Using the power ratio as an early warning signal to detect critical transitions for infectious disease emergence and eradication

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Goal

It has recently been shown that infectious disease emergence and elimination may be preceded by statistical fluctuations that function as early warning signals. However, such early warning signals are known to have low power and perform poorly in the presence of periodic dynamics such as are common in infectious diseases. **The goal of this project was to determine if *power ratio* can be used as a reliable early warning signal to predict disease emergence or eradication for varying levels of disease case reporting levels.**

Overview

- Eradication of human infectious diseases has been a public health initiative for more than a century
- Emerging and re-emerging infectious diseases, such as Ebola, multi-drug-resistant TB, and pertussis, continually threaten lives of people across the world
- Infectious disease data is often under-reported, thus methods to predict emergence and eradication need to be robust enough to function without entire set of cases
- Predicting when eradication of a disease is "almost" achieved or when emergence events are likely could give policy makers specific evidence to stop the disease emergence or continue eradication efforts[1].

What are Early Warning Signals (EWS)?

Early warning signals (EWS) are statistical properties that change prior to a *critical transition*, which is an abrupt change in qualitative behavior of a system due to a small environmental change. Mathematically, these transitions correspond to correspond to bifurcations in the mean field dynamics. EWS have been studied in systems such as fishery collapses and climate change[2].

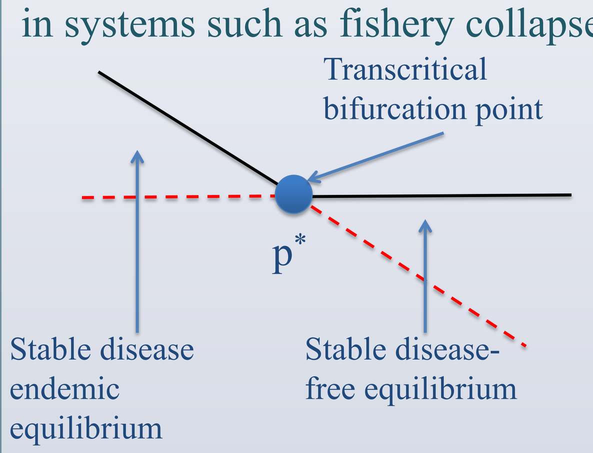

Fig. 1) An illustration transcritical bifurcation. Detecting this critical transition is the goal of EWS. Ideally, this would allow us to predict emergence and eradication events for disease systems. Figure courtesy of Dr. Suzanne O'Regan.

In the case of infectious diseases, however, EWS are difficult to use because of inherent periodicities (seasonality or multi-yearly cycling) and under-reporting issues in the datasets along with violations of normality, independence, and stationarity assumptions[3].

What is a power ratio?

- Power ratios come from wavelet methods which make fewer assumptions about datasets than other EWS[3] and allow us to study frequencies not affected by inherent periodicities in data
- *Wavelets* represent a time-series in terms of coefficients (*power*) that are associated with a particular time and a particular frequency[3]
- We defined the *power ratio* as the number calculated by dividing a low frequency power by a high frequency power throughout the entire time series (see Detailed Methods)
- Here, power ratios are evaluated for potential use as an EWS

