Using models to link surveillance and global air transportation data

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Diseases have been moving around for a while

It first began, it is said, in the parts of Ethiopia above Egypt, and thence descended into Egypt and Libya and into most of the [Persian] King's country. Suddenly falling upon Athens, it first attacked the population in Piraeus [..] and afterwards appeared in the upper city, when the deaths became much more frequent.

Thucydides (c. 460 BC - c. 395 BC)
History of the Peloponnesian War
(plague of Athens of 430 BC)

Several types of mobilities

- Long term (> 6 months): relocation, immigration, refugees
  Typically change of place of main residence

- Middle range (1–6 months): migrant workers (domestic and foreign)
  Typically maintain two places of residence (or strong attachment to one of the two)

- Short term (< 1 month): travel (work or leisure).
  Travel away from the main place of residence. **Focus here**

Spatio-temporal spread of SARS in 2003

SARS gets onto the GATN in March 2003

- propagation to 27 countries in Asia, North and South America, Europe, in a matter of months

36 cities imported SARS cases

- 24 had direct nonstop flights from Hong Kong (HKG)
- 12 were 1 stop away from HKG

137 cases showed to have crossed national boundaries while infected

- 129 travelled by air
- 8 people went China $\rightarrow$ Mongolia by ground transportation

Spatial spread of nH1N1 in 2009

March and April 2008 (surrogate for 2009 data):

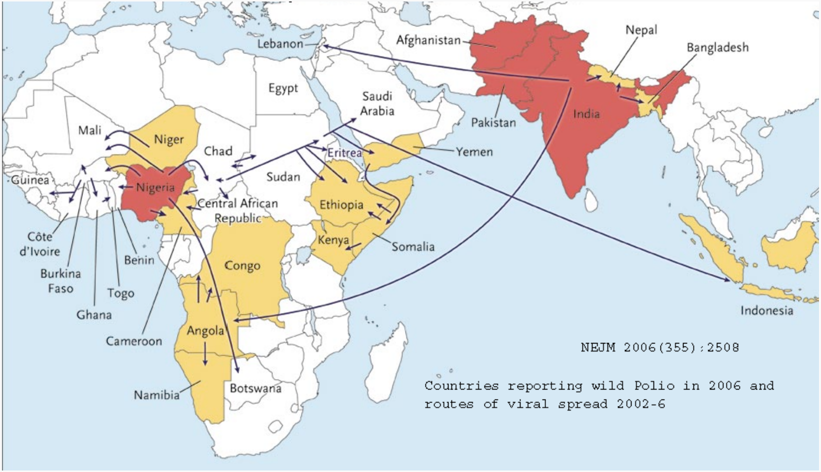
- 2.35M PAX flew from MX to 1018 cities in 164 countries
    - 80.7% to USA and Canada
    - 8.8% to South and Central America
    - 8.7% to Europe

- countries receiving more than 1400 passengers from MX at significantly elevated risk for importation (ROC curve). Using this passenger threshold, international air-traffic volume alone was a
    - more than 92% sensitive
    - more than 92% specific

  predictor of importation (area under the ROC curve of 0.97)

Khan, Arino, Hu et al, New England J Med, July 2009

Polio after 2002



Internet (trawling) disease surveillance

Principle

Internet (trawling) surveillance uses automatic processing of internet sources (news, blogs, etc.) to monitor and provide early warning about the emergence or re-emergence of diseases

- HealthMap
- Global Public Health Information Network (GPHIN, Public Health Agency of Canada)

Another example, specific to influenza: Google Flu Trends, uses google searches about influenza to guesstimate flu activity

It works!

Health officials outside of Mexico were potentially aware of what was eventually determined to be the 2009 H1N1 pandemic as early as April 1, when HealthMap first disseminated local media reports about a "mysterious" influenza-like illness in La Gloria.

April 6: Veratect

On April 10, GPHIN notified WHO of acute respiratory illness in La Gloria, and on the following day the PAHO IHR focal point (the point of contact with the WHO under the IHR) requested verification.

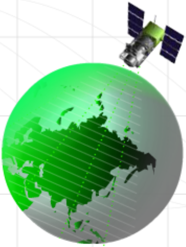
Y. Zhang et al, PLoS One, 8(4), April 2013

However..

Because they trawl the internet, these systems generate a lot of noise

$\Rightarrow$ Human analysts go through the alerts to eliminate the irrelevant ones and help rank the alerts

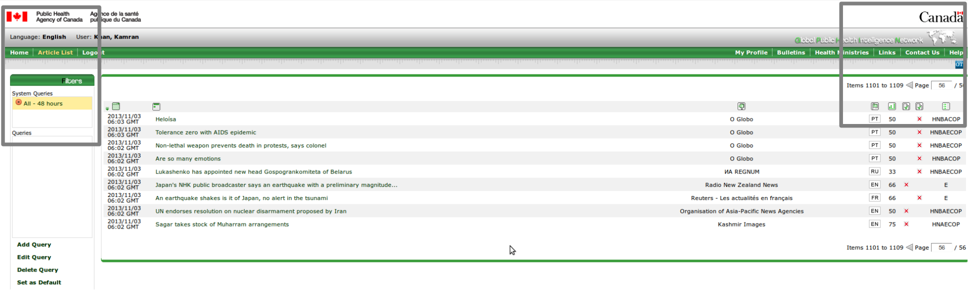
RÉSEAU
MONDIAL
D'
INFORMATION
EN
SANTÉ
PUBLIQUE



GLOBAL
PUBLIC
HEALTH
INTELLIGENCE
NETWORK

English ☐ default language **Enter**

عن GPHIN 简体中文 繁體中文 About GPHIN RMISP en bref درباره جیفن Sobre o sistema GPHIN О ССГИОЗ Acerca de la RIMSP


