

COLD SPRING HARBOR, NEW YORK—How many genes does an organism need to survive? Last week at the genome meeting here,* two genome researchers with radically different approaches presented complementary views of the basic genes needed for life. One research team, using computer analyses to compare known genomes, concluded that today's organisms can be sustained by just 250 genes, and that the *Escherichia coli* genome required a mere 128 genes. The other researcher mapped genes in a simple parasite and estimated that for this organism, 800 genes are plenty to do the job—but that anything short of 100 wouldn't be enough.

Although the numbers don't match precisely, those predictions

"are not all that far apart," especially in comparison to the 75,000 genes in the human genome, notes Siv Andersson of Uppsala University in Sweden, who arrived at the 800 number. But coming up with a consensus answer may be more than just a genetic numbers game, particularly as more and more genomes are completely mapped and analyzed. "It may be a way of organizing the genome," explains Arcady Mushegian, a computational molecular biologist at the National Center for Biotechnology Information (NCBI) in Bethesda, Maryland. Comparing an

Topic Models



November 9

Genes needed
for biochemical
pathways
+22 genes

Redundant and
parasite-specific
genes removed
- 4 genes

Related and
modern genes
removed
-122 genes

256
genes

Ancestral
gene set

Minimal
gene set
250 genes

128
genes

Stripping down. Computer analysis yields an estimate of the minimum modern and ancient gene sets.

Yale

* Genome Mapping and Sequencing, Cold Spring Harbor, New York, May 8 to 12.

Checkpoint

- Assignment 5 (Embeddings) due Thursday
- Assignment 6 (Topic models) posted Thursday
- Quiz 3 next Tuesday: LMs, embeddings, Bayes, topic models

Probabilistic modeling

- ① Data are assumed to be observed from a generative probabilistic process that includes hidden variables.
 - *In text, the hidden variables are the thematic structure.*
- ② Infer the hidden structure using posterior inference
 - *What are the topics that describe this collection?*
- ③ Situate new data into the estimated model.
 - *How does a new document fit into the topic structure?*

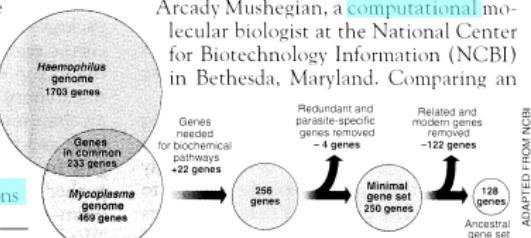
Latent Dirichlet allocation (LDA)

Seeking Life's Bare (Genetic) Necessities

COLD SPRING HARBOR, NEW YORK—How many genes does an organism need to survive? Last week at the genome meeting here,* two genome researchers with radically different approaches presented complementary views of the basic genes needed for life. One research team, using computer analyses to compare known genomes, concluded that today's organisms can be sustained with just 250 genes, and that the earliest life forms required a mere 128 genes. The other researcher mapped genes in a simple parasite and estimated that for this organism, 800 genes are plenty to do the job—but that anything short of 100 wouldn't be enough.

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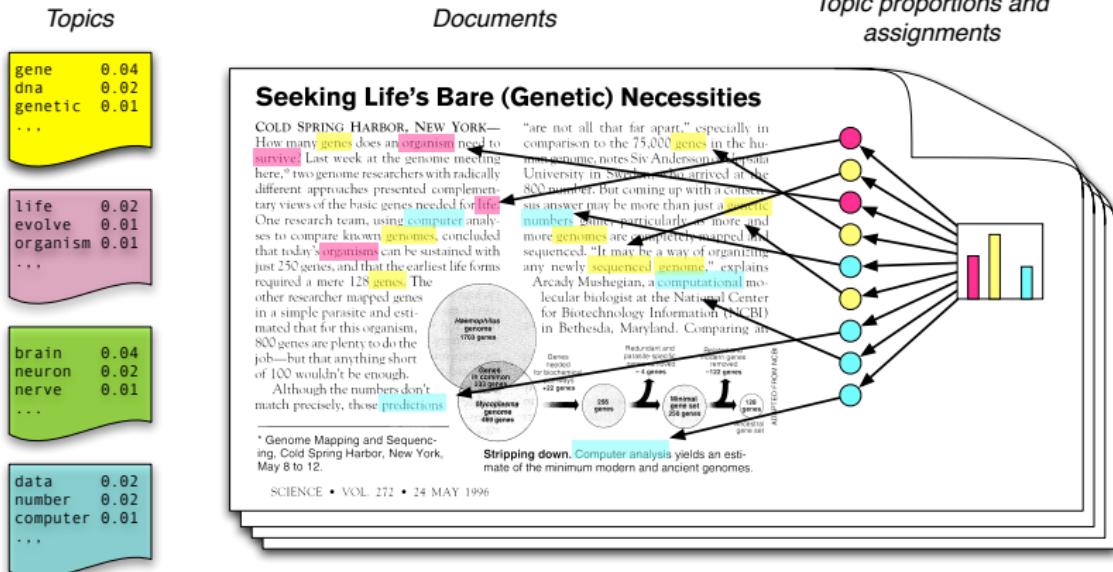


ADAPTED FROM NCBI

Stripping down. Computer analysis yields an estimate of the minimum modern and ancient genomes.

Simple intuition: Documents exhibit multiple topics.

Generative model for LDA



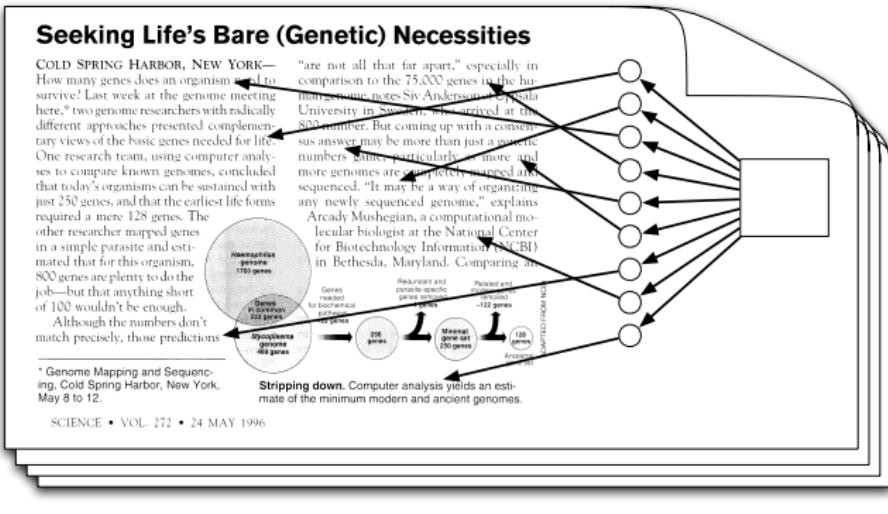
- Each **topic** is a distribution over words
- Each **document** is a mixture of corpus-wide topics
- Each **word** is drawn from one of those topics