Emergence

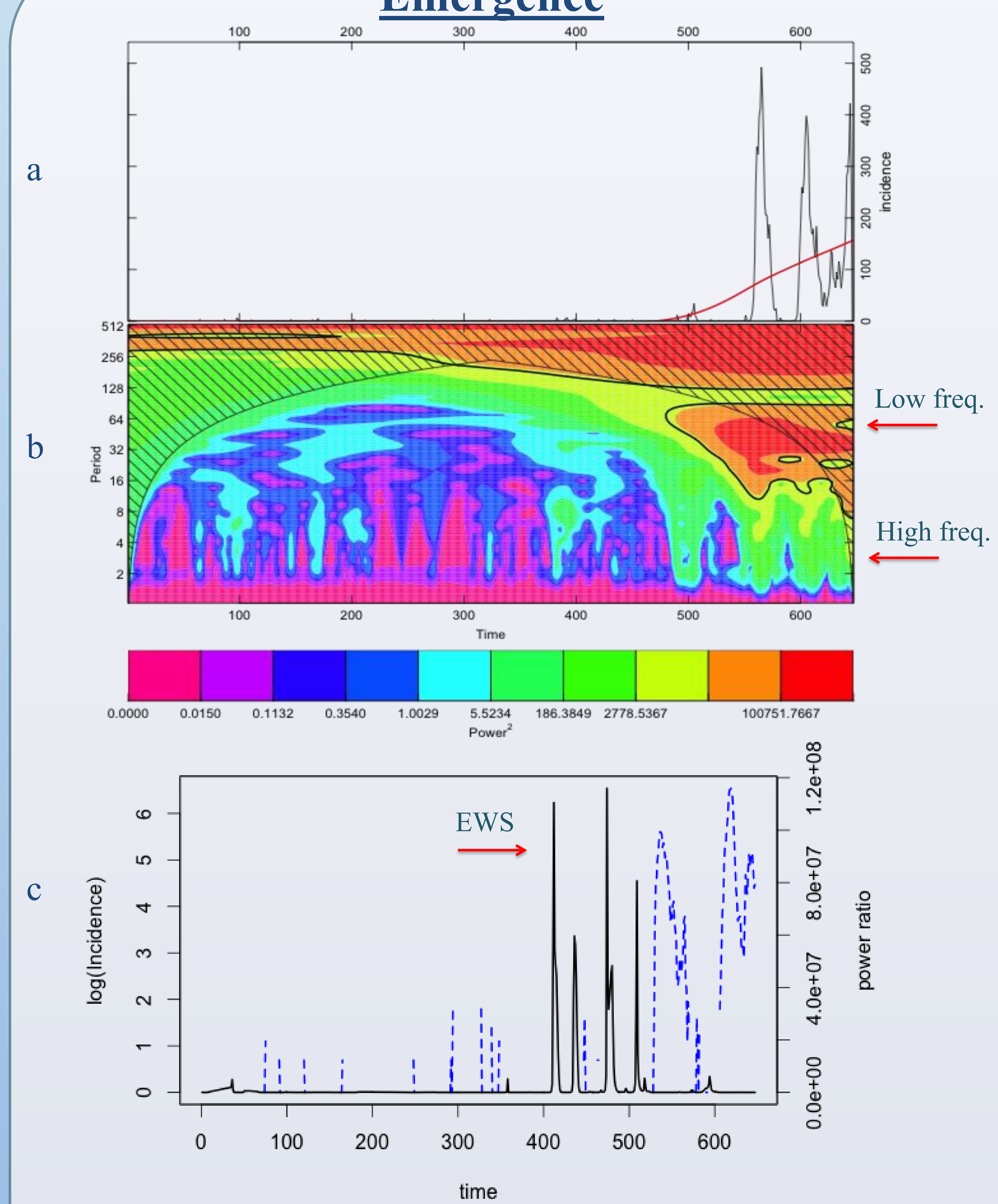

Fig. 2) Stochastic SIR simulation of a disease emerging due to an increase in population size (staring at year 360), exceeding the threshold for emergence (year 480). a) Incidence data from a single simulation. Time steps here are years. **b)** Wavelet plot showing how low frequencies (on y-axis; period=~64) begin to dominate before crit. trans.. **c)** Power ratio (black line) and time-series data (dashed blue line) from a single simulation. Power ratio increases prior to crit. trans., demonstrating its use as an EWS.

