Modeling the Ebola Outbreak in West Africa, 2014

August 4th Update

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Technical Report #14-096

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Overview

- Epidemiological Update
  - Country by country analysis
  - Details from Liberian outbreak
- Compartmental Model
  - Description
  - Comparisons with different disease parameters
  - Long term projections
- Preliminary back of envelope look at US

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Epidemiological Update

- Confirmed case imported into Lagos via air travel – 59 contacts being monitored, but many others are lost to followup
- Outbreak in Guinea has picked up again
- Two new areas of Liberia are reporting cases
- 83 new cases in Sierra Leone from July 20-27
- 2 American Health workers now cases
  - One in Atlanta being treated

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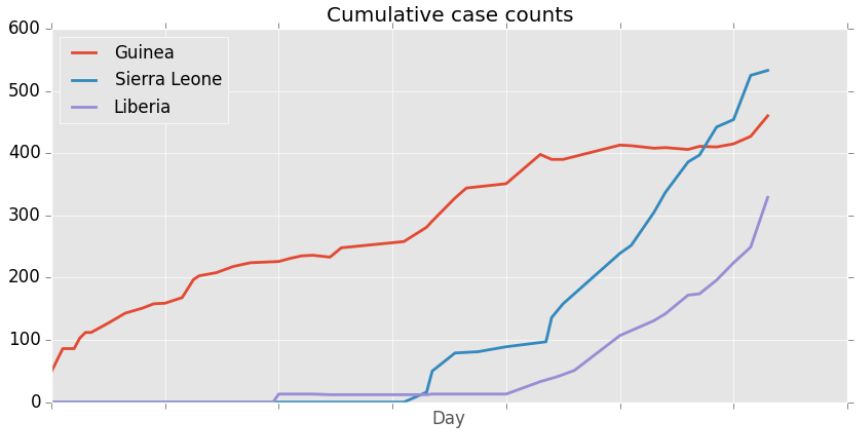
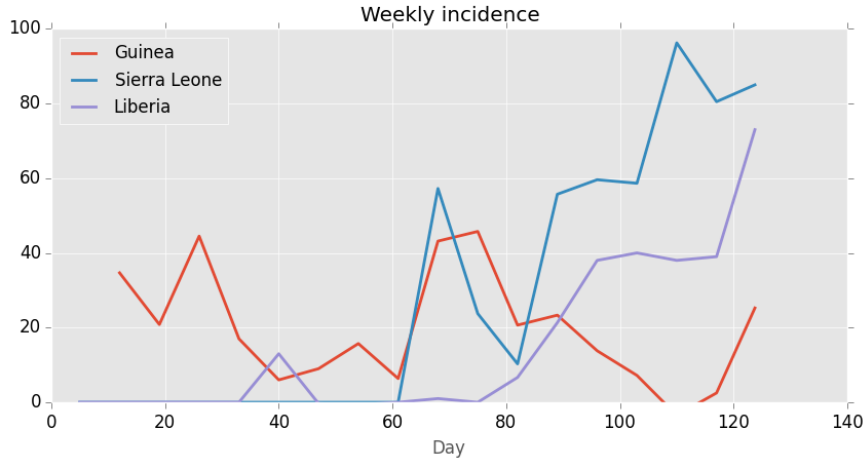
Epidemiological Update

	Cases	Deaths
Guinea	460	339
Liberia	329	156
Sierra Leone	533	233
Total	**1322**	**728**

- Data reported by WHO on July 31 for cases as of July 27
- Sierra Leone case counts censored up to 4/30/14.
- Time series was filled in with missing dates, and case counts were interpolated.





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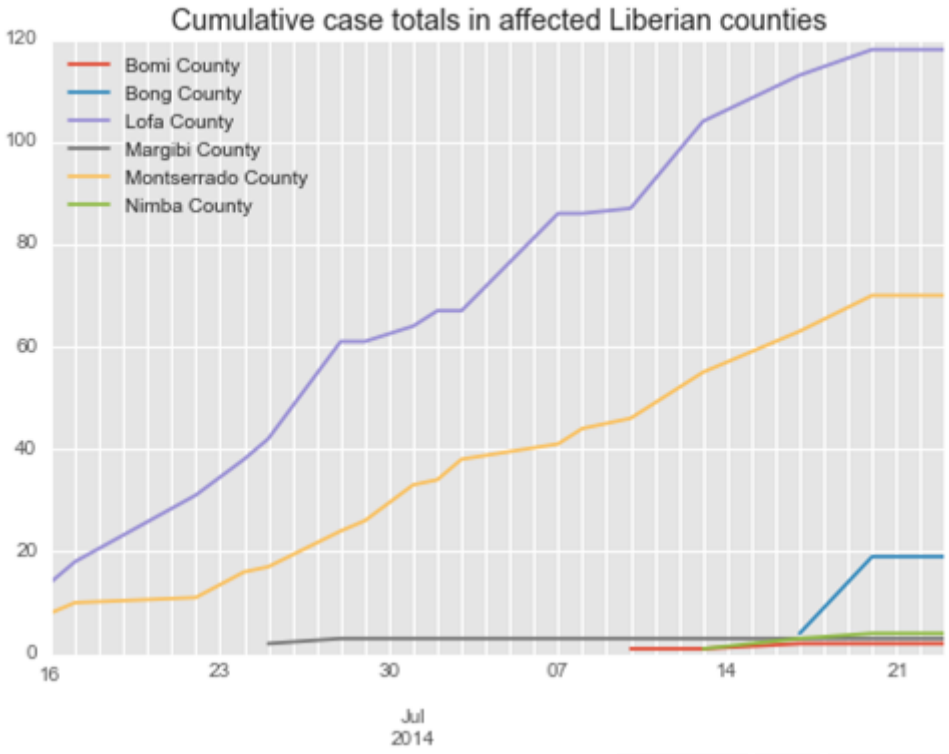
Liberia



- Major ports of entry are now closed
- Two previously unaffected counties are investigating suspected cases
- Continued transmission via funerary practices still suspected
- Transmission among healthcare workers continued
- Significant resistance in the community, particularly Lofa county. Patients are concealed, refuse follow up, buried secretly.

