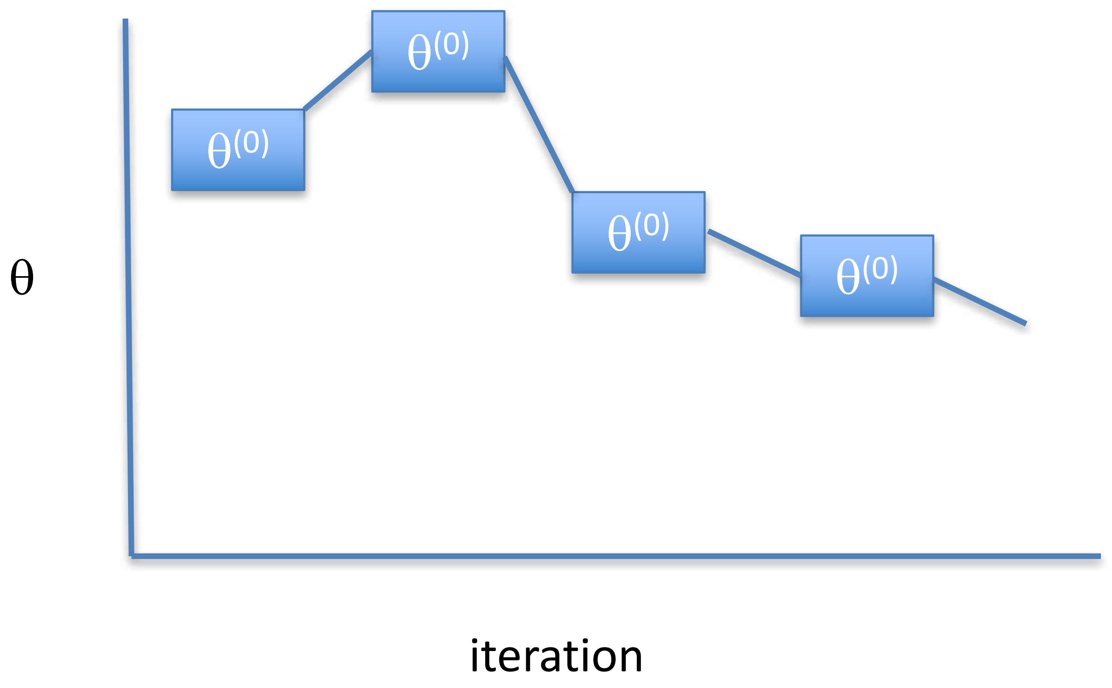


Posterior Beliefs
Evidence
Prior Beliefs

MCMCの実際, PyMCの実際

Malkov Chain

$$P(\theta^{(i)} = a \mid \theta^{(i-1)}, \theta^{(i-2)}, \ldots \theta^{(0)}) = P(\theta^{(i)} = a \mid \theta^{(i-1)})$$