The posterior distribution

Topics



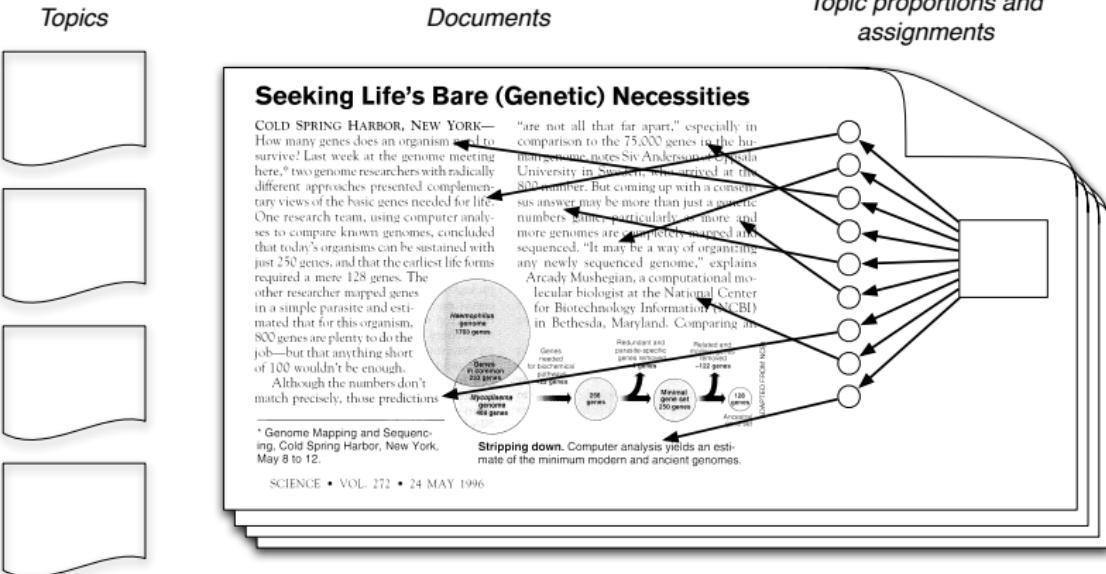
Documents



Topic proportions and assignments

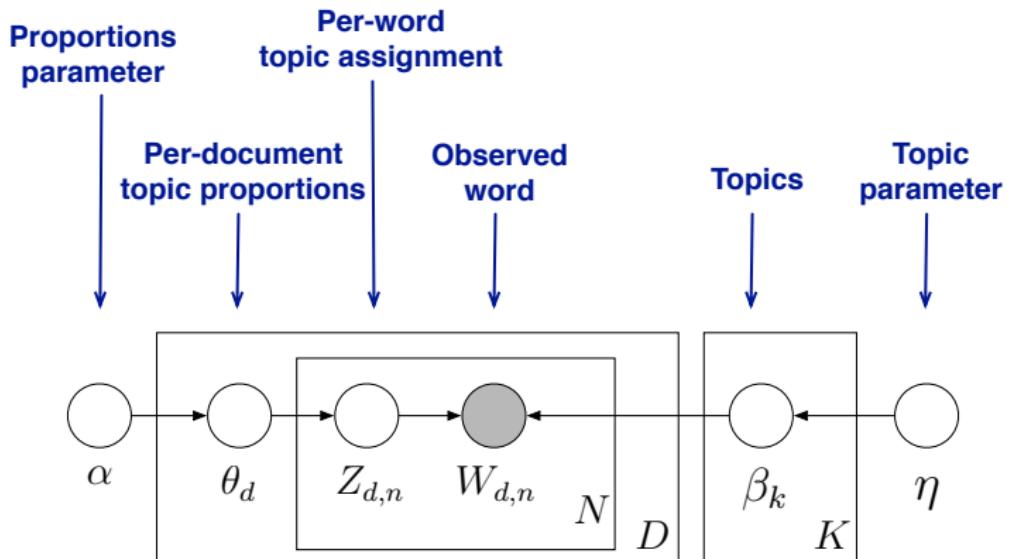
- In reality, we only observe the documents
 - The other structure are **hidden variables**

The posterior distribution



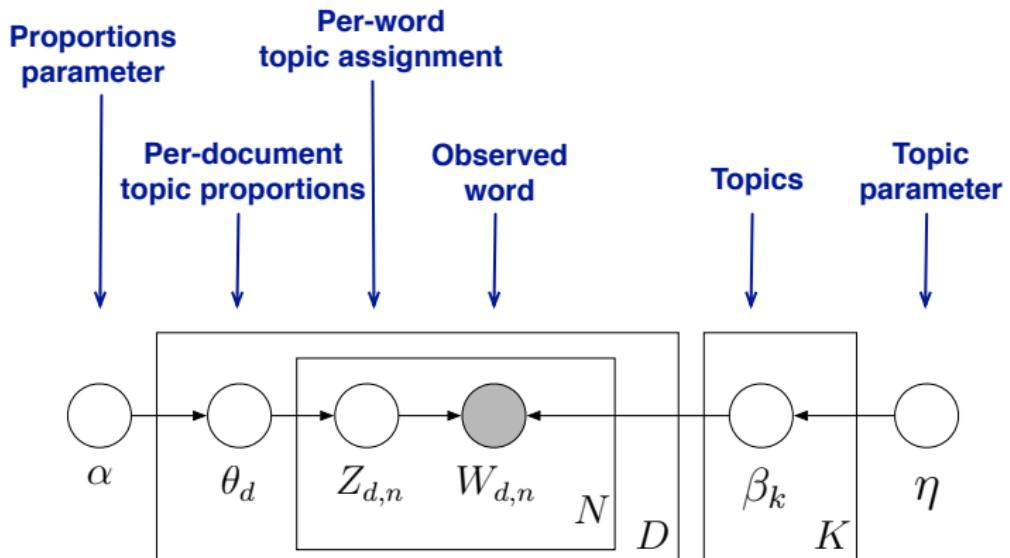
- Our goal is to **infer** the hidden variables
 - I.e., compute their distribution conditioned on the documents
- $$p(\text{topics, proportions, assignments} \mid \text{documents})$$