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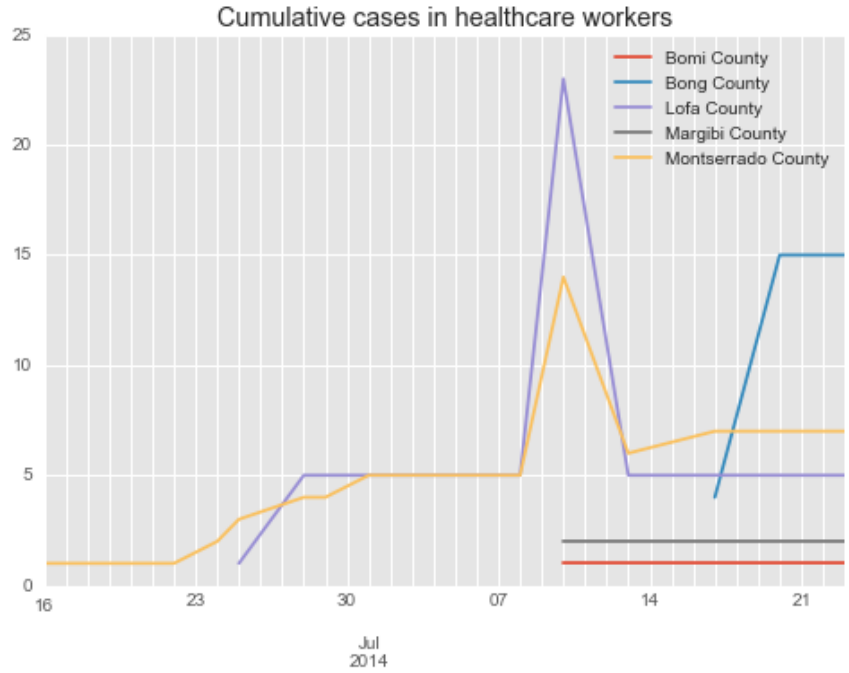
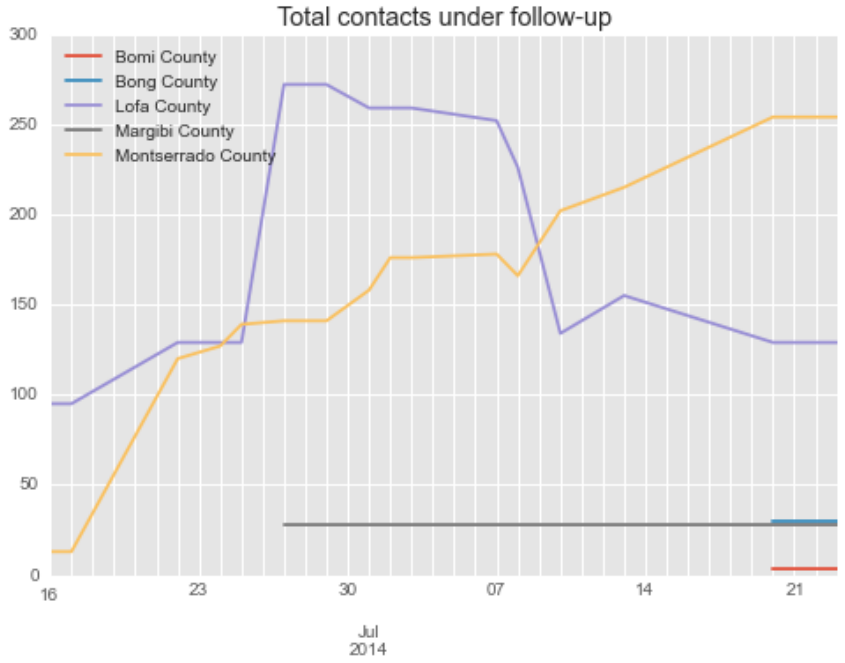
Detailed data from Liberia





- Healthcare work infections and contact tracing info captured
- More details than aggregates could help with estimates

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Sierra Leone

- 83 new cases were reported between July 20 and 27, a massive increase.
- Sierra Leone now has the most cases of the three affected countries
- A confirmed patient left isolation in the capital city, reportedly due to “fear and mistrust of health workers”

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Guinea

- Worrying spike in cases from July 20-27 reporting period, after a prolonged lull.
- WHO asserts this suggests “undetected chains of transmission existed in the community”

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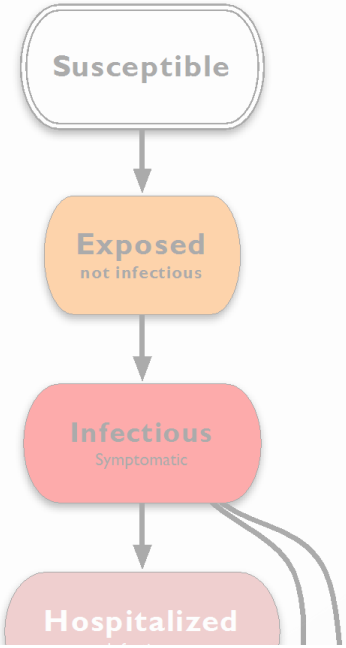


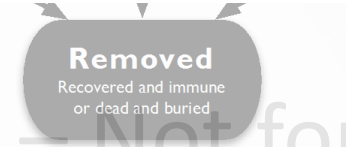
$$-\frac{1}{N}(\beta_{\mathrm{I}}\mathrm{SI}+\beta_{\mathrm{H}}\mathrm{SH}+\beta_{\mathrm{F}}\mathrm{SF})$$

$$\frac{1}{N}(\beta_{\mathrm{I}}\mathrm{SI}+\beta_{\mathrm{H}}\mathrm{SH}+\beta_{\mathrm{F}}\mathrm{SF})-\alpha\mathrm{E}$$

$$\alpha\mathrm{E}-(\gamma_{\mathrm{h}}\theta_1+\gamma_i(1-\theta_1)(1-\delta_1)+\gamma_{\mathrm{d}}(1-\theta_1)\delta_1)\mathrm{I}$$

$$\gamma_{\mathrm{h}}\theta_1\mathrm{I}-(\gamma_{d\mathrm{h}}\delta_2+\gamma_{i\mathrm{h}}(1-\delta_2))\mathrm{H}$$

MODEL DESCRIPTION



$$\gamma_i(1-\theta_1)(1-\delta_1)\mathrm{I}+\gamma_{i\mathrm{h}}(1-\delta_2)\mathrm{H}+\gamma_{\mathrm{f}}\mathrm{F}$$

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Compartmental Approach

- Extension of model proposed by Legrand et al.

Epidemiol. Infect. (2007), **135**, 610–621. © 2006 Cambridge University Press
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Understanding the dynamics of Ebola epidemics

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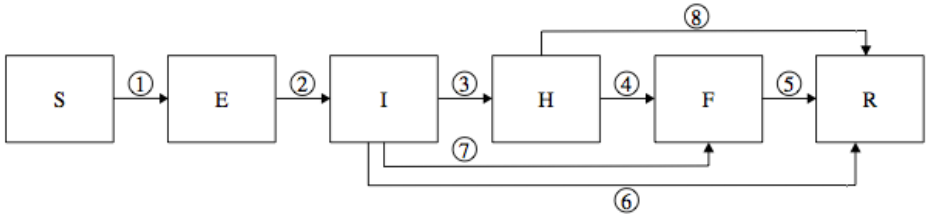
(*Accepted 14 July 2006; first published online 26 September 2006*)

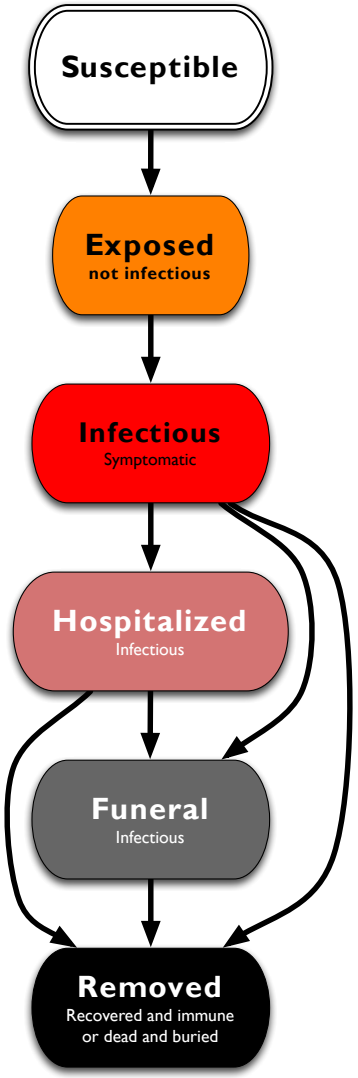
Legrand, J, R F Grais, P Y Boelle, A J Valleron, and A Flahault. "Understanding the Dynamics of Ebola Epidemics" *Epidemiology and Infection* 135 (4). 2007. Cambridge University Press: 610–21. doi:10.1017/S0950268806007217.