Public Health
Agency of Canada
Canada
Global Public
ntelligence Network
Language: English
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Article List
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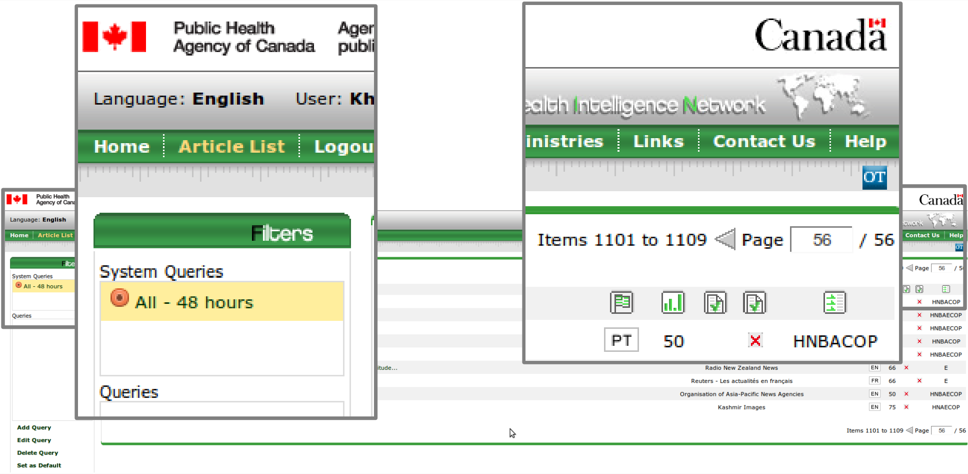
Bulletins
Links
Contact Us
Help
Filters
System Queries
All - 48 hours
Queries
Add Query
Edit Query
Delete Query
Set as Default
Items 1101 to 1109 Page 56
2013/11/03 06:03 GMT | Heloísa | O Globo | PT | 50 | HNBACOP
2013/11/03 06:03 GMT | Tolerance zero with AIDS epidemic | O Globo | PT | 50 | HNBAECOP
2013/11/03 06:02 GMT | Non-lethal weapon prevents death in protests, says colonel | O Globo | PT | 50 | HNBAECOP
2013/11/03 06:02 GMT | Are so many emotions | O Globo | PT | 50 | HNBACOP
2013/11/03 06:02 GMT | Lukashenko has appointed new head Gospogrankomiteta of Belarus | ИА REGNUM | RU | 33 | HNBAECOP
2013/11/03 06:02 GMT | Japan's NHK public broadcaster says an earthquake with a preliminary magnitude... | Radio New Zealand News | EN | 66 | E
2013/11/03 06:02 GMT | An earthquake shakes is it of Japan, no alert in the tsunami | Reuters - Les actualités en français | FR | 66 | E
2013/11/03 06:02 GMT | UN endorses resolution on nuclear disarmament proposed by Iran | Organisation of Asia-Pacific News Agencies | EN | 50 | HNBAECOP
2013/11/03 06:02 GMT | Sagar takes stock of Muharram arrangements | Kashmir Images | EN | 75 | HNAECOP
Items 1101 to 1109 Page 56 / 56



Public Health Agency of Canada
Language: English
User: Kh
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All - 48 hours
Queries
Add Query
Edit Query
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Links
Contact Us
Help
Items 1101 to 1109
Page 56 / 56
PT
50
HNBACOP
HNBAECOP
Radio New Zealand News
Reuters - Les actualités en français
Organisation of Asia-Pacific News Agencies
Kashmir Images
HNAECOP