LDA as a graphical model



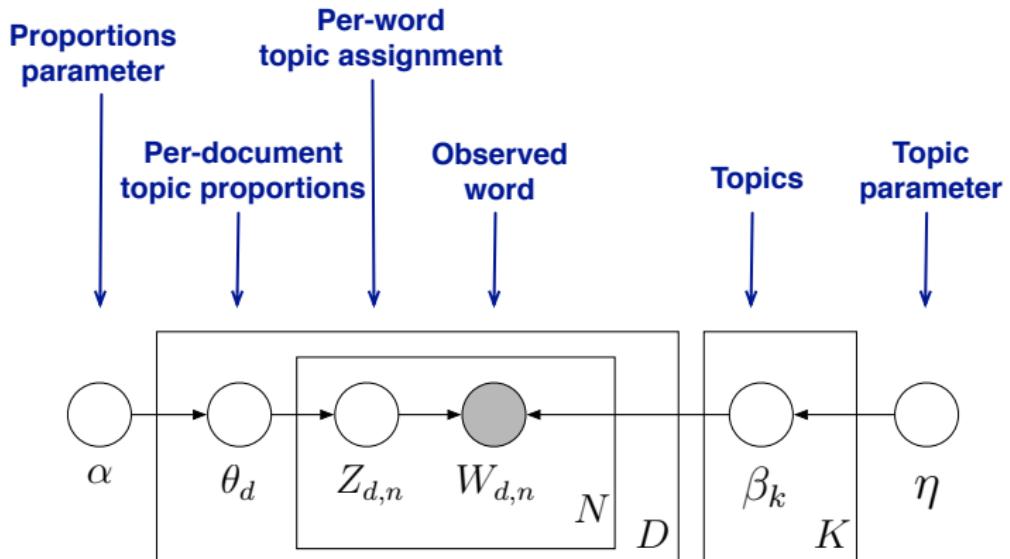
- Encodes our assumptions about the data
- Connects to algorithms for computing with data
- See *Pattern Recognition and Machine Learning* (Bishop, 2006).

LDA as a graphical model



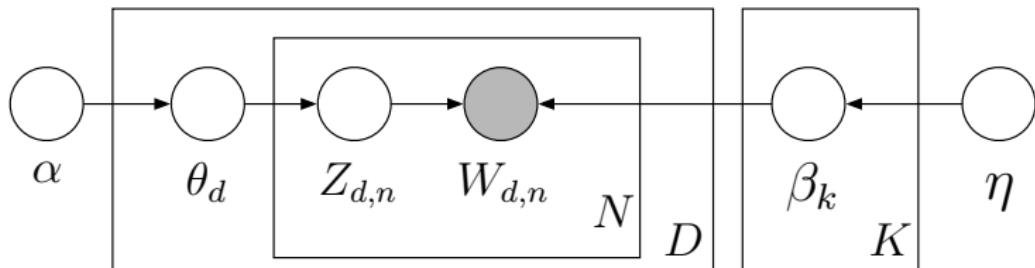
- Nodes are random variables; edges indicate dependence.
- Shaded nodes are observed.
- Plates indicate replicated variables.

LDA as a graphical model



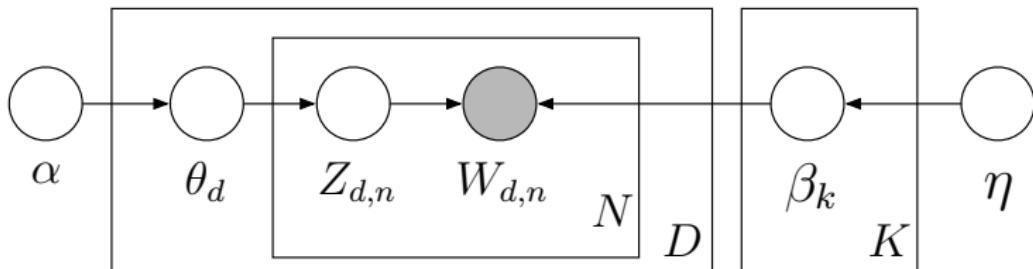
$$\prod_{i=1}^K p(\beta_i | \eta) \prod_{d=1}^D p(\theta_d | \alpha) \left(\prod_{n=1}^N p(z_{d,n} | \theta_d) p(w_{d,n} | \beta_{1:K}, z_{d,n}) \right)$$

LDA



- This joint defines a posterior.
- From a collection of documents, infer
 - Per-word topic assignment $Z_{d,n}$
 - Per-document topic proportions θ_d
 - Per-corpus topic distributions β_k
- Then use posterior expectations to perform the task at hand, e.g., information retrieval, document similarity, exploration, ...

Example inference



- **Data:** The OCR'ed collection of *Science* from 1990–2000
 - 17K documents
 - 11M words
 - 20K unique terms (stop words and rare words removed)
- **Model:** 100-topic LDA model using variational inference.

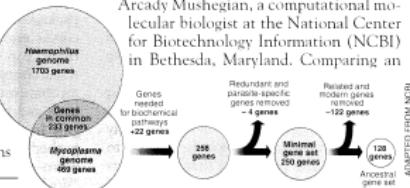
Example inference

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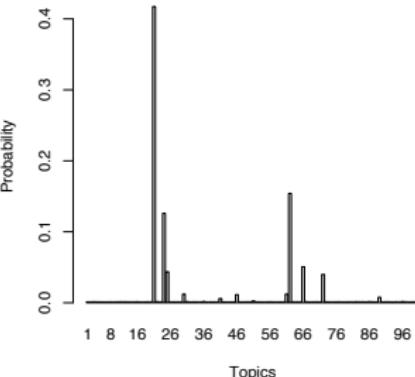
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* Genome Mapping and Sequencing, Cold Spring Harbor, New York, May 8 to 12.