Transition		Transition rate (λ_i)
1	(S, E)→(S − 1, E + 1)	$(\beta_I SI + \beta_H SH + \beta_F SF)/N$
2	(E, I)→(E − 1, I + 1)	αE
3	(I, H)→(I − 1, H + 1)	$\gamma_h \theta_1 I$
4	(H, F)→(H − 1, F + 1)	$\gamma_{dh} \delta_2 H$
5	(F, R)→(F − 1, R + 1)	$\gamma_f F$
6	(I, R)→(I − 1, R + 1)	$\gamma_i (1 - \theta_1)(1 - \delta_1) I$
7	(I, F)→(I − 1, F + 1)	$\delta_1 (1 - \theta_1) \gamma_d I$
8	(H, R)→(H − 1, R + 1)	$\gamma_{ih} (1 - \delta_2) H$



Virginia Tech
Virginia Bioinformatics Institute
Network Dynamics & Simulation Science Laboratory

Legrand et al. Model Description



$$-\frac{1}{N}(\beta_{\mathrm{I}}\mathrm{SI}+\beta_{\mathrm{H}}\mathrm{SH}+\beta_{\mathrm{F}}\mathrm{SF})$$

$$\frac{1}{N}(\beta_{\mathrm{I}}\mathrm{SI}+\beta_{\mathrm{H}}\mathrm{SH}+\beta_{\mathrm{F}}\mathrm{SF})-\alpha\mathrm{E}$$

$$\alpha\mathrm{E}-(\gamma_{\mathrm{h}}\theta_1+\gamma_i(1-\theta_1)(1-\delta_1)+\gamma_{\mathrm{d}}(1-\theta_1)\delta_1)\mathrm{I}$$

$$\gamma_{\mathrm{h}}\theta_1\mathrm{I}-(\gamma_{\mathrm{dh}}\delta_2+\gamma_{i\mathrm{h}}(1-\delta_2))\mathrm{H}$$

$$\gamma_{\mathrm{d}}(1-\theta_1)\delta_1\mathrm{I}+\gamma_{\mathrm{dh}}\delta_2\mathrm{H}-\gamma_{\mathrm{f}}\mathrm{F}$$

$$\gamma_i(1-\theta_1)(1-\delta_1)\mathrm{I}+\gamma_{i\mathrm{h}}(1-\delta_2)\mathrm{H}+\gamma_{\mathrm{f}}\mathrm{F}$$

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Legrand et al. Approach

- Behavioral changes to reduce transmissibilities at specified days
- Stochastic implementation fit to two historical outbreaks
  - Kikwit, DRC, 1995
  - Gulu, Uganda, 2000
- Finds two different "types" of outbreaks
  - Community vs. Funeral driven outbreaks

Table 4. *Parameter estimates of the model*

Parameters	Estimates (95% CI)
DRC, 1995	
Decrease in transmission in the community after interventions, $1-z$ (%)	12 (0–78)
Basic reproduction number, R_0	2·7 (1·9–2·8)
R_{0I} (community component)	0·5 (0·4–1·9)
β_I (week^{-1})	0·588 (0·420–2·191)
R_{0H} (hospitalization component)	0·4 (0–2·2)
β_H (week^{-1})	0·794 (0·001–4·091)
R_{0F} (traditional burial component)	1·8 (0–2·3)
β_F (week^{-1})	7·653 (0·001–9·997)
Uganda, 2000	
Decrease in transmission in the community after interventions, $1-z$ (%)	88 (1–92)
Basic reproduction number, R_0	2·7 (2·5–4·1)
R_{0I} (community component)	2·6 (0·3–2·8)
β_I (week^{-1})	3·532 (0·403–3·774)
R_{0H} (hospitalization component)	0·01 (0–3·5)
β_H (week^{-1})	0·012 (0·0–6·427)
R_{0F} (traditional burial component)	0·1 (0–3·2)
β_F (week^{-1})	0·462 (0·0–21·257)

CI, Confidence interval.

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Parameters of two historical outbreaks

Table 5. *Values of parameters for the multivariate sensitivity analysis*

Parameters	Values from the 1995 DRC epidemic	Values from the 2000 Uganda epidemic
Size of the population (N)	100 000	100 000
R_{0I} (community component)	0·5	2·6
R_{0H} (hospitalization component)	0·4	0·01
R_{0F} (traditional burial component)	1·8	0·1
Number of index cases	1	1
Duration of the incubation period ($1/\alpha$)	7 days (mean)	12 days (mean)
From onset to hospitalization for $t<T$ ($1/\gamma_h$)	5 days (mean)	4·2 days (mean)
From onset to death ($1/\gamma_d$)	9·6 days (mean)	8 days (mean)
From onset to end of infectiousness for survivors ($1/\gamma_i$)	10 days (mean)	10 days (mean)
Duration of the traditional burial ($1/\gamma_f$)	2 days (mean)	2 days (mean)
Hospitalization rate θ for $t<T$ (%)	80	80
Case-fatality ratio, δ (%)	81	53
Decrease of β_I after interventions ($1-z$), (%)	12	88
Decrease of β_H after interventions ($1-z_H$), (%)	**50–100**	**50–100**
Decrease of β_F after interventions ($1-z_F$), (%)	**75–100**	**75–100**
Time to intervention (T) in weeks	**4–10**	**4–10**
From onset to hospitalization for $t>T$ ($1/\gamma_h$) in days	**1–5**	**1–5**
Hospitalization rate θ for $t>T$ (%)	**0–100**	**0–100**

Bold text corresponds to the intervention parameters studied in the multivariate sensitivity analysis.

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NDSSL Extensions to Legrand Model

- Multiple stages of behavioral change possible during this prolonged outbreak
- Optimization of fit through automated method
- Experiment:
  - Explore “degree” of fit using the two different outbreak types for each country in current outbreak

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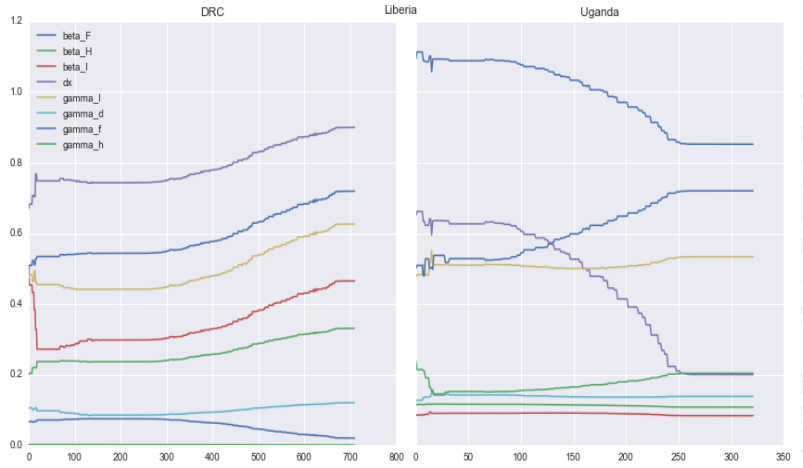
Optimized Fit Process

- Parameters to explored selected
  - Diag_rate, beta_I, beta_H, beta_F, gamma_I, gamma_D, gamma_F, gamma_H
  - Initial values based on two historical outbreak
- Optimization routine
  - Runs model with various permutations of parameters
  - Output compared to observed case count
  - Algorithm chooses combinations that minimize the difference between observed case counts and model outputs, selects “best” one



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Fitted Model Caveats

- Assumptions:
  - Behavioral changes effect each transmission route similarly
  - Mixing occurs differently for each of the three compartments but uniformly within
- These models are likely “overfitted”
  - Guided by knowledge of the outbreak to keep parameters plausible
  - Structure of the model is published and defensible
  - Many combos of parameters will fit the same curve