Situation awareness and information overload

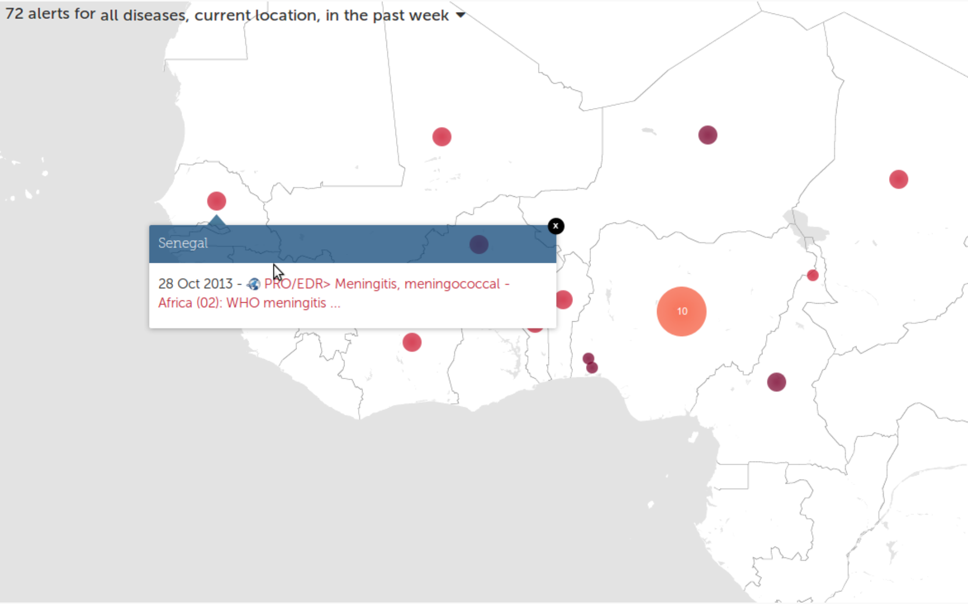
A lot of alerts

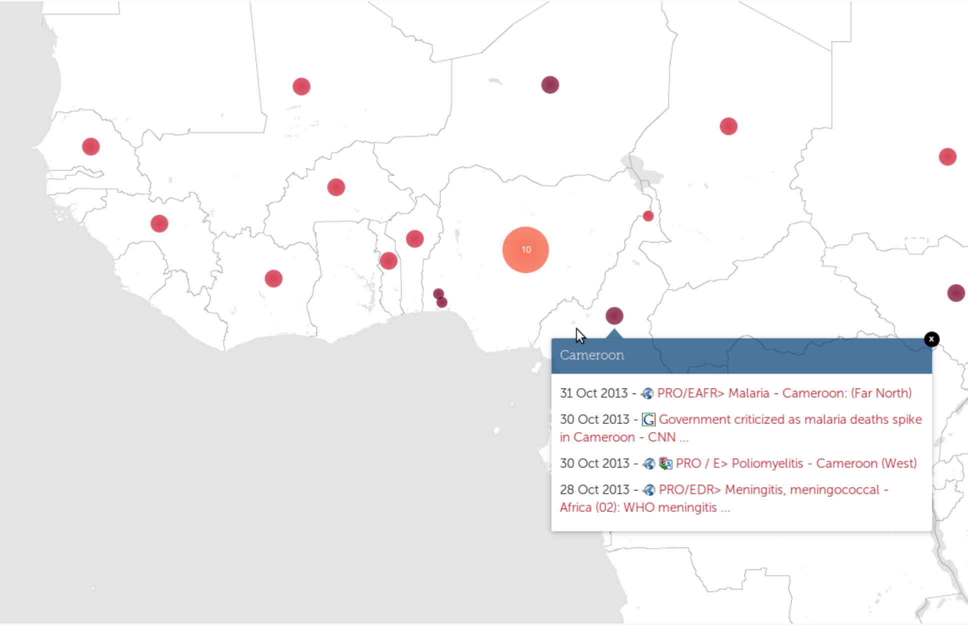
Geographically located

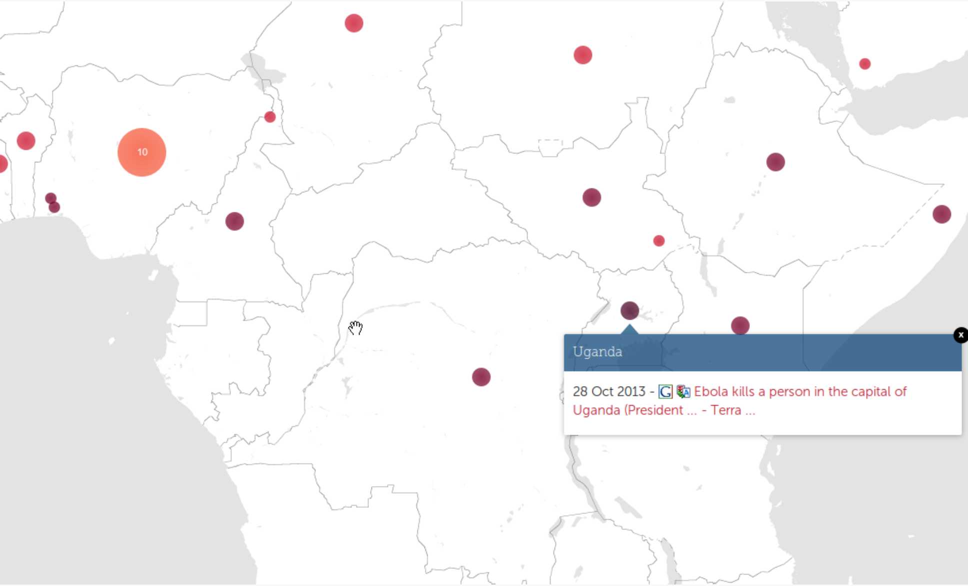
If alerts concern somewhere close, local PHA will be made aware soon

If alerts are far away, do they really all represent the same risk to a given PHA?

(Following figures from HealthMap)


72 alerts for all diseases, current location, in the past week
Senegal
28 Oct 2013 - PRO/EDR> Meningitis, meningococcal - Africa (02): WHO meningitis ...
10


10
Cameroon
31 Oct 2013 - PRO/EAFR> Malaria - Cameroon: (Far North)
30 Oct 2013 - Government criticized as malaria deaths spike in Cameroon - CNN ...
30 Oct 2013 - PRO / E> Poliomyelitis - Cameroon (West)
28 Oct 2013 - PRO/EDR> Meningitis, meningococcal - Africa (02): WHO meningitis ...


10
Uganda
28 Oct 2013 - Ebola kills a person in the capital of Uganda (President ... - Terra ...

Do these alerts represent the same risk?

If not, which to monitor in priority?

$\Rightarrow$ Use our knowledge of the GATN and modelling to “rank” alerts

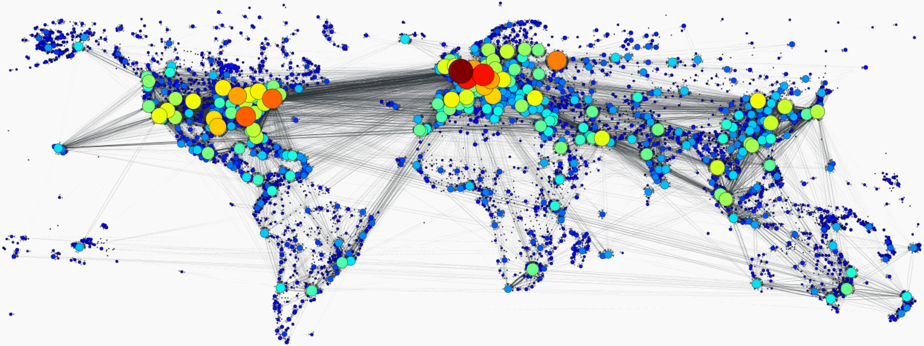
1. Mobility and pathogens
2. Internet (trawling) disease surveillance
3. Global air transportation network
4. Connection through metapopulation modelling

BioDiaspora Project – SMH (Toronto)

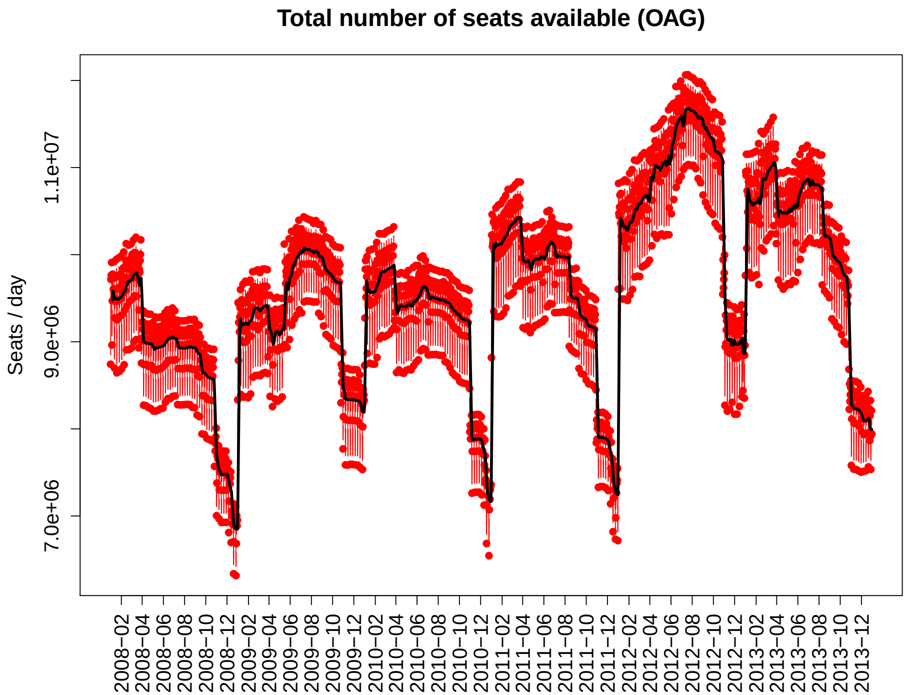
Objective

Suppose an infectious agent is introduced naturally or artificially somewhere on earth. Can we

- provide information about the capacity of the Global Air Transportation Network (GATN) to facilitate the global spread of this infectious agent?
- provide public health authorities with an evaluation of the risk they run of importing this agent into their system?