Stripping down. Computer analysis yields an estimate of the minimum modern and ancient genomes.



Example inference

human	evolution	disease	computer
genome	evolutionary	host	models
dna	species	bacteria	information
genetic	organisms	diseases	data
genes	life	resistance	computers
sequence	origin	bacterial	system
gene	biology	new	network
molecular	groups	strains	systems
sequencing	phylogenetic	control	model
map	living	infectious	parallel
information	diversity	malaria	methods
genetics	group	parasite	networks
mapping	new	parasites	software
project	two	united	new
sequences	common	tuberculosis	simulations

Example inference (II)

Chaotic Beetles

Charles Godfray and Michael Hassell

Ecologists have known since the pioneering work of May in the mid-1970s (1) that the population dynamics of animals and plants can be exceedingly complex. This complexity arises from two sources: The tangled web of interactions that constitute any natural community provide a myriad of different pathways for species to interact, both directly and indirectly. And even in isolated populations the nonlinear feedback processes present in all natural populations can result in complex dynamic behavior. Natural populations can show persistent oscillatory dynamics and chaos, the latter characterized by extreme sensitivity to initial conditions. If such chaotic dynamics were common in nature, then this would have important ramifications for the management and conservation of natural resources. On page 389 of this issue, Costantino *et al.* (2) provide the most

convincing evidence to date of complex dynamics and chaos in a biological population—of the flour beetle, *Tribolium castaneum* (see figure).

It has proven extremely difficult to demonstrate complex dynamics in populations in the field. By its very nature, a chaotically fluctuating population will superficially resemble a stable or cyclic population buffeted by the normal random perturbations experienced by all species. Given a long enough time series, diagnostic tools from nonlinear mathematics can be used to identify the telltale signatures of chaos. In phase space, chaotic trajectories come to lie on “strange attractors,” curious geometric objects with fractal structure and hence noninteger dimension. As they

move over the surface of the attractor, sets of adjacent trajectories are pulled apart, then stretched and folded, so that it becomes impossible to predict exact population densities into the future. The strength of the mixing that gives rise to the extreme sensitivity to initial conditions can be measured mathematically estimating the Liapunov exponent, which is positive for chaotic dynamics and nonpositive otherwise. There have been many attempts to estimate attractor dimension and Liapunov exponents from time series data, and some candidate chaotic population have been identified (some insects, rodents, and most convincingly, human childhood diseases), but the statistical difficulties preclude any broad generalization (3).

An alternative approach is to parameterize population models with data from natural populations and then compare their predictions with the dynamics in the field. This technique has been gaining popularity in recent years, helped by statistical advances in parameter estimation. Good ex-



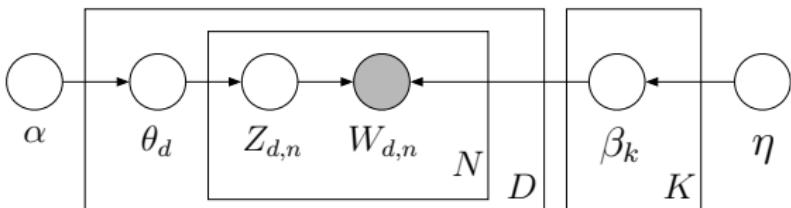
Cannibalism and chaos.
The flour beetle, *Tribolium castaneum*, exhibits chaotic population dynamics when the amount of cannibalism is altered in a mathematical model.

The authors are in the Department of Biology, Imperial College at Silwood Park, Ascot, Berks, SL5 7PZ UK. E-mail: m.hassell@ic.ac.uk

Example inference (II)

problem	model	selection	species
problems	rate	male	forest
mathematical	constant	males	ecology
number	distribution	females	fish
new	time	sex	ecological
mathematics	number	species	conservation
university	size	female	diversity
two	values	evolution	population
first	value	populations	natural
numbers	average	population	ecosystems
work	rates	sexual	populations
time	data	behavior	endangered
mathematicians	density	evolutionary	tropical
chaos	measured	genetic	forests
chaotic	models	reproductive	ecosystem

Posterior inference for LDA



- There is a large literature on approximating the posterior.
- We will focus on
 - Gibbs sampling
 - Mean-field variational methods (batch and online)



Markov chain Monte Carlo

- Construct a **Markov chain** on the hidden variables, whose limiting distribution is the posterior.
- Collect **independent samples** from that distribution; approximate the posterior with them
- In **Gibbs sampling** the chain is defined by the conditional distribution of each hidden variable given observations and the current setting of the other hidden variables.

Toy example: 3 topics, 3 docs

w	z	w	z	w	z
meth	2	drug	3	inning	1
father	1	baseball	2	mother	3
divorce	3	hit	1	son	1
drug	1	inning	2	hit	2
illegal	1	steroids	1	baseball	3

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drug	1	inning	2	hit	2
illegal	1	steroids	1	baseball	2

Extensions

Modeling richer assumptions

- Correlated topic model
- Dynamic topic model

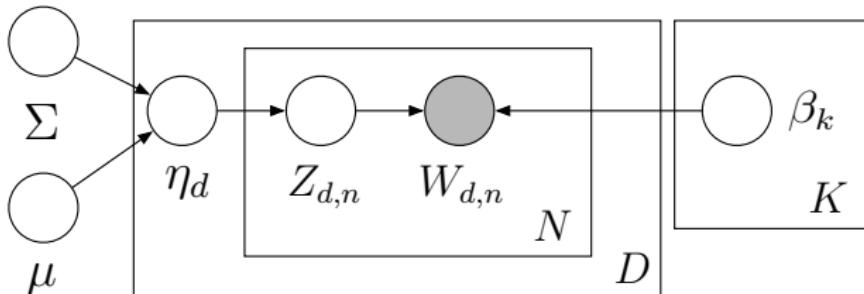
Shortcoming of the Dirichlet

- Dirichlet for topic proportions:

$$p(\theta | \alpha) \propto \prod_{j=1}^k \theta_j^{\alpha_j - 1}$$

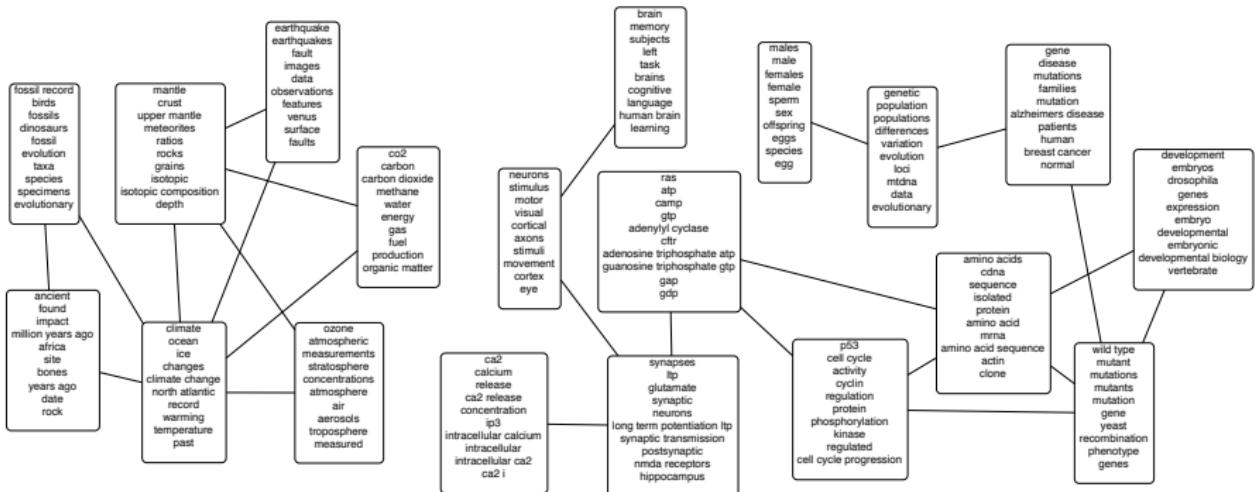
- Near independence of components makes it an unrealistic model
 - ▶ An article about *fossil fuels* is more likely to also be about *geology* than about *genetics*

Correlated topic model

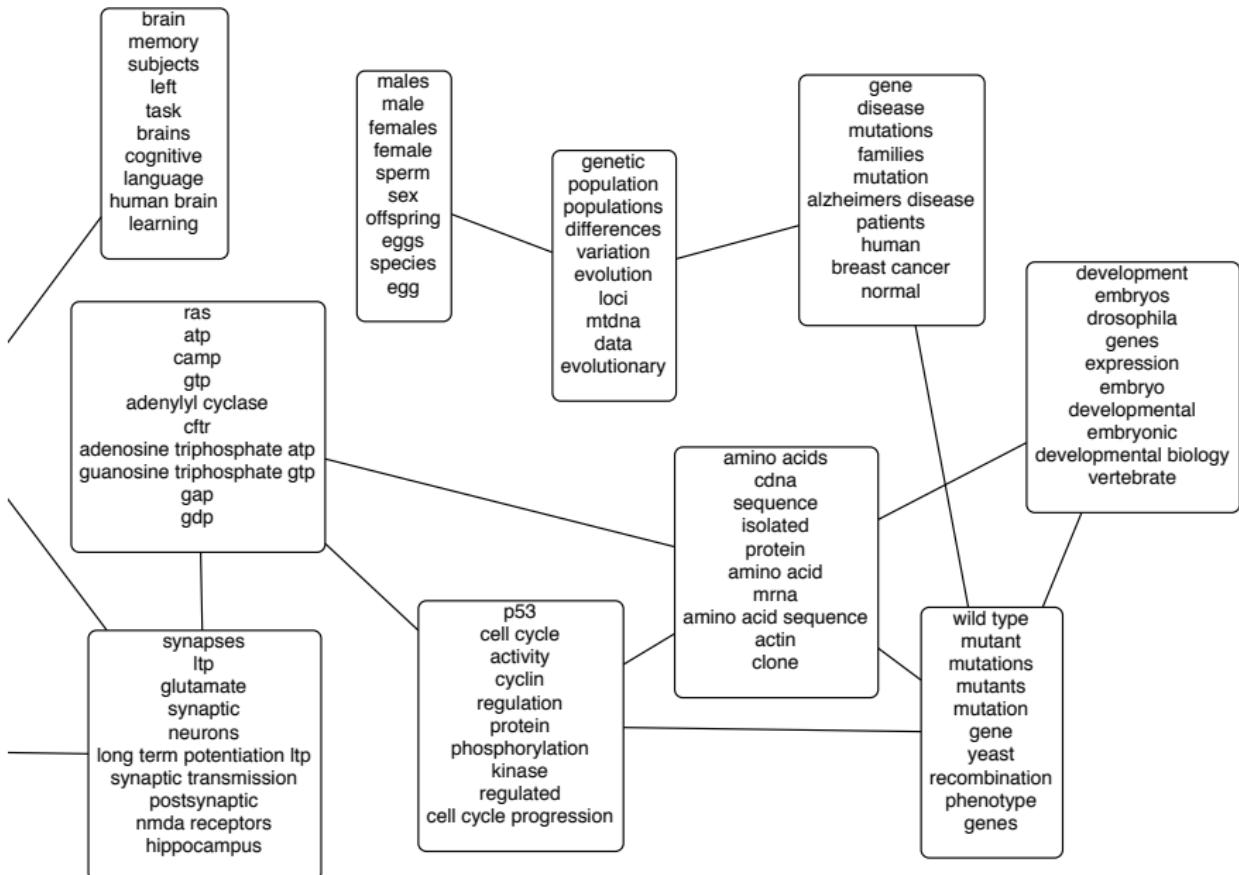


- Draw topic proportions from a logistic normal.
- Useful for:
 - ▶ providing a “map” of topics and how they are related;
 - ▶ better prediction via correlated topics.
- Sacrifice conjugacy: Posterior over θ does not have same form

Topic graphs



Topic graphs



Modeling Evolution of Topics

- In LDA, document order doesn't matter
- The topics should *evolve* over time
 - ▶ “Cleaning Birds” (1883)
 - ▶ “Interspecific Brood Parasitism in Blackbirds (Icterinae): A Phylogenetic Perspective” (1992)
- Many document collections have such dynamics: emails, query logs, news articles, etc.