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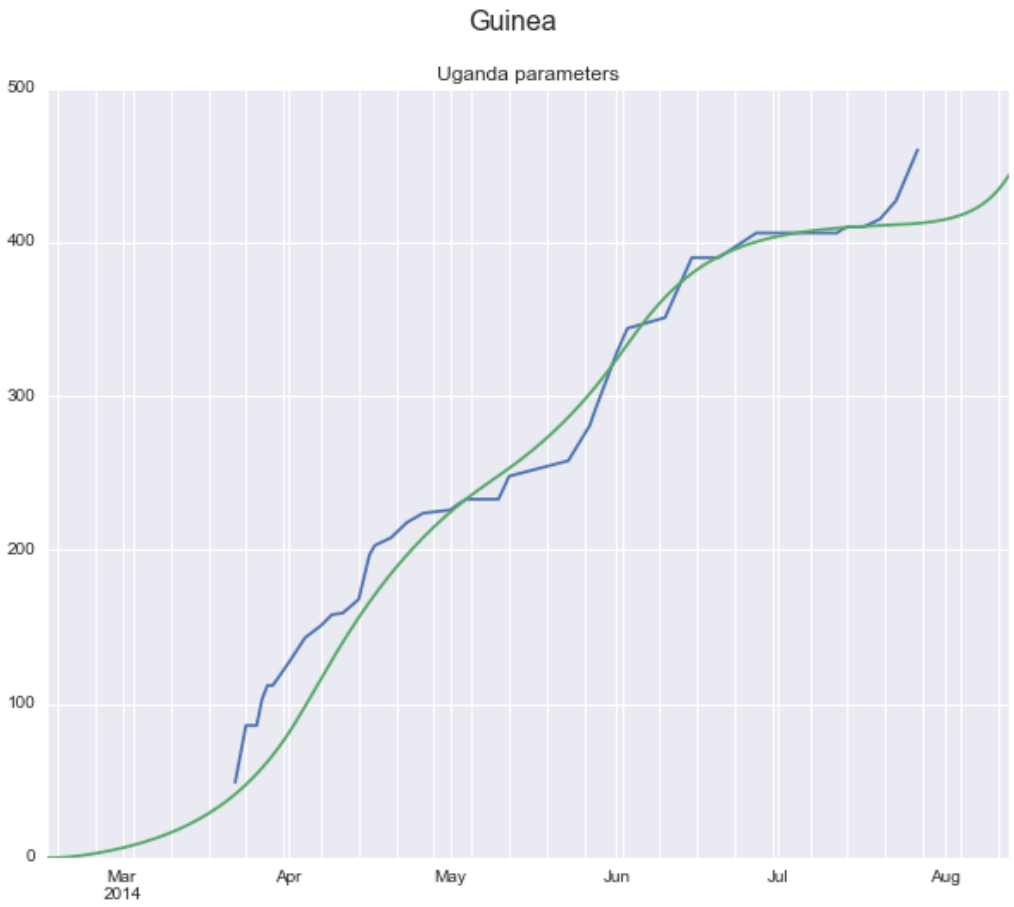
Guinea Fitted Model



This outbreak is difficult to fit, with so many seeming behavioral shifts

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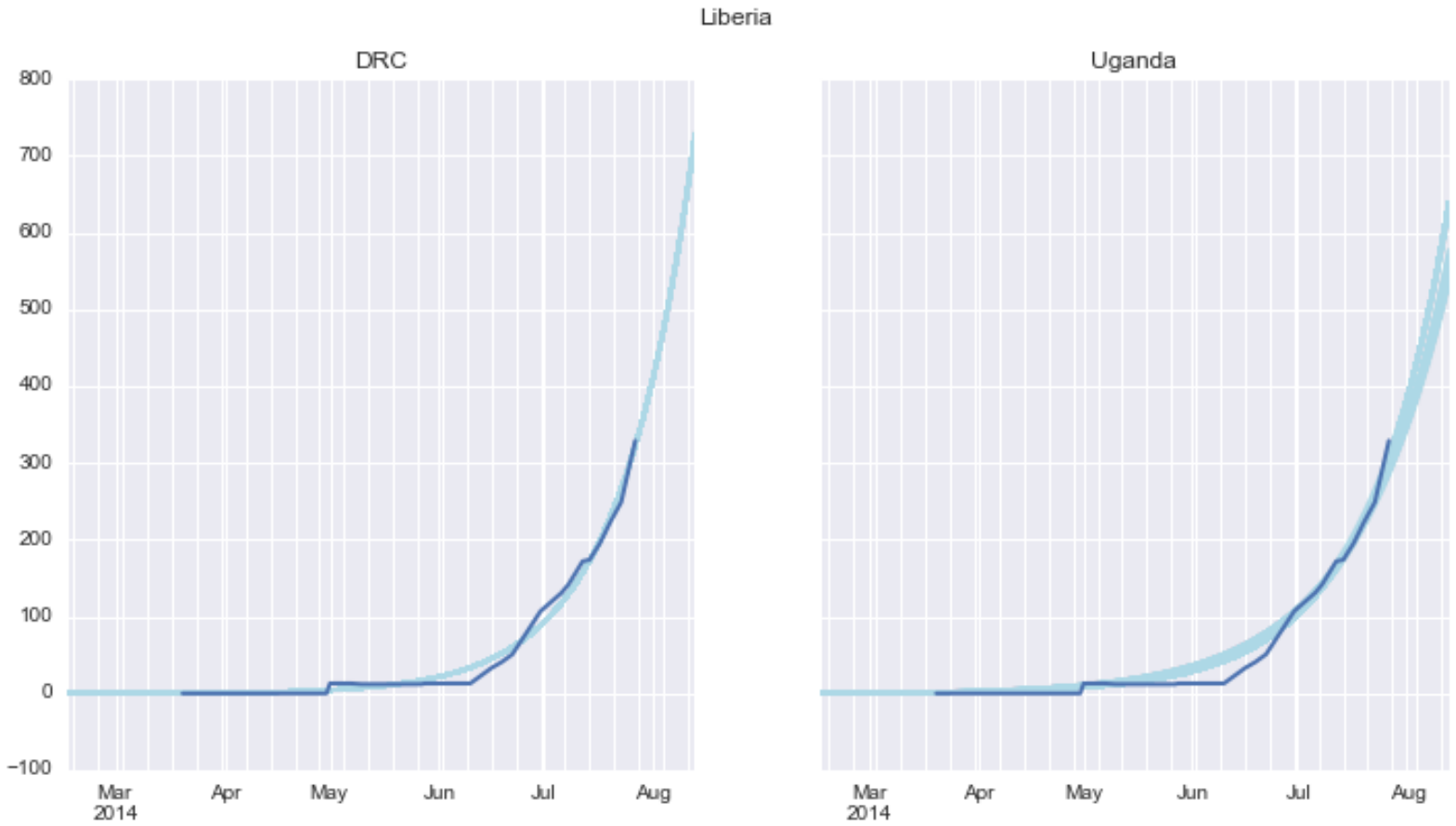
Liberia Fitted Models



Assuming no impact from ongoing response and DRC parameter fit is correct:
83 cases in next 14 days

Assuming no impact from ongoing response and Uganda parameter fit is correct:
63 cases in next 14 days