The volumes are variable



Total number of seats available (OAG)
Seats / day
7.0e+06
9.0e+06
1.1e+07
2008−02
2008−04
2008−06
2008−08
2008−10
2008−12
2009−02
2009−04
2009−06
2009−08
2009−10
2009−12
2010−02
2010−04
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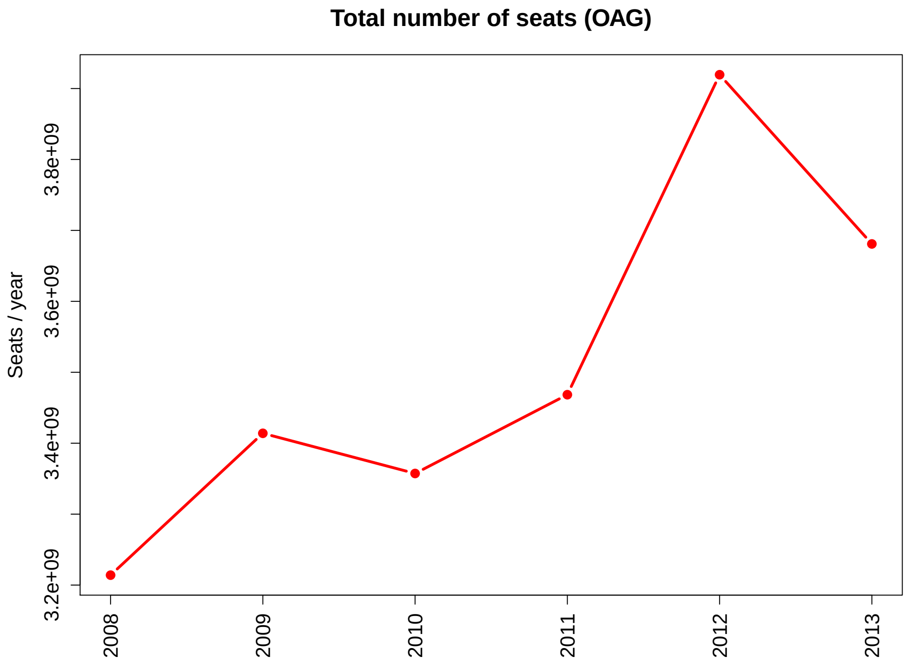
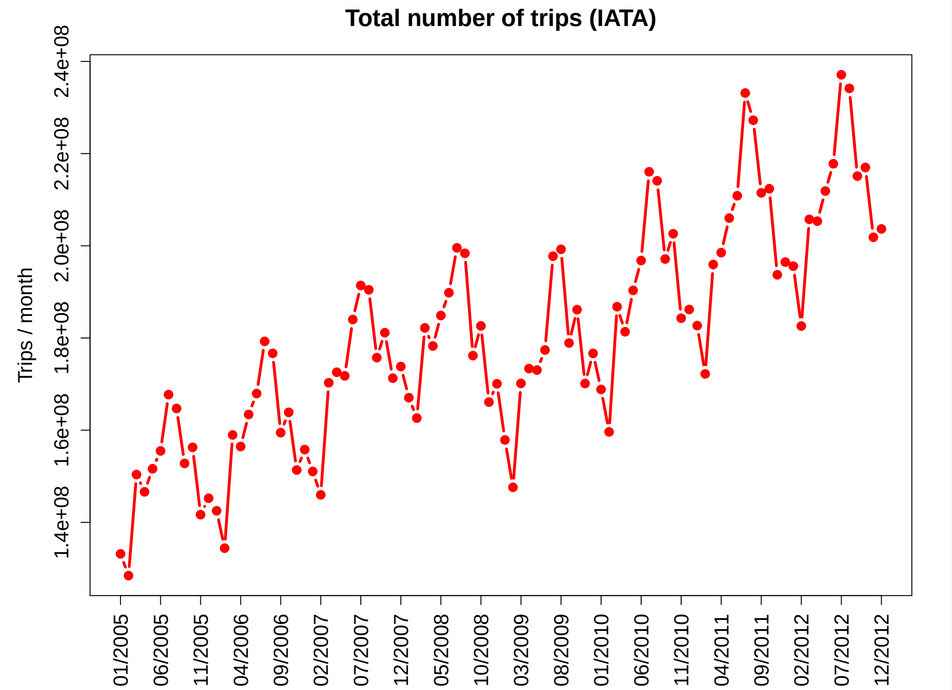
2013−08
2013−10
2013−12


Total number of seats (OAG)
Seats / year
3.2e+09
3.4e+09
3.6e+09
3.8e+09
2008
2009
2010
2011
2012
2013


Total number of trips (IATA)
Trips / month
1.4e+08
1.6e+08
1.8e+08
2.0e+08
2.2e+08
2.4e+08
01/2005
06/2005
11/2005
04/2006
09/2006
02/2007
07/2007
12/2007
05/2008
10/2008
03/2009
08/2009
01/2010
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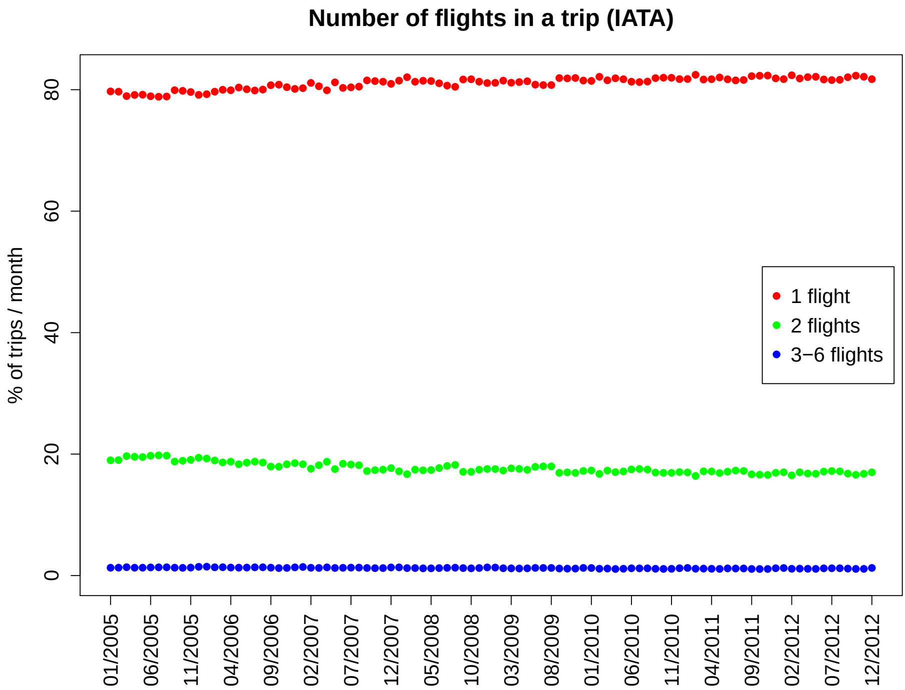
04/2011
09/2011
02/2012
07/2012
12/2012