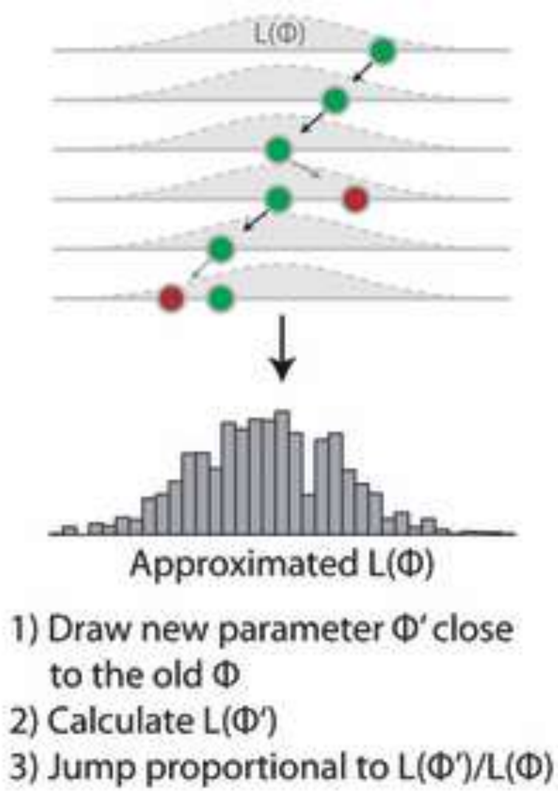


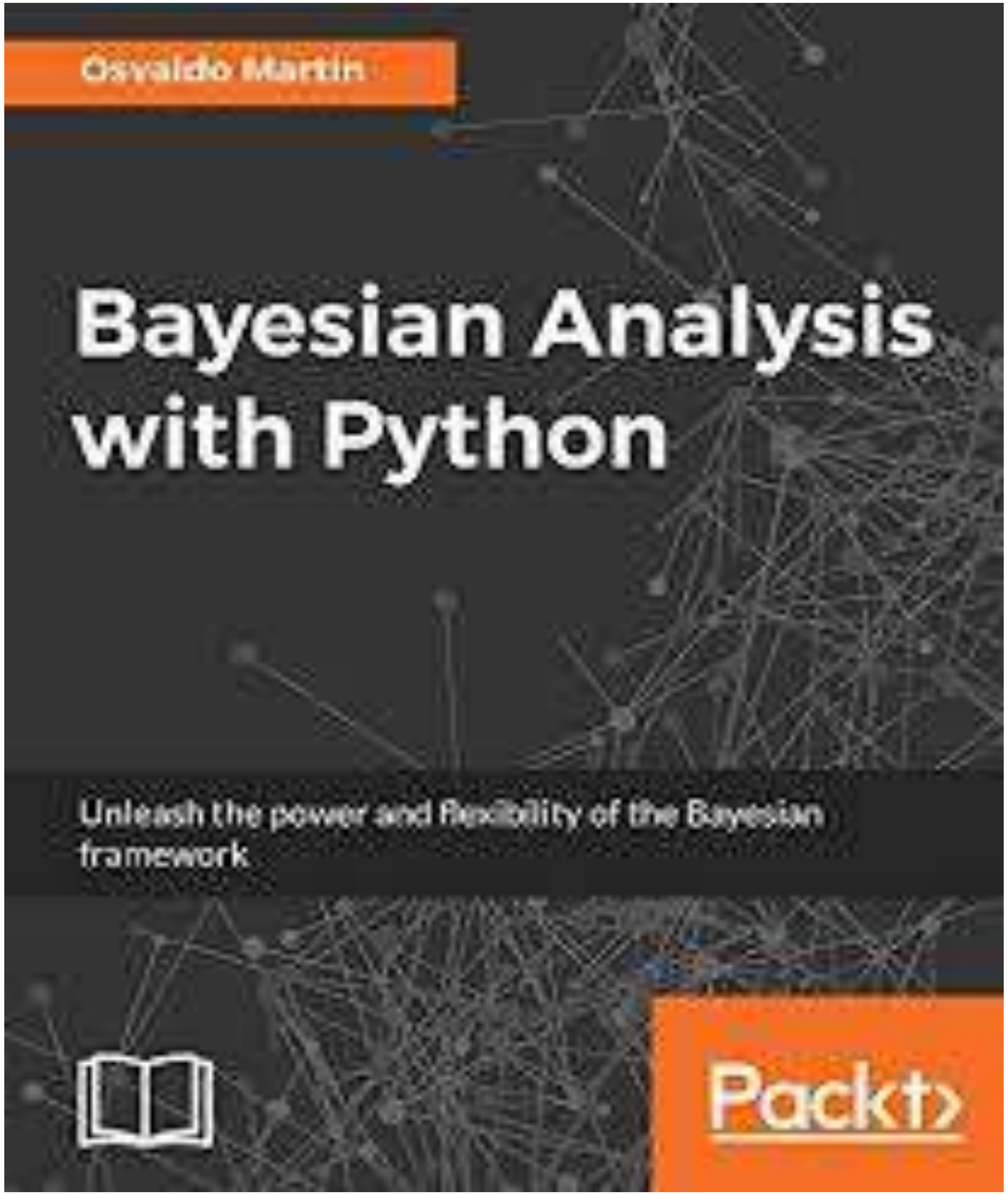
Metropolis sampling

$$\theta^* = \theta^{(i)} + Q, \quad Q \sim N(0,1)$$

$$\theta^{(i+1)} = \begin{cases} \theta^* & \text{if } U < \alpha, \quad U \sim U([0,1]) \\ \theta^{(i)} & \text{otherwise} \end{cases}$$

$$\alpha = \min \{ [P(\theta^*|y) / P(\theta^{(i)}|y)], 1\}$$





https://www.packtpub.com/product/bayesian-analysis-with-python-second-edition/9781789341652

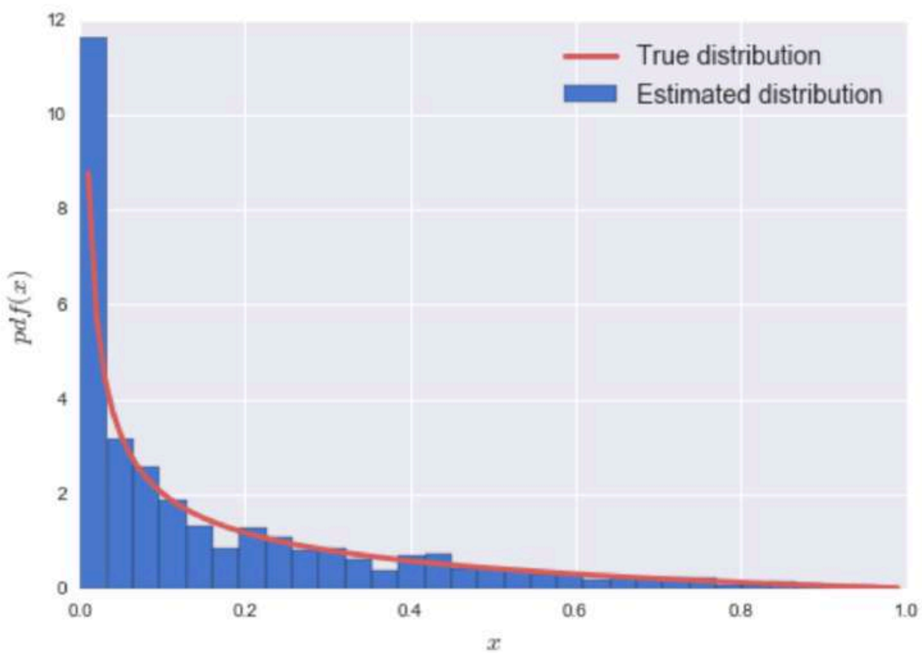
MCMC using PyMC3

```python
def metropolis(func, steps=10000):
    """A very simple Metropolis implementation"""
    samples = np.zeros(steps)
    old_x = func.mean()
    old_prob = func.pdf(old_x)

    for i in range(steps):
        new_x = old_x + np.random.normal(0, 1)
        new_prob = func.pdf(new_x)
        acceptance = new_prob/old_prob
        if acceptance >= np.random.random():
            samples[i] = new_x
            old_x = new_x
            old_prob = new_prob
        else:
            samples[i] = old_x
    return samples
```

Source:
https://www.packtpub.com/product/bayesian-analysis-with-python-second-edition/9781789341652

```
np.random.seed(345)
func = stats.beta(0.4, 2)
samples = metropolis(func=func)
x = np.linspace(0.01, .99, 100)
y = func.pdf(x)
plt.xlim(0, 1)
plt.plot(x, y, 'r-', lw=3, label='True distribution')
plt.hist(samples, bins=30, normed=True, label='Estimated distribution')
plt.xlabel('$x$', fontsize=14)
plt.ylabel('$pdf(x)$', fontsize=14)
plt.legend(fontsize=14)
plt.savefig('B04958_02_03.png', dpi=300, figsize=(5.5, 5.5));
```