Reliability of EWS on detecting emergence

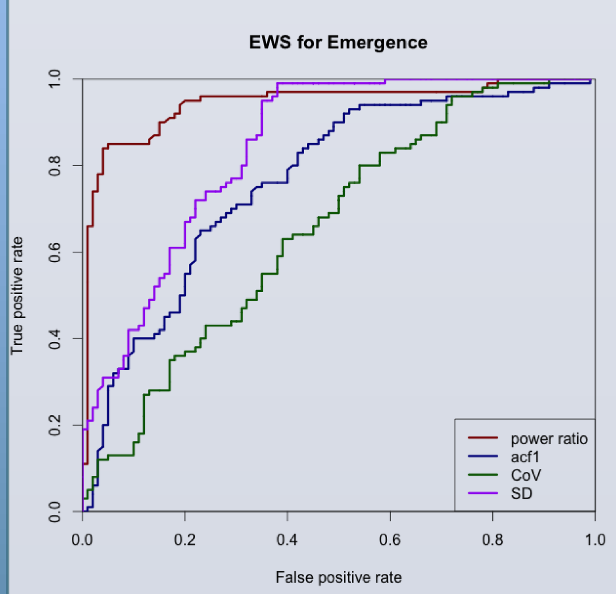

Fig. 3) ROC curves for detecting emergence with 100% reporting. ROC analysis tests a null interval (not approaching crit. trans.) against a test interval (approaching crit. trans.) to predict crit. trans. Perfect detection would return an Area Under Curve (AUC) value of 1. No detection ability would return an AUC value of 0.5. AUC values for power ratio, autocorrelation at lag-1 (acf1), coefficient of variation (CoV), and standard deviation (SD) were 0.92, 0.67, 0.66, and 0.92, respectively.

Detecting emergence with under-reporting

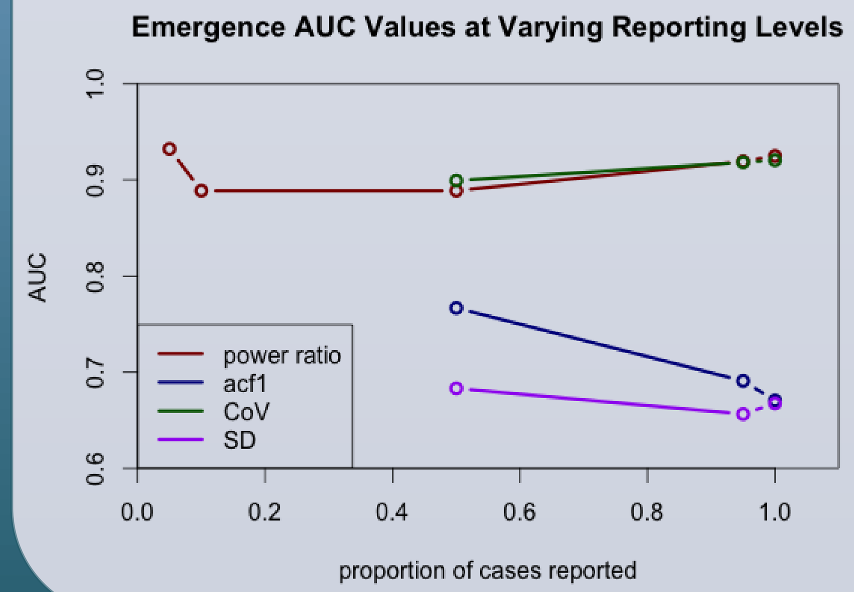

Fig. 4) AUC values for prediction of emergence events at varying levels of case reporting. The power ratio remains reliable even at very low levels of case reporting. CoV also remains as a reliable indicator at low reporting levels.