Number of flights in a trip (IATA)
% of trips / month
0
20
40
60
80
1 flight
2 flights
3−6 flights
01/2005
06/2005
11/2005
04/2006
09/2006
02/2007
07/2007
12/2007
05/2008
10/2008
03/2009
08/2009
01/2010
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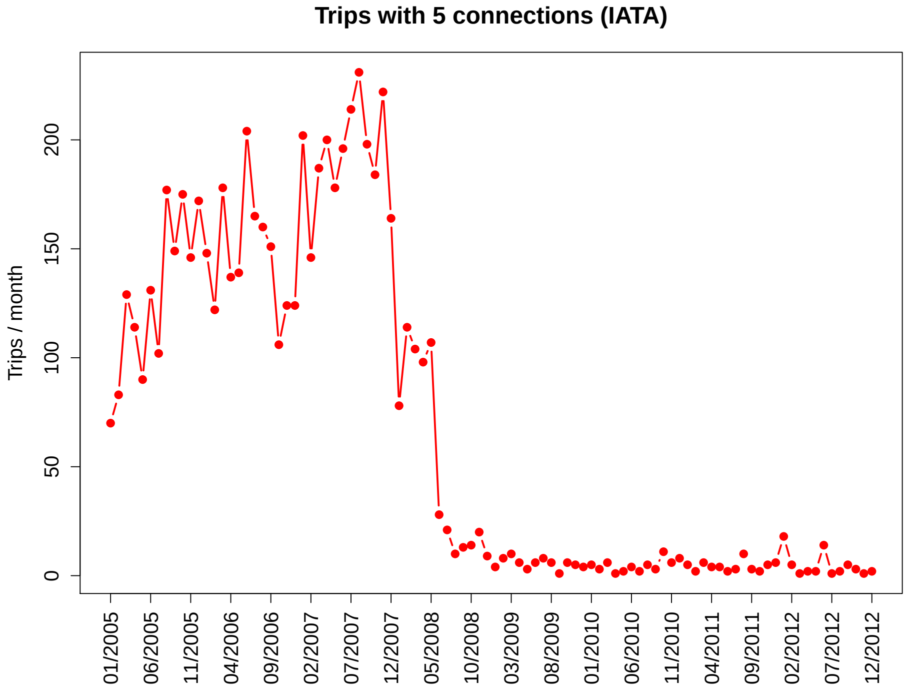
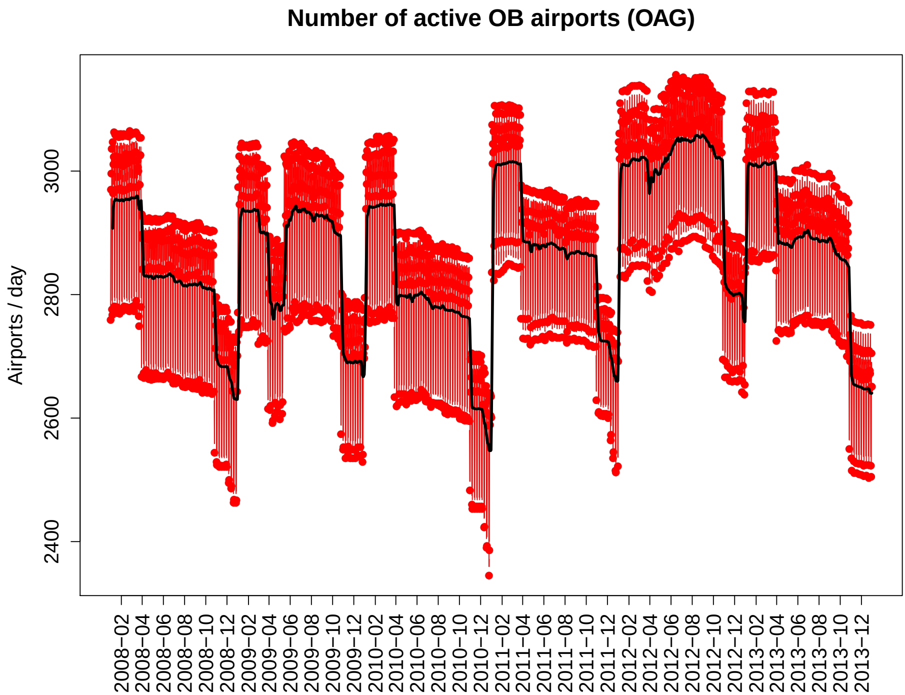
04/2011
09/2011
02/2012
07/2012
12/2012



Trips with 5 connections (IATA)
Trips / month
0
50
100
150
200
01/2005
06/2005
11/2005
04/2006
09/2006
02/2007
07/2007
12/2007
05/2008
10/2008
03/2009
08/2009
01/2010
06/2010
11/2010
04/2011
09/2011
02/2012
07/2012
12/2012

The graph itself is variable


Number of active OB airports (OAG)
Airports / day
2400
2600
2800
3000
2008−02
2008−04
2008−06
2008−08
2008−10
2008−12
2009−02
2009−04
2009−06
2009−08
2009−10
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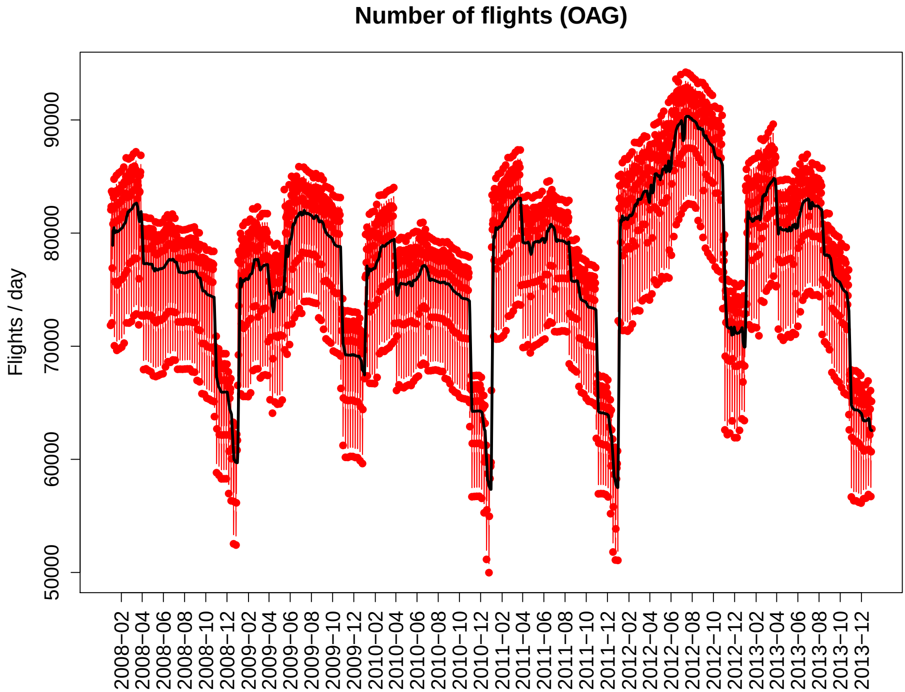