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Liberia Fitted Models

Model Parameters

Liberia Disease Parameters for Model Fitting

	UgandaOut	Uganda_in	DRCOut	DRC_in
beta_F	0.852496	1.093286	0.020287	0.066
beta_H	0.107974	0.113429	0.00057	0.001714
beta_I	0.083646	0.084	0.465238	0.504571
dx	0.2	0.65	0.9	0.67
gamma_I	0.533852	0.474164	0.626551	0.474164
gamma_d	0.138182	0.125	0.120216	0.104167
gamma_f	0.720525	0.5	0.719349	0.5
gamma_h	0.203924	0.238095	0.330794	0.2
Score	14742	NA	9694	NA

No behavioral Changes included

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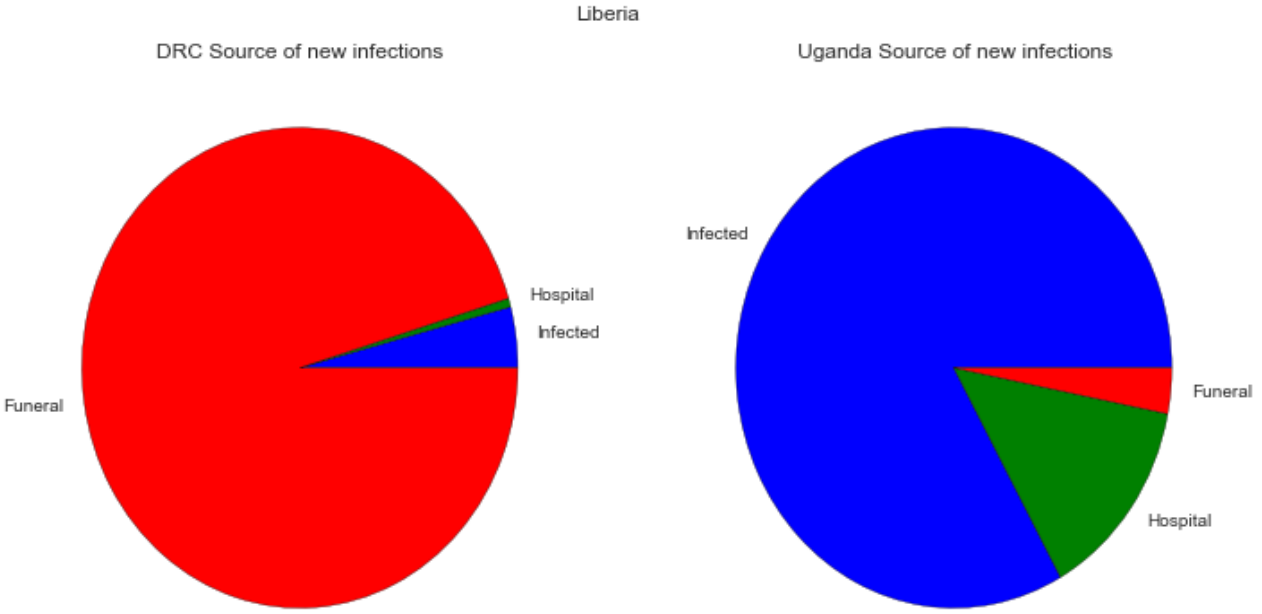
Liberia Fitted Models

Sources of Infections



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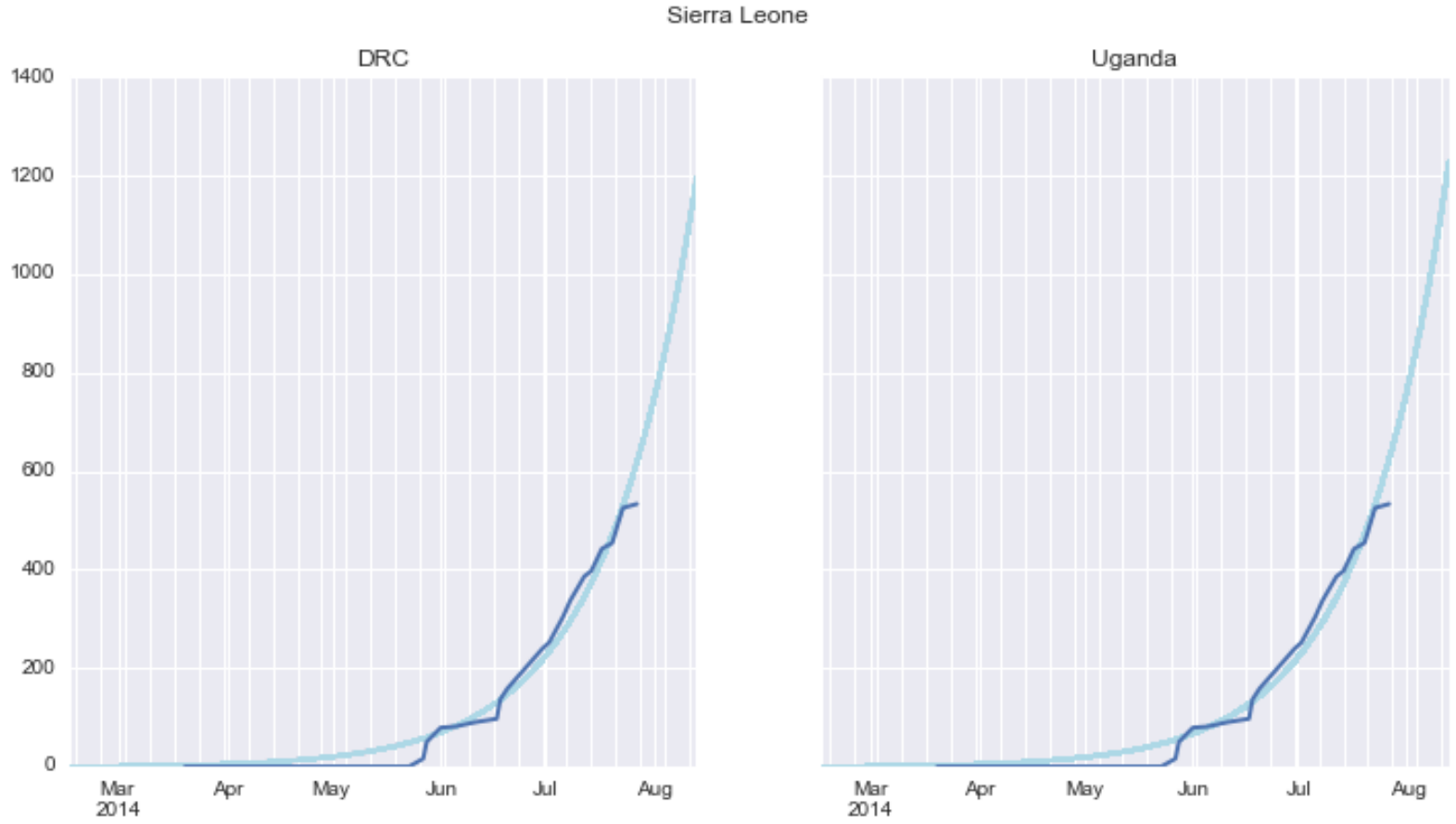
Sierra Leone Fitted Model



Assuming no impact from ongoing response and DRC parameter fit is correct:
101 cases in next 14 days

Assuming no impact from ongoing response and Uganda parameter fit is correct:
107 cases in next 14 days

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Sierra Leone Fitted Model

Model Parameters

Sierra Leone Disease Parameters for Model Fitting

	UgandaOut	Uganda_in	DRCOut	DRC_in
beta_F	1.253475	1.093286	0.058504	0.066
beta_H	0.067821	0.113429	0.000000	0.001714
beta_I	0.090063	0.084	0.308796	0.504571
dx	0.669891	0.65	0.604919	0.67
gamma_I	0.460938	0.437148	0.687977	0.437148
gamma_d	0.159662	0.125	0.090552	0.104167
gamma_f	0.550443	0.5	0.596496	0.5
gamma_h	0.159662	0.238095	0.226723	0.2
Score	78487	NA	76891	NA