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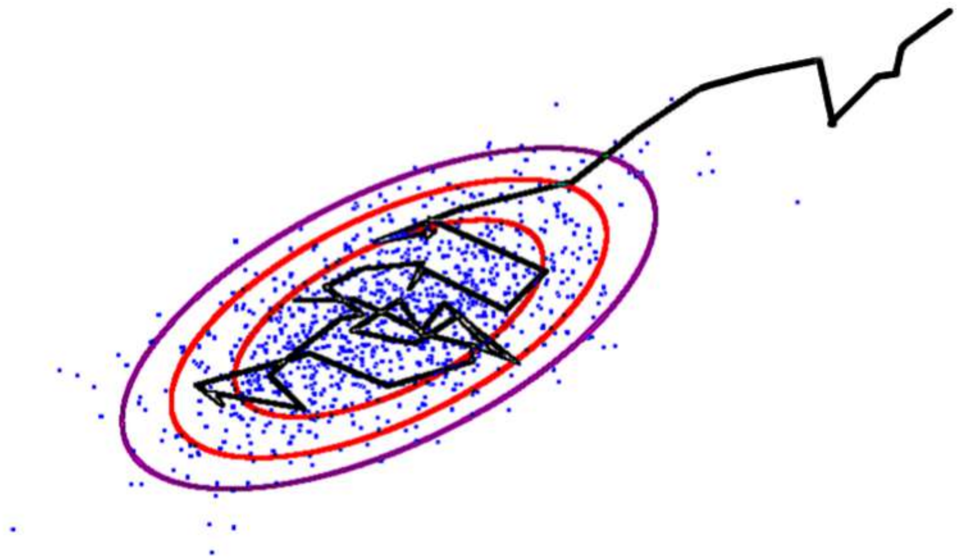
Markov chain Monte Carlo

Construct a biased random walk that explores target dist $P^\star(x)$

Markov steps, $x_t \sim T(x_t \leftarrow x_{t-1})$



MCMC gives approximate, correlated samples from $P^\star(x)$

Metropolis-Hastings sampling, Gibbs sampling, Hamiltonian Sampling

ある人が病気の確率: θ

４人サンプルした結果

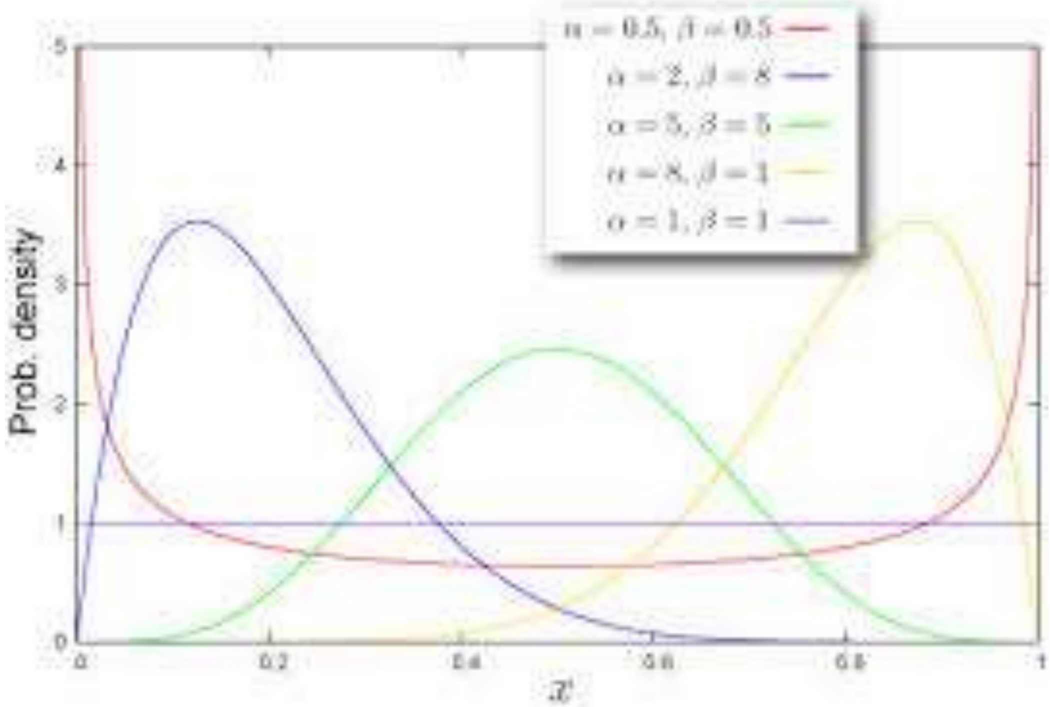
Data: (1, 0, 0, 0)