Science 1893 ⇒ Science 1976

Administration	Limnology	Astronomy	Psychology
association	water	observatory	mind
meeting	lake	observations	nature
american	sea	stars	say
committee	waters	time	science
congress	lakes	made	psychology
members	gulf	astronomical	work
held	great	comet	knowledge
international	depth	star	truth
meetings	river	observed	religion
section	stream	telescope	human

Administration	Limnology	Astronomy	Psychology
house	water	mass	human
congress	concentrations	radio	attempts
science	mercury	objects	theory
bill	fish	astronomy	learning
nsf	samples	xray	ideas
president	soil	stars	new
budget	lake	astronomical	memory
office	ppm	sources	psychology
committee	concentration	observations	behavior
new	waters	observatory	complex

Time series topic model

1. Allow topics evolve between time slices
3. For each document in the current time slice:
 - a. Select a distribution over topics;
 - b. Generate the words from the resulting topic mixture.

Time-corrected document similarity

The Brain of the Orang (1880)

300

EXTRACTIVE

In this issue there are three papers which have submitted to us for publication in the *Journal of Geriatric Psychiatry and Neurology*: one objecting to the changes we have made in its *Instructions to Authors*, another objecting to the changes we have made in our *Code of Practice*. We have asked that the writers under whose names these articles are published clarify their position. We therefore request one reader of each article to respond.

George E. Barker, Frederick G. Marder and Priscilla J. H. Blaustein are preparing more elaborate responses to these important papers, and promise them as soon as possible.

THE MEAN OF THE SAMPLE

BY HENRY C. DUNHAM, M.D.

The state of China has been figured by Tabin, and the Chinese have been described by Gutzlaff, Klaproth, etc. On the other, however, of the literature, and of the importance of the subject, it is remarkable that there are few recent views of my own. The last few years were from results of Dr. L. C. Liao, who was removed from his post in 1903, to his return, which was about 1907. In 1908, Dr. Liao, and a little of the work of the left hemisphere had been described by Dr. S. S. Chang, and good results. It weighed only one month. The author of this paper, however, has not mentioned Dr. Liao's work, nor the author of the Chinese paper, nor the author of the paper which Dr. Chang has published, and which I have seen, has he ever made change in his original statement? The author of the Chinese paper, however, has not mentioned Dr. Liao's work, nor the author of the paper which Dr. Chang has published, and which I have seen, has he ever made change in his original statement? The author of the Chinese paper, however, has not mentioned Dr. Liao's work, nor the author of the paper which Dr. Chang has published, and which I have seen, has he ever made change in his original statement? The author of the Chinese paper, however, has not mentioned Dr. Liao's work, nor the author of the paper which Dr. Chang has published, and which I have seen, has he ever made change in his original statement?



1

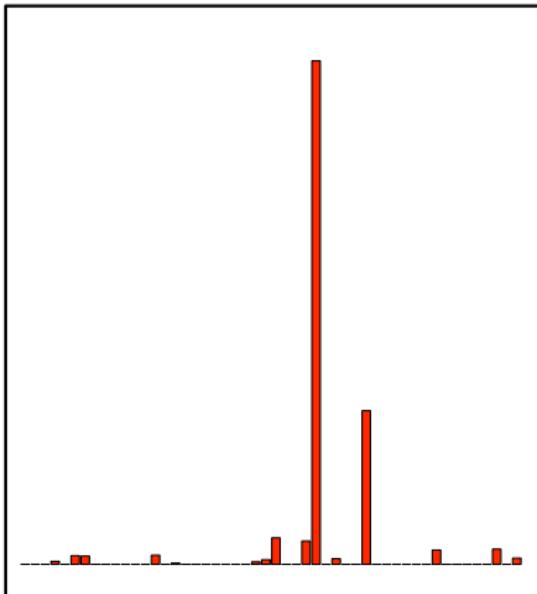
The brain of the orang, chimpanzee, and man are the same; they are certain racial differences, however, in the development in all three. The fissure of Sylvius in the orang is much deeper than in the chimpanzee, and contains only a single, broadened division; the anterior part of the fissure is, therefore, of greater depth than the posterior, and the corpus callosum is correspondingly larger in the orang than in man. It differentiates the two hemispheres more completely in the orang than in man, and is well marked; bordered on one side by the longitudinal sulcus, it descends laterally on the mesial side of the hemisphere.



6

acipenser fissure: externally it is continuous with the capital lobe, as the first acipenser gyrus, anteriorly it is separated from the posterior cerebral convolution more completely than is usual, by a fissure which runs parallel to the cerebral commissure. In the orangutan the fissure is continued with the parieto-occipital sulcus which divides the upper parietal lobe into lateral and median portions. The paroxysm, or the space on the median side of the parietal lobe between the parieto-occipital

* From the Proceedings of the Academy of Natural Sciences, Philadelphia, etc.



Time-corrected document similarity

Representation of the Visual Field on the Medial Wall of Occipital-Parietal Cortex in the Owl Monkey (1976)

present by recording responses of the medial occipital-parietal cortex were plotted with描记technique using techniques in five owl monkeys (2). The monkeys were anesthetized, killed, and prepared for recording. Tissue and pterygomastoid-mastoidectomy were used to expose the medial occipital-parietal cortex or occasionally from single resections it was exposed by resecting the temporal lobe and softening all surrounding connective tissue. Recording fields were plotted by moving microelectrodes across the surface of the cortex on the surface of a translucent plastic hemisphere centered in front of the contralateral eye. A translucent plastic disk was projected onto the plane hemispherical screen with the aid of Fernand and Chou (5). The preferred eye usually was

covered with a opaque shield. Electrode tracks and recorded receptive fields were extracted from histological sections and photographs of the intact brain.