No behavioral Changes included

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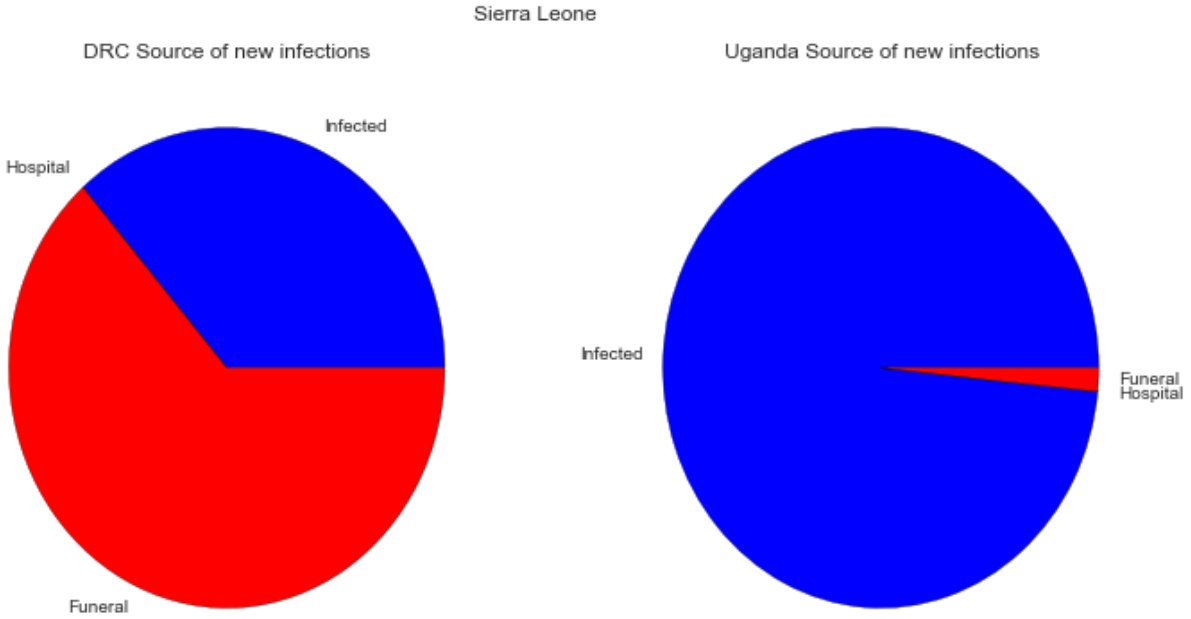
Sierra Leone Fitted Models

Sources of Infections



DRC R0 estimates
rI: 1.40278302774
rH: 2.85436942329e-10
rF: 0.151864780392
Overall: 1.55464780842

Uganda R0 estimates
rI: 0.424081180257
rH: 6.70236711791e-10
rF: 1.4124823235
Overall: 1.83656350443

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Model Fitting Conclusions

- Given:
  - Many sets of parameters can yield “reasonable” fits with totally different transmission drivers
  - These different parameter sets offer similar estimated projections of future cases
  - Coarseness of the case counts and inability to estimate under/over case ascertainment
- Can not account for all uncertainty, thus estimates are very uncertain:
  - Model structure and parameters allow for over-fitting
  - Not enough information in current case count curve to limit this uncertainty
  - Need more information to characterize the type of outbreak

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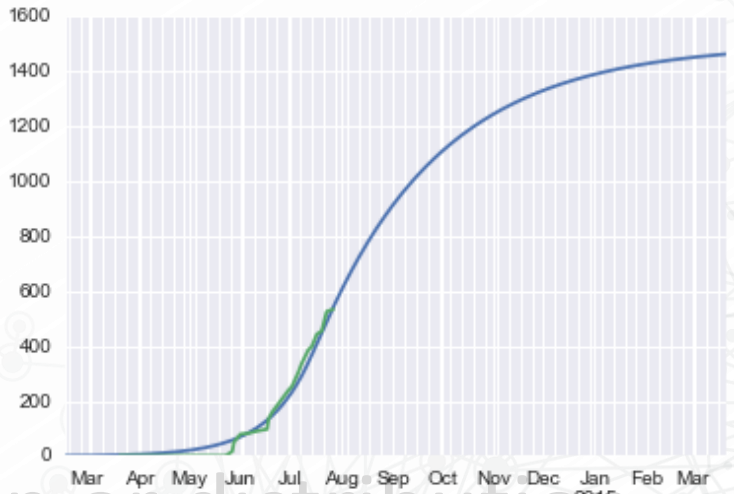
Notional Long-term Projections

- Start with “best” fit model (example purposes: Sierra Leone model fit from Uganda params)
- Induce behavioral change in 2 weeks that bends epidemic over such that it ends at 6m, 12m, 18m
- Estimate impact
  - Example: Sierra Leone @ 6m
  - Cases: ~900 more



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Notional US estimates

- Under assumption that Ebola case, arrives and doesn't seek care and avoids detection throughout illness
- CNIMS based simulations
  - Agent-based models of populations with realistic social networks, built up from high resolution census, activity, and location data
- Assume:
  - Reduced transmission routes in US

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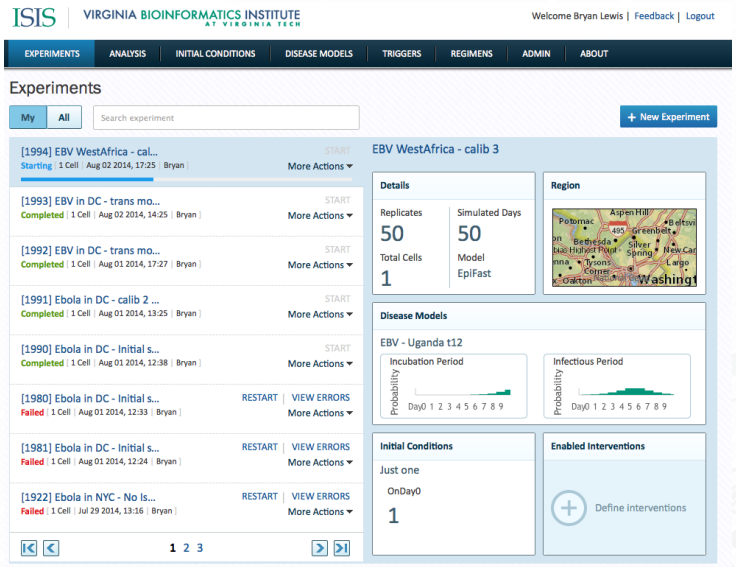
Notional US estimates Approach

- Get disease parameters from fitted model in West Africa
- Put into CNIMS platform
  - ISIS simulation GUI
  - Modify to represent US
- Example Experiment:
  - 100 replicates
  - One case introduction into Washington DC
  - Simulate for 3 weeks