Model: Binomial Distribution（２項分布）

Prior of θ（事前確率): 一様分布

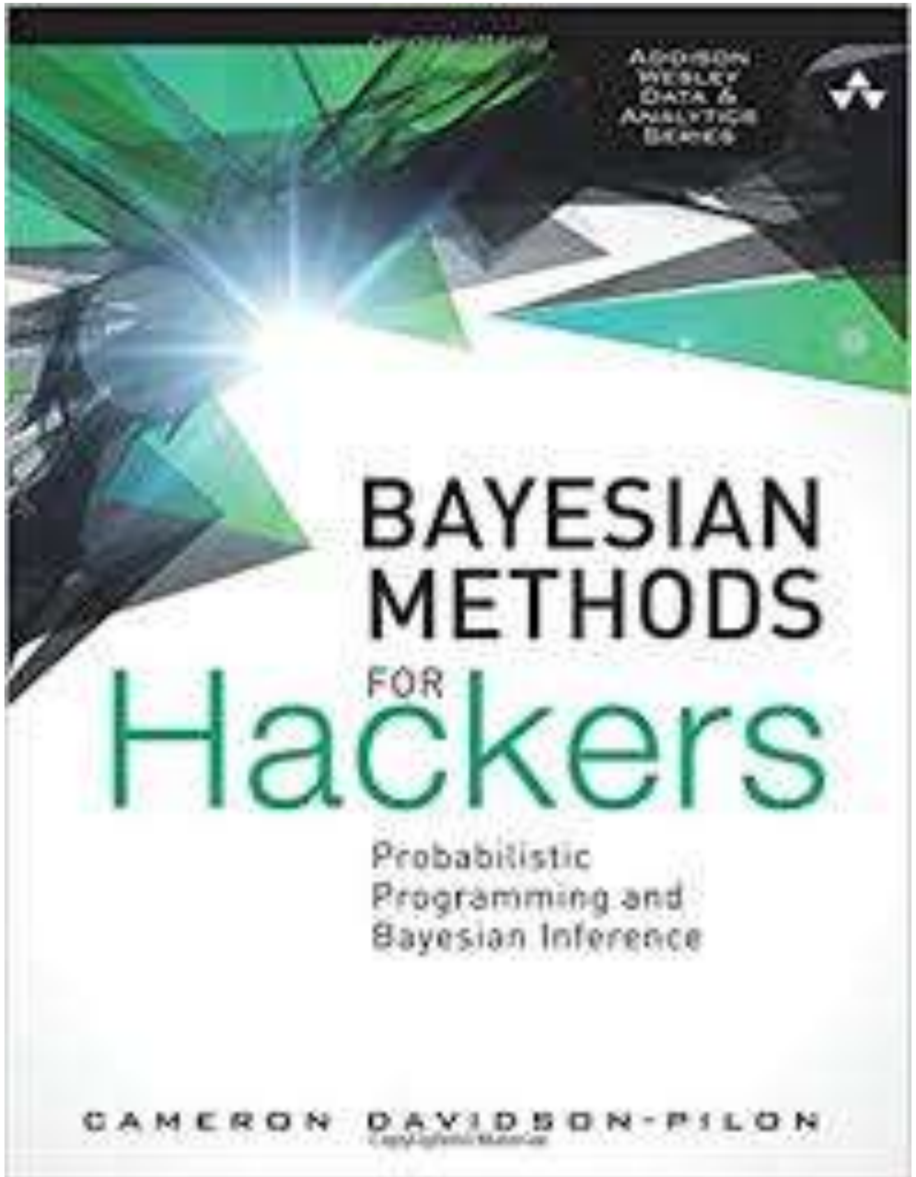
$\theta \sim \mathit{Beta}(\alpha, \beta)$