In the present report we focus our most complete mapping of the visual field area, data obtained in the other four experiments are described elsewhere. The cortical organization of the visual field area in the owl monkey is similar to that in the rhesus monkey (6). In Fig. 2, which illustrates the organization of the other cortical visual areas that have been mapped by the cat monkey, the border between the visual area and the auditory area is roughly at the upper one-third portion of the horizontal meridian. In other experiments in the macaque area, the visual field area is roughly bounded near its caudal border with the medial geniculate nucleus and optic radiations and near its lateral border and projected in a broad loop in the periphery toward the contralateral eye. In the experiments shown in Figs. 1 and 2, the anterior border between the dorsomedial and the medial occipital-parietal cortex is roughly bounded in the lower quadrant near the vertical meridian about 30° to 40° from the center (6). Thus, as is shown in Fig. 1, and

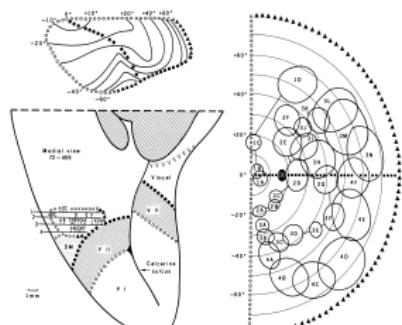
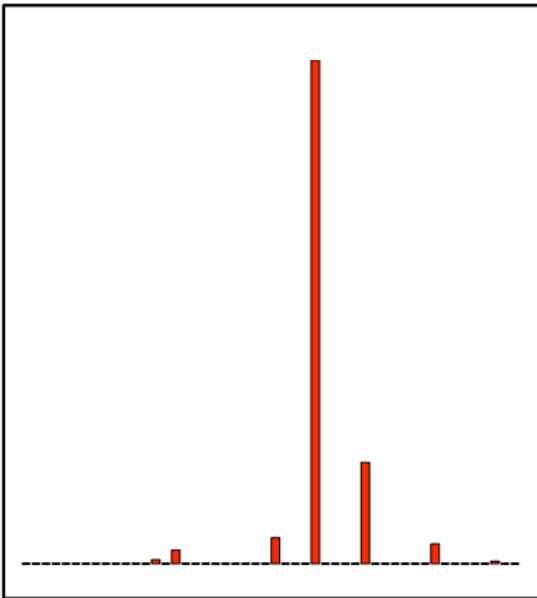


Fig. 1. Microelectrode recording penetrations and receptive field data for the medial visual area in owl monkey 72-415. The diagram on the lower left is a medial view of the left hemisphere of the owl monkey with the brainstem and cerebellum removed. An arrow is used to indicate the direction of descent to the left in this diagram. Microelectrode penetrations are shown as small dots in the medial wall. The upper-left is a polar plot of the receptive fields in the left visual field on the right. The upper-left is a polar plot of the visual field representation of the medial visual area. The numbers in the circles represent the number of microelectrode penetrations in each receptive field. V1 is the first visual area; V2 is the second visual area. PM = posterior medial area. DM = dorsomedial visual area.



Exploring the UN General Debates with Dynamic Topic Models



Luke Lefebvre [Follow](#)
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Credit: [Vladislav Klapin on Unsplash](#)

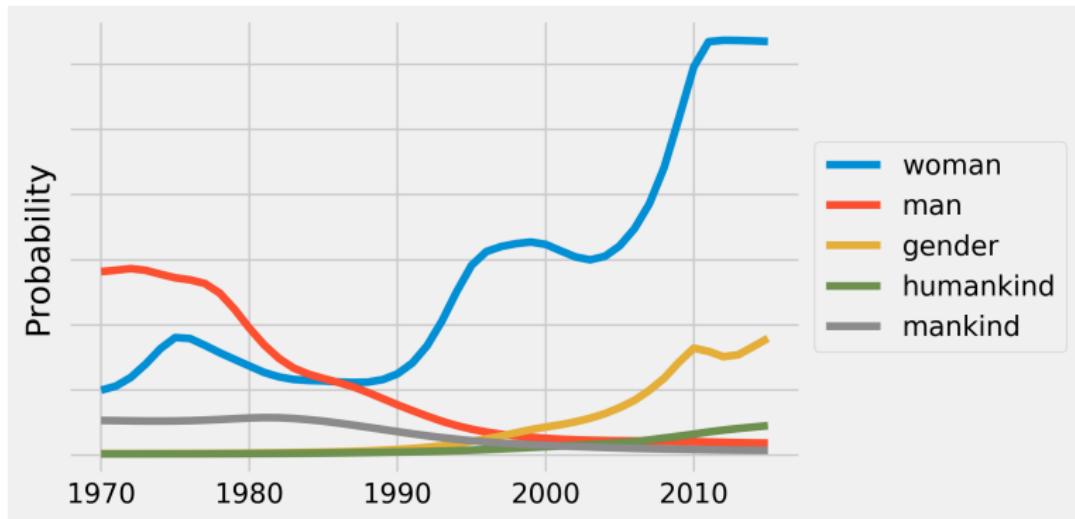
<https://towardsdatascience.com/>

[exploring-the-un-general-debates-with-dynamic-topic-models-72dc0e307696](https://towardsdatascience.com/exploring-the-un-general-debates-with-dynamic-topic-models-72dc0e307696)

Human rights

	1970	1980	1990	2000	2010
0	right	right	right	right	right
1	human	human	human	human	human
2	people	people	freedom	law	law
3	international	freedom	people	democracy	woman
4	principle	international	democracy	respect	freedom
5	justice	political	respect	international	respect
6	freedom	principle	law	people	people
7	law	respect	international	freedom	democracy
8	state	justice	principle	principle	rule
9	must	social	state	must	international

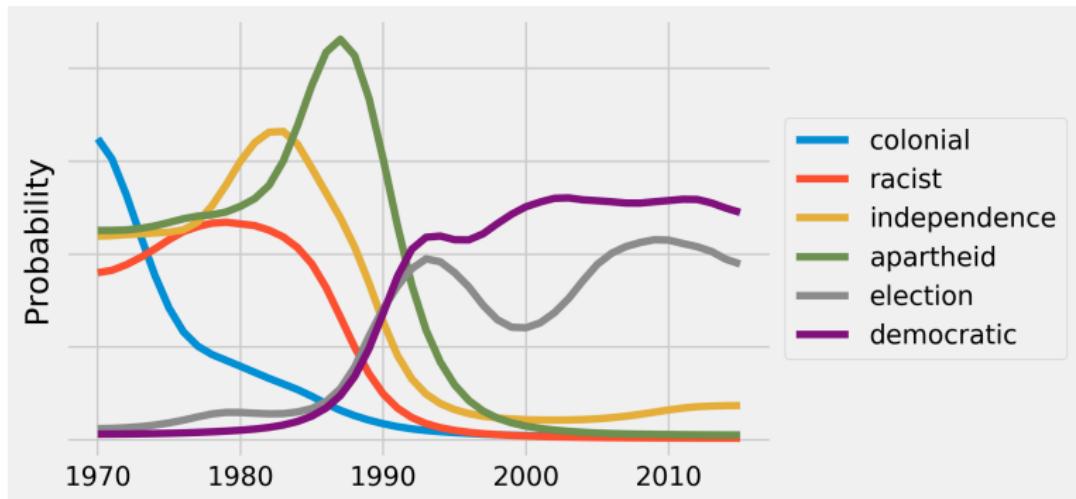
Human rights



Apartheid

	1970	1980	1990	2000	2010
0	africa	africa	africa	african	african
1	african	south	south	peace	country
2	south	african	african	africa	government
3	colonial	namibia	apartheid	country	africa
4	people	people	people	government	people
5	regime	regime	government	community	peace
6	southern	independence	country	democratic	political
7	government	apartheid	namibia	international	community
8	territory	racist	community	republic	democratic
9	apartheid	southern	process	effort	national