Number of flights (OAG)
Flights / day
50000
60000
70000
80000
90000
2008−02
2008−04
2008−06
2008−08
2008−10
2008−12
2009−02
2009−04
2009−06
2009−08
2009−10
2009−12
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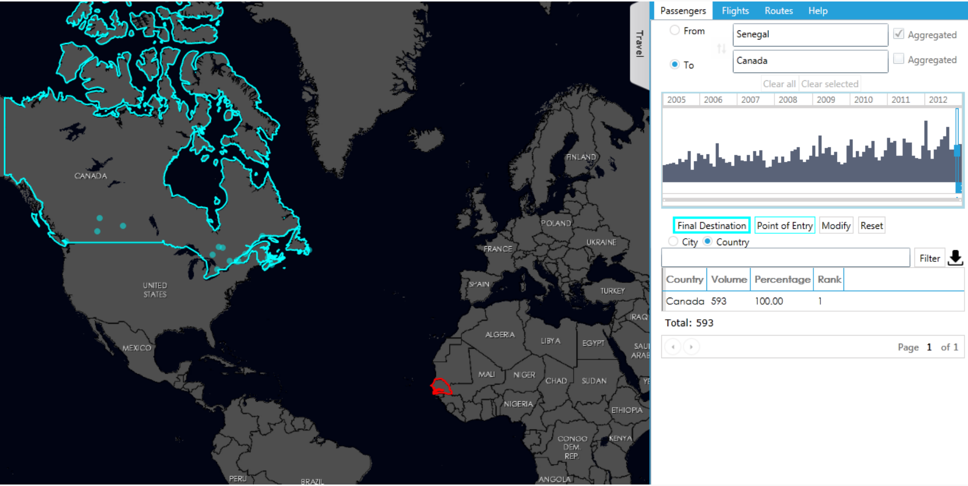

CANADA
UNITED STATES
MEXICO
PERU
BRAZIL
FINLAND
POLAND
UKRAINE
FRANCE
SPAIN
TURKEY
IRAQ
ALGERIA
LIBYA
EGYPT
MALI
NIGER
CHAD
SUDAN
NIGERIA
ETHIOPIA
CONGO DEM. REP.
KENYA
ANGOLA
Travel
Passengers
Flights
Routes
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Senegal
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To
Canada
Aggregated
Clear all
Clear selected
2005
2006
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2008
2009
2010
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2012
Final Destination
Point of Entry
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Reset
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593
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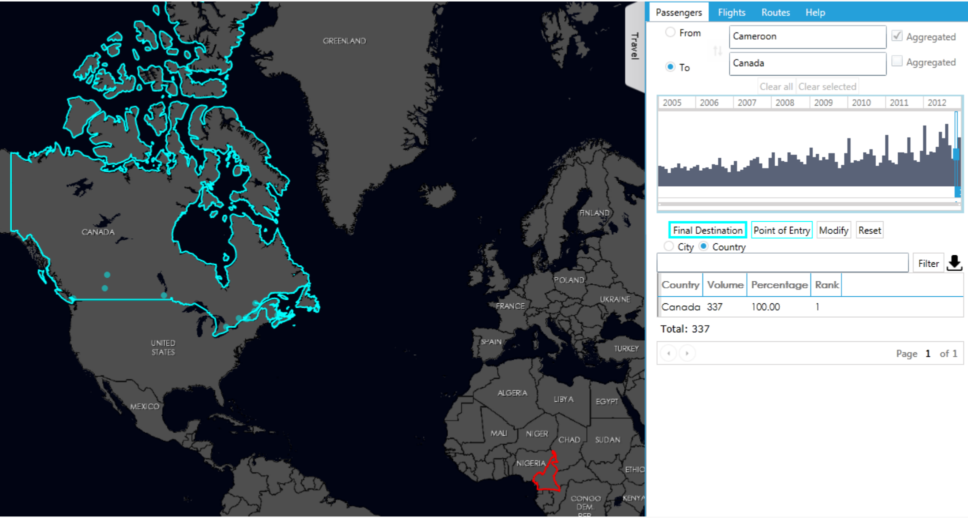
1
Total: 593
Page 1 of 1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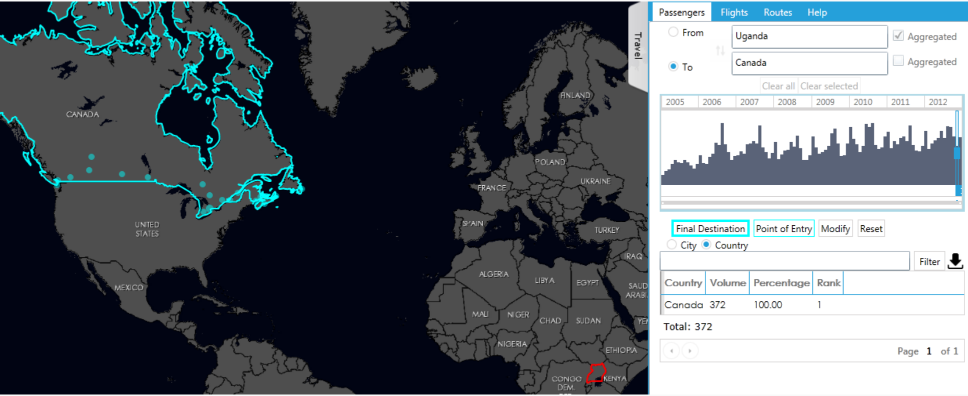
NIGER
CHAD
SUDAN
NIGERIA
CONGO DEM. REP.
KENYA
Travel
Passengers
Flights
Routes
Help
From
Cameroon
Aggregated
To
Canada
Aggregated
Clear all
Clear selected
2005
2006
2007
2008
2009
2010
2011
2012
Final Destination
Point of Entry
Modify
Reset
City
Country
Filter
Country
Volume
Percentage
Rank
Canada
337
100.00
1
Total: 337
Page 1 of 1



Passengers
Flights
Routes
Help
Travel
From
Uganda
Aggregated
To
Canada
Aggregated
Clear all
Clear selected
2005
2006
2007
2008
2009
2010
2011
2012
Final Destination
Point of Entry
Modify
Reset
City
Country
Filter
Country | Volume | Percentage | Rank
Canada | 372 | 100.00 | 1
Total: 372
Page 1 of 1
CANADA
UNITED STATES
MEXICO
FINLAND
POLAND
UKRAINE
FRANCE
SPAIN
TURKEY
IRAQ
ALGERIA
LIBYA
EGYPT
SAUDI ARABIA
MALI
NIGER
CHAD
SUDAN
NIGERIA
ETHIOPIA
CONGO DEM.
KENYA