$$f(x;\alpha,\beta) = \frac{x^{\alpha-1}(1-x)^{\beta-1}}{B(\alpha,\beta)}$$



y = *Bin*(n=1, p=θ)

实例： Jupyter notebook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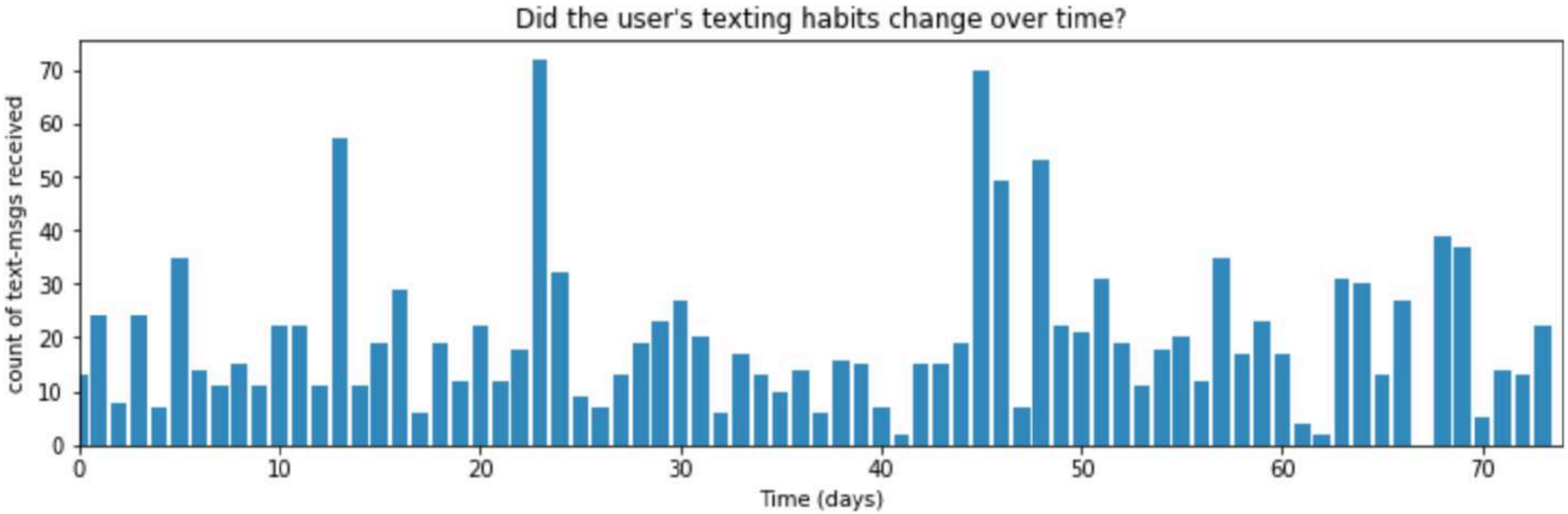
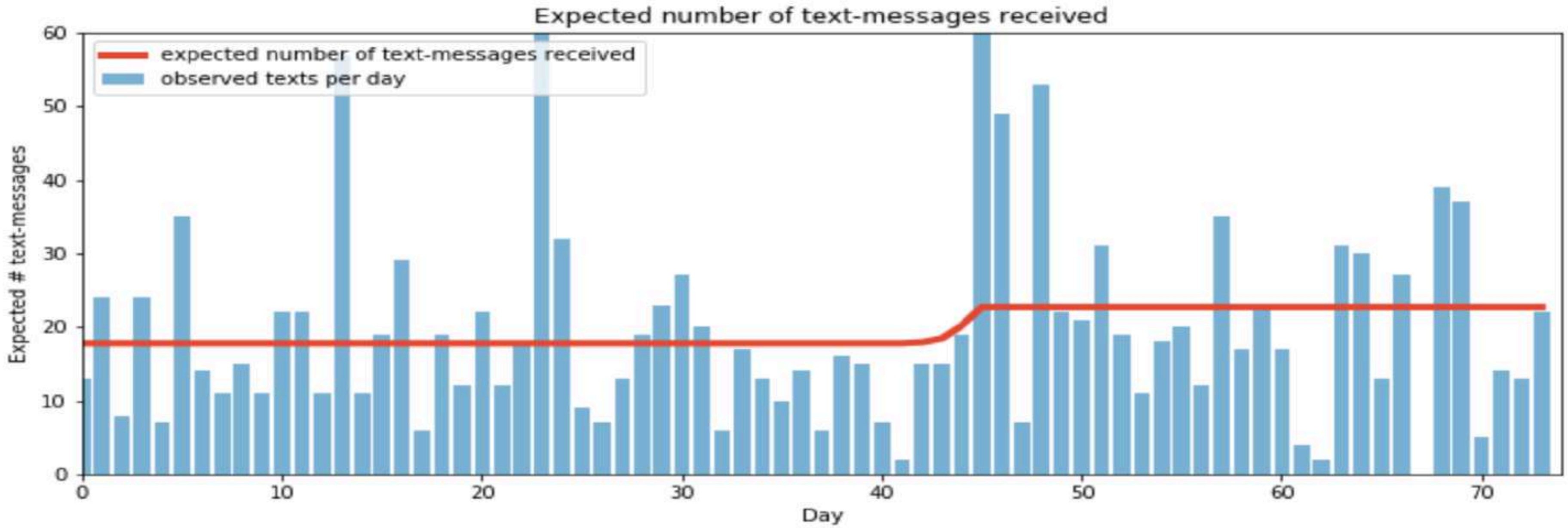