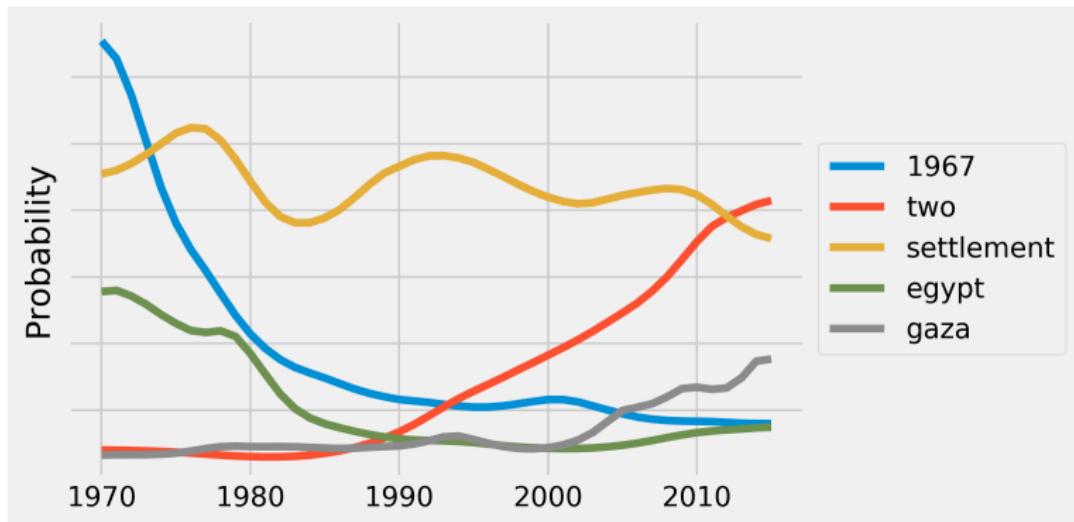
Apartheid



Arab-Israeli conflict

	1970	1980	1990	2000	2010
0	arab	palestinian	peace	peace	peace
1	israel	israel	east	east	state
2	east	right	middle	resolution	palestinian
3	middle	east	arab	palestinian	solution
4	peace	people	people	middle	east
5	territory	arab	palestinian	security	international
6	resolution	middle	international	people	israel
7	1967	peace	israel	israel	middle
8	palestinian	territory	kuwait	state	arab
9	israeli	state	right	international	people

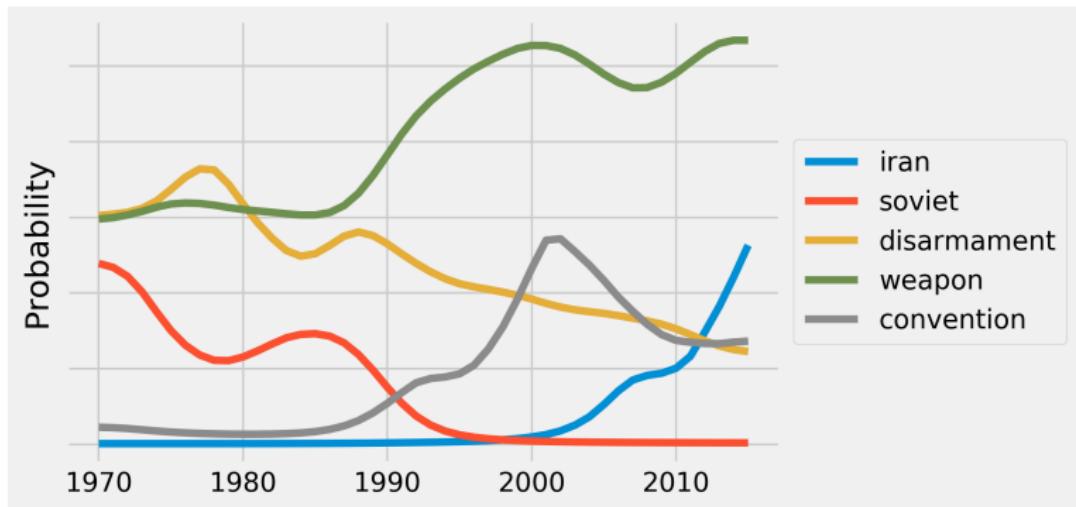
Arab-Israeli conflict



Nuclear arms

	1970	1980	1990	2000	2010
0	nuclear	nuclear	nuclear	weapon	nuclear
1	disarmament	disarmament	weapon	nuclear	weapon
2	weapon	weapon	disarmament	convention	non
3	soviet	arm	treaty	arm	proliferation
4	arm	state	arm	treaty	arm
5	treaty	race	state	disarmament	treaty
6	union	military	chemical	proliferation	international
7	agreement	treaty	agreement	international	disarmament
8	power	soviet	proliferation	non	convention
9	state	power	soviet	destruction	state

Nuclear arms



Tutorials

<https://medium.com/@lettier/how-does-lda-work-ill-explain-using-emoji-108abf40fa7d>

<https://towardsdatascience.com/>

[latent-dirichlet-allocation-intuition-math-implementation-and-visualisation-63ccb616e094](https://towardsdatascience.com/latent-dirichlet-allocation-intuition-math-implementation-and-visualisation-63ccb616e094)

Summary

- Topic models automatically extract “semantic themes” from large document collections
- Use mixtures and latent variables
- Estimating Bayesian posterior done with Gibbs sampling
- Many extensions are possible