Metapopulations in 20 seconds

$\bar{p}$ geographical locations (*patches*)

Compartments *may* move between patches and

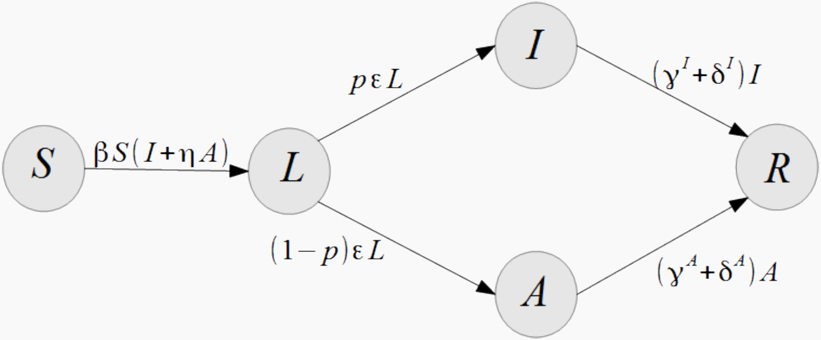
$$m_{cqp}$$

is rate of movement of individuals from compartment $c \in \mathcal{C}$ from patch $p \in \mathcal{P}$ to patch $q \in \mathcal{P}$

Assume **infected** (i) and **uninfected** (s) compartments $\mathcal{I}$ and $\mathcal{U}$ ($\mathcal{I} \cup \mathcal{U} = \mathcal{C}$). For all $k \in \mathcal{U}$, $\ell \in \mathcal{I}$ and $p \in \mathcal{P}$

$$s'_{kp} = f_{kp}(S_p, I_p) + \sum_{q=1}^{\bar{p}} m_{kpq} s_{kq}$$
$$i'_{\ell p} = g_{\ell p}(S_p, I_p) + \sum_{q=1}^{\bar{p}} m_{\ell pq} i_{\ell q}$$

Base model in each patch



Arino, Brauer, van den Driessche, Watmough & Wu, PRS-I, 2006

Getting rates of movement between ACAs

Consider Winnnipeg (Manitoba, Canada, IATA code YWG) and Toronto (Ontario, Canada, aggregate IATA code YTO)

Want actual number of trips between the two ACAs

For short time interval (eg., 1 day), can neglect other sources of variation of population in origin ACA as well as other flows, so

$$N'_{\mathrm{YWG}}(t) = -m_{\mathrm{YTO,YWG}}(t)N_{\mathrm{YWG}}(t)$$

where $m_{\mathrm{YTO,YWG}}(t)$ rate of movement of individuals from Winnipeg to Toronto at time t

After one day, population in Winnipeg has changed according to

$$N_{\mathrm{YWG}}(1) = e^{-m_{\mathrm{YTO,YWG}}} N_{\mathrm{YWG}}(0)$$

$N_{\mathrm{YWG}}(1) - N_{\mathrm{YWG}}(0)$: loss of population in Winnipeg from trips to Toronto (in one day)

Example: November 2012, average of 865 people per day, so

$$m_{\mathrm{YTO,YWG}} = -\ln\left(1 - \frac{865}{N_{\mathrm{YWG}}(0)}\right),$$

where $N_{\mathrm{YWG}}(0)$ population of Winnipeg obtained from catchment area computation

Getting ACAs: Dirichlet tessellation

$\mathcal{P}$ finite set of points on a sphere (*sources*). For each $P, Q \in \mathcal{P}$, define

$$H_{PQ} = \left\{ X : \frac{|X-P|}{\sigma(P)} \leq \frac{|X-Q|}{\sigma(Q)} \right\}$$

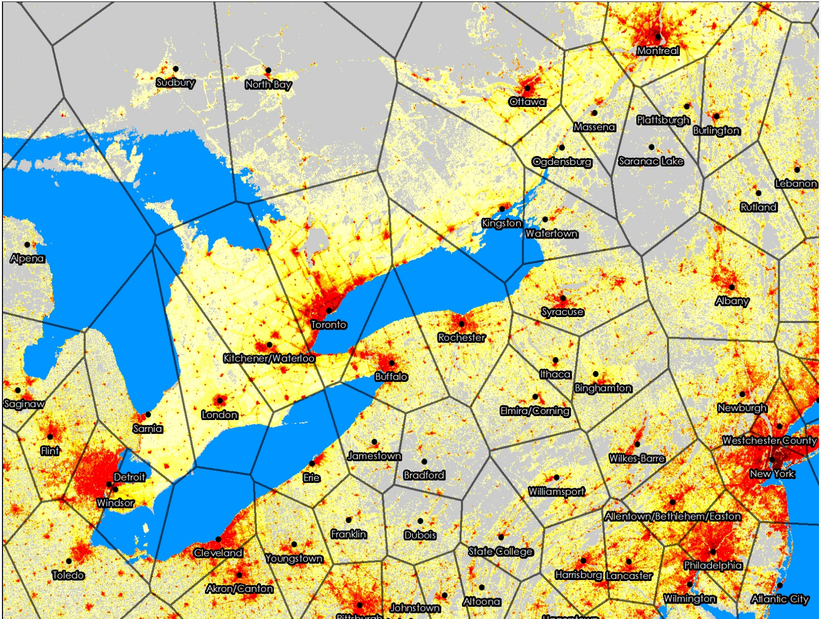
where $\sigma(P) > 0$, and

$$K_{PQ} := H_{PQ} \cap H_{QP} = \left\{ X : \frac{|X-P|}{\sigma(P)} = \frac{|X-Q|}{\sigma(Q)} \right\}$$