Source:
https://github.com/CamDavidsonPilon/Probabilistic-Programming-and-Bayesian-Methods-for-Hackers



Source:
https://github.com/CamDavidsonPilon/Probabilistic-Programming-and-Bayesian-Methods-for-Hackers

ベイズ推定 （Bayes inference)

$$P(\theta|\mathrm{data}) = [P(\mathrm{data}|\theta) \times P(\theta)] / P(\mathrm{data})$$

θ ： 確率分布のパラメータ

(例： Poisson分布の λ)

Maximum Likelihood 最尤推定値

$L(\theta|X=10, N=100) = {}_{10}C_{100}\ \theta^{10}(1-\theta)^{90}$

Log likelihood

$l = Log(L(\theta|X=10, N=100)\ ) = Log({}_{10}C_{100}\ )+Log(\theta^{10})+Log(1-\theta)^{90}$

$= Log({}_{10}C_{100}\ )+10Log(\theta)+90Log(1-\theta)$

$\partial l/\ \partial\theta = 10 \text{ x } 1/\theta - 90 \text{ x } 1/1-\theta$

$\partial l/\ \partial\theta = 0 \quad \rightarrow \theta = 1/10$

$\partial l^2/\ \partial\theta^2 = -10/\theta^2 - 90/(1-\theta)^2$ with $\theta = 1/10 \ \rightarrow < 0$