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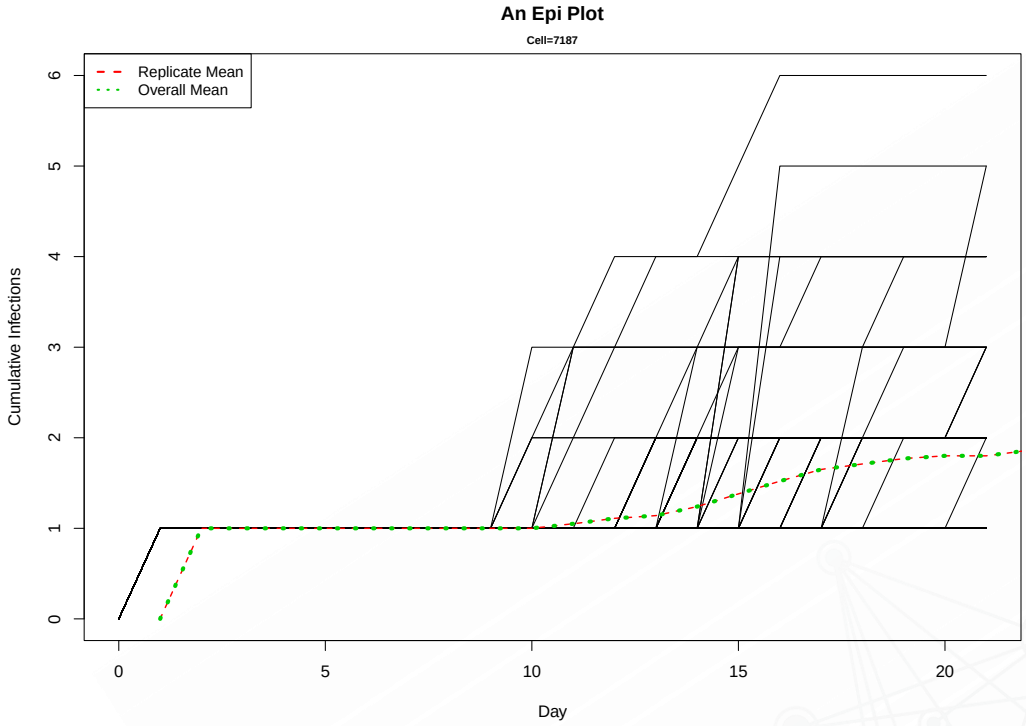
Notional US estimates Example



100 replicates

- Mean of 1.8 cases
- Max of 6 cases
- Majority only one initial case

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Next steps

- Seek data to choose most appropriate model
  - Detailed Liberia MoH with HCW data
  - Parse news reports to estimate main drivers of transmission
- Patch modeling with flows between regions from road networks
- Refine estimates for US
  - Find more information on characteristics of disease, explore parameter ranges
- Gather more data for West African region

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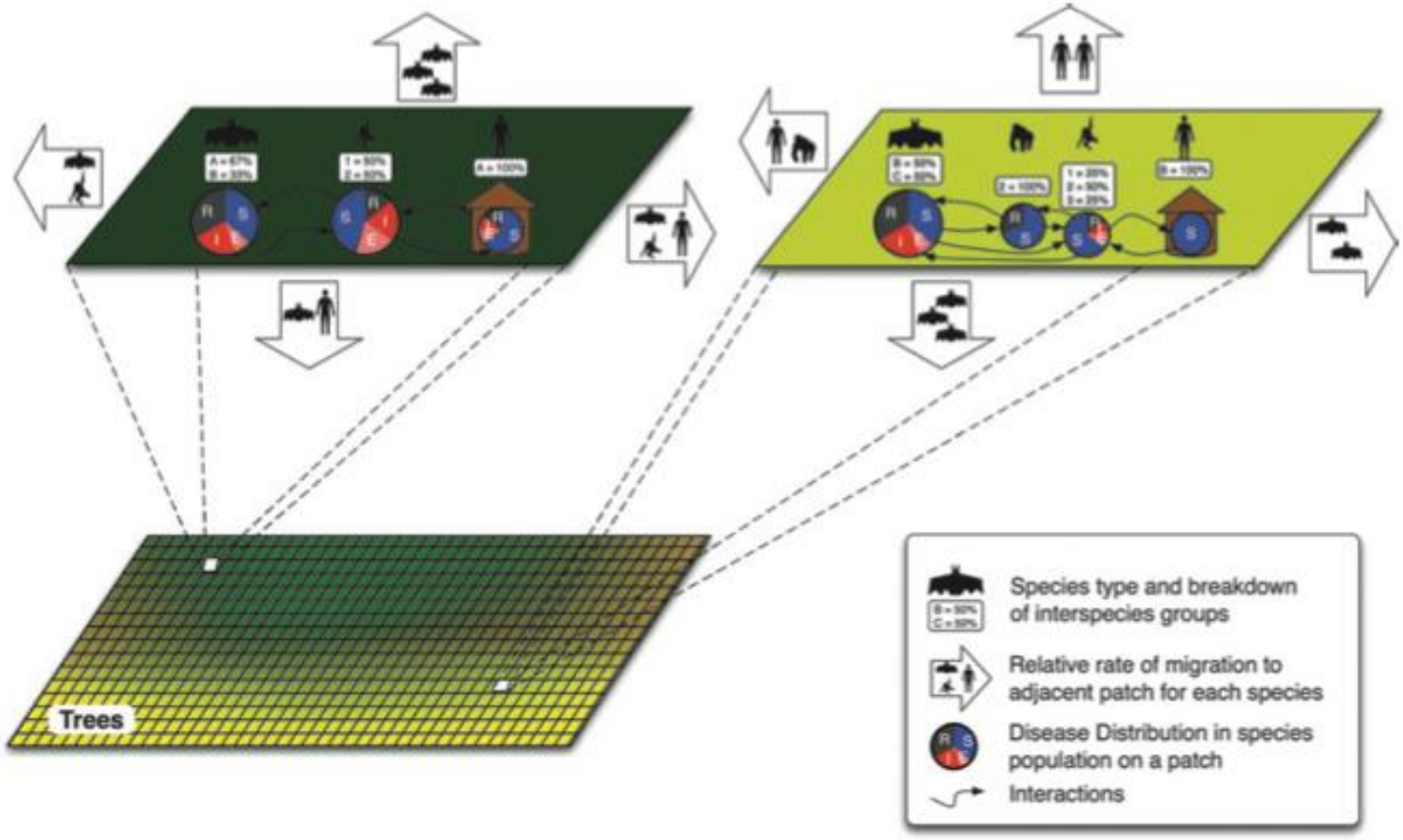
Patch Modeling



Combines compartmental models with Niche modeling to explore larger scale dynamics. Can help understand