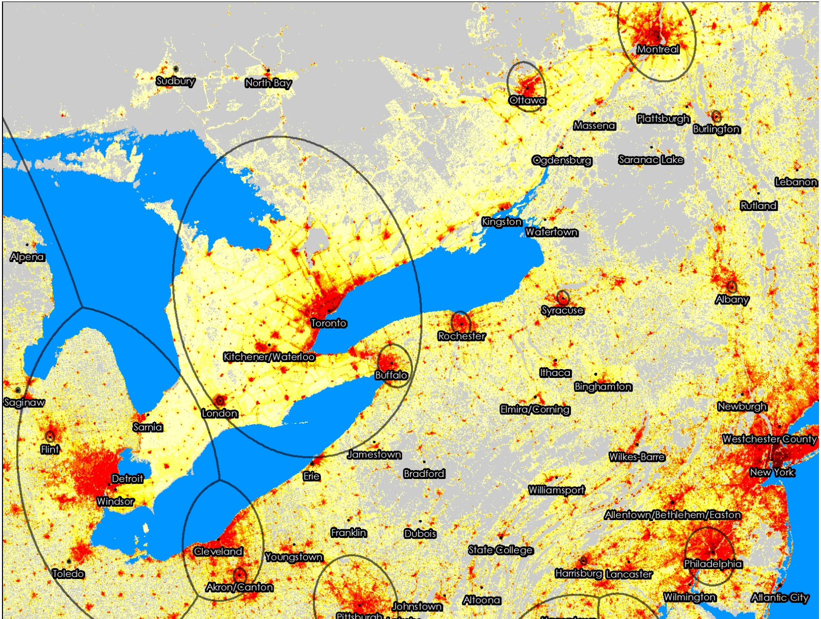
For each $P \in \mathcal{P}$, let $R_p = \bigcap_{Q \neq P} H_{PQ}$ and $R = \{R_P, P \in \mathcal{P}\}$

Then $R(\mathcal{P})$ is the Dirichlet (or weighted Voronoi) tessellation of the sphere

Case $\sigma(P) = 1$ for all P



$$\sigma(P) = v_i(t)$$


Montreal
Sudbury
North Bay
Ottawa
Massena
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Burlington
Ogdensburg
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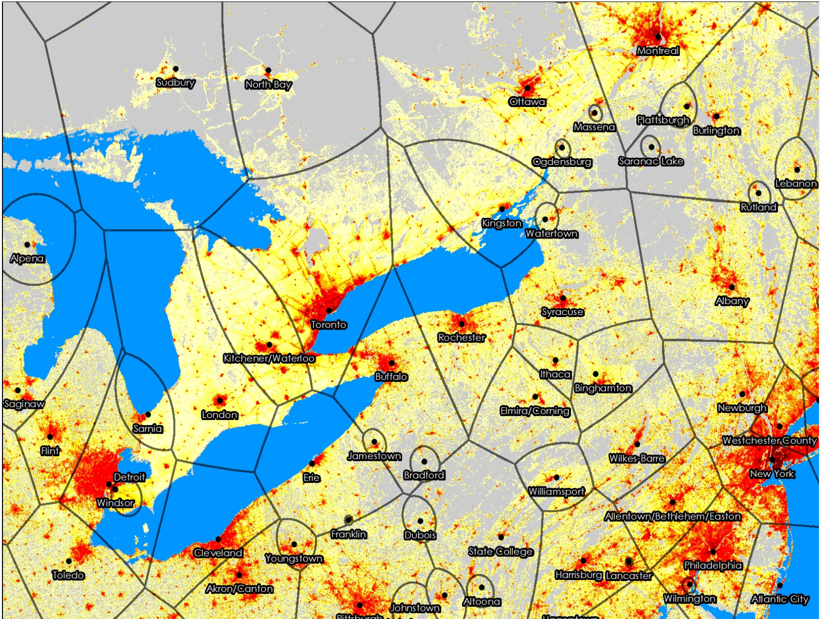
Lebanon
Rutland
Kingston
Watertown
Alpena
Albany
Syracuse
Toronto
Rochester
Kitchener/Waterloo
Buffalo
Ithaca
Binghamton
Saginaw
London
Elmira/Corning
Newburgh
Sarnia
Westchester County
Flint
Jamestown
Wilkes-Barre
Detroit
Erie
Bradford
New York
Windsor
Williamsport
Allentown/Bethlehem/Easton
Franklin
Dubois
State College
Cleveland
Youngstown
Philadelphia
Toledo
Harrisburg
Lancaster
Akron/Canton
Johnstown
Altoona
Wilmington
Atlantic City

$$\sigma(P) = v_{max}(t)v_i(t)/(v_i(t) + v_{med}(t))$$



So what happens when we get something like this..

From: GPHIN Alert <GPHIN-ALERT@opentext.com>
Date: November 6, 2013 at 2:10:34 PM EST
To: <KhanK@smh.ca>
Subject: EN / Spain reports first case of deadly MERS coronavirus

This is an automated alert from the GPHIN System, please do not reply to this e-mail.

The following article is brought to your attention and may require action on your part:

Publication Language: English
Unique ID: 10844193
Received Date: 2013/11/06 19:06:00 GMT
Publication Date: 2013/11/06 19:06:00 GMT
Place Name: Spain
SPAIN
40°23' N
3°65' W
News Provider:
News Source: Expatica
Title: Spain reports first case of deadly MERS coronavirus
Article Text: Spain reports first case of deadly MERS coronavirus

Spain said Wednesday that a woman who just returned from Saudi Arabia has been infected by the MERS coronavirus in the country's first case of the deadly disease.
The patient, who was born in Morocco but lives in Spain, is receiving treatment at a Madrid hospital and is in a "stable" condition, the health ministry said in a statement.

Mechanism of the simulation system

Initial alert. Given alert $a_{t_0} = (\mathrm{lat}_{t_0}, \mathrm{lon}_{t_0}, \mathrm{event\ type}_{t_0})$

1. Select $\mathrm{ACA}_{\mathrm{XYZ}}$ of airport XYZ closest to $(\mathrm{lat}_{t_0}, \mathrm{lon}_{t_0})$
2. Initiate CTMC simulations in $\mathrm{ACA}_{\mathrm{XYZ}}$ with parameters compatible with $\mathrm{event\ type}_{t_0}$ (if known, otherwise use several sets of parameters for comparable diseases), going forward 3 weeks

Subsequent alerts

3. Track alerts for $\mathrm{event\ type}_{t_0}$, giving a_{t_1}, a_{t_2}, etc.
4. Incorporate these alerts (with space/time) into the data
5. Mix of ODE/CTMC at the local level to establish prevalence at time t of start of simulation, $t > t_n > \cdots > t_1 > t_0$ in ACAs with alerts
6. Initiate CTMC simulations in ACAs with alerts, IC as given by previous step

Ongoing work

τ-leaping and other speedups

Mixing models (determininistic and stochastic)

Criterion for including non-detected ACAs

Time from location to airport in ACA as function of local transportation network

For more information – Methodology

- Khan et al. *An analysis of Canada's vulnerability to emerging infectious disease threats via the global airline transportation network*. Report to PHAC, 2009
- Arino et al. *Some methodological aspects involved in the study by the Bio.Diaspora Project of the spread of infectious diseases along the global air transportation network*. CAMQ, 2011
- Arino et al. *Using mathematical modelling to integrate disease surveillance and global air transportation data*. To appear in "Spatial and Temporal Dynamics of Infectious Diseases", Chen, Moulin & Wu, Eds.

For more information – Work using and about GATN

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