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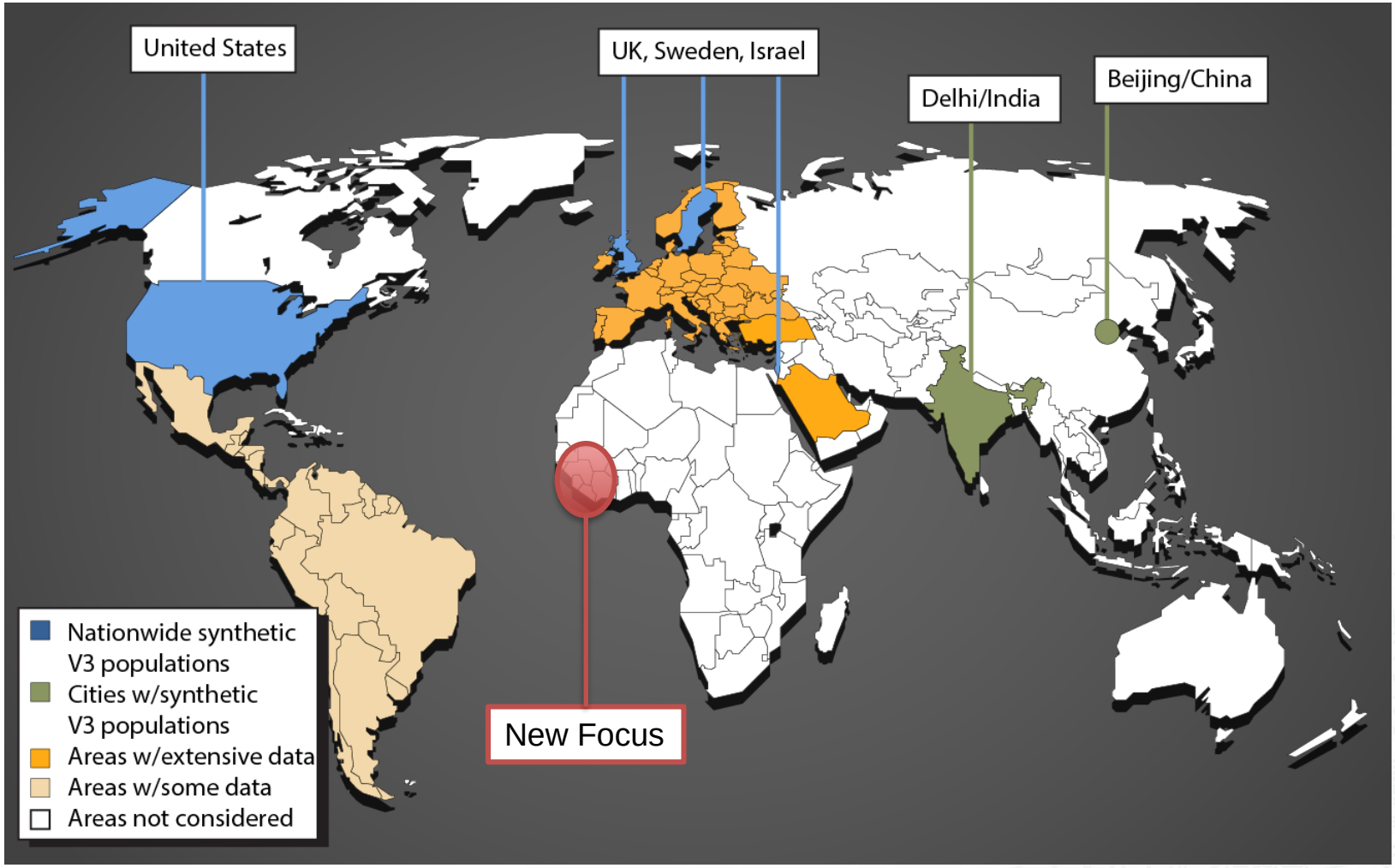
Population Construction - Global



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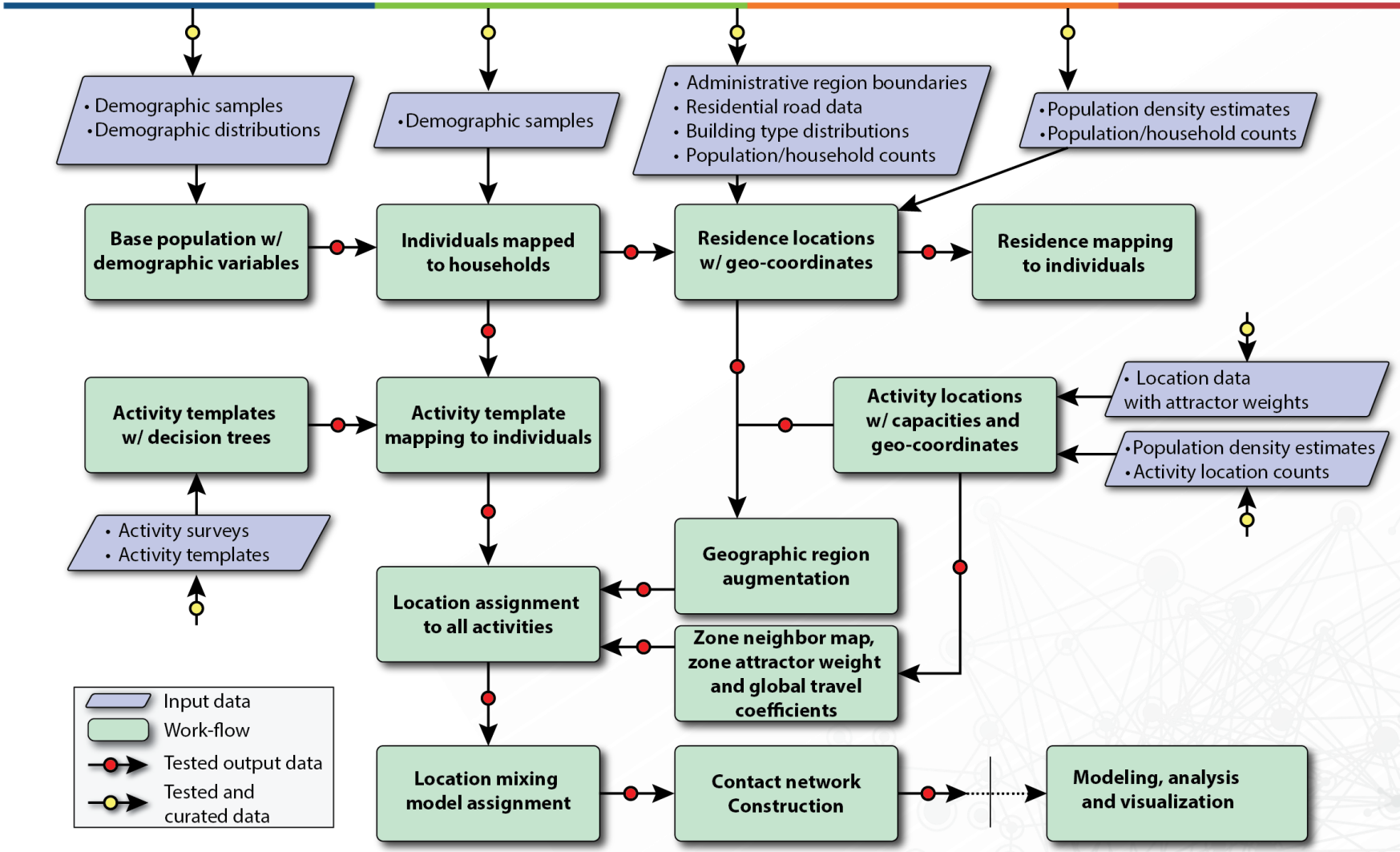
Population Construction - Pipeline



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Pop Construction – New Countries

Liberia:

- Limited demographic information
  - http://www.tlcafrica.com/lisgis/lisgis.htm
  - http://www.nationmaster.com/country-info/profiles/Liberia/People
- OpenStreetMap data (OSM data file is 4.1 MB, so limited)
  - http://download.geofabrik.de/africa.html

Sierra Leone:

- Some demographic information
  - http://www.statistics.sl
  - http://www.nationmaster.com/country-info/profiles/Sierra-Leone/People
  - http://www.statistics.sl/reports_to_publish_2010/population_profile_of_sierra_leone_2010.pdf
- OpenStreetMap data (OSM data file is 10.2 MB)

Guinea:

- Some demographic information
  - http://www.stat-guinee.org (french)
  - http://www.nationmaster.com/country-info/profiles/Guinea/People
- OpenStreetMap data (OSM data file is 15.6 MB)

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Conclusions

- Still need more data
  - Working on gathering West Africa population and movement data
  - News reports and official data sources need to be analyzed to better understand the major drivers of infection
- From available data and in the absence of significant mitigation outbreak in Africa looks to continue to produce significant numbers of cases
- Expert opinion and preliminary simulations support limited spread in US context

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