Eradication

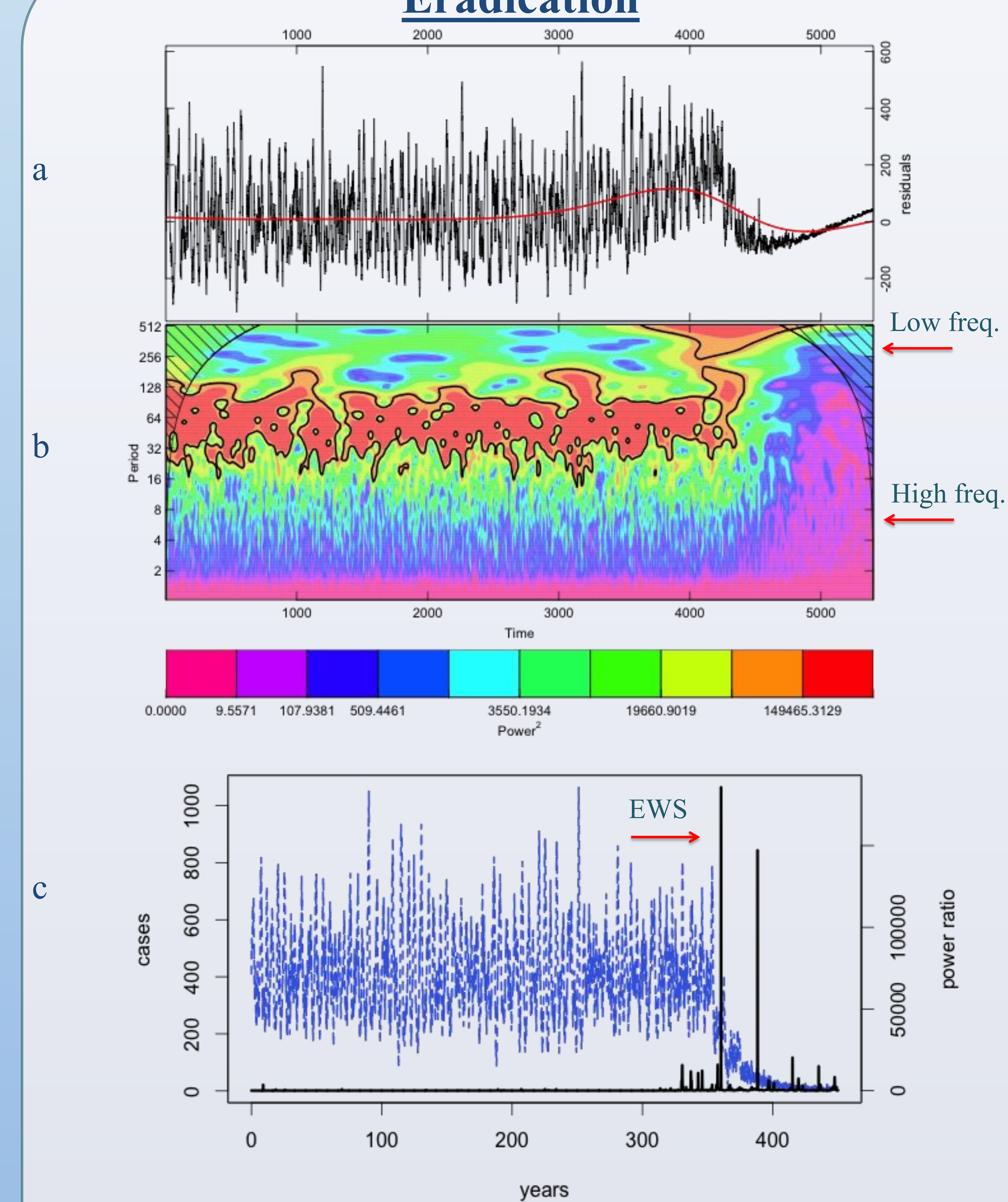

Fig. 5) Stochastic SIR simulation of a disease that becomes eradicated due to an increase in vaccinations starting in year 350[4]. a) Residuals calculated from the smoothed curve of time series data. Time steps here are monthly. **b)** Wavelet plot showing how low frequencies (on y-axis; period=~256) begin to dominate before crit. trans., around time step (in months) 4200. **c)** An example of the log power ratio (black line) and time-series data (dashed blue line). Power ratio increases before crit. trans.

Reliability of EWS on detecting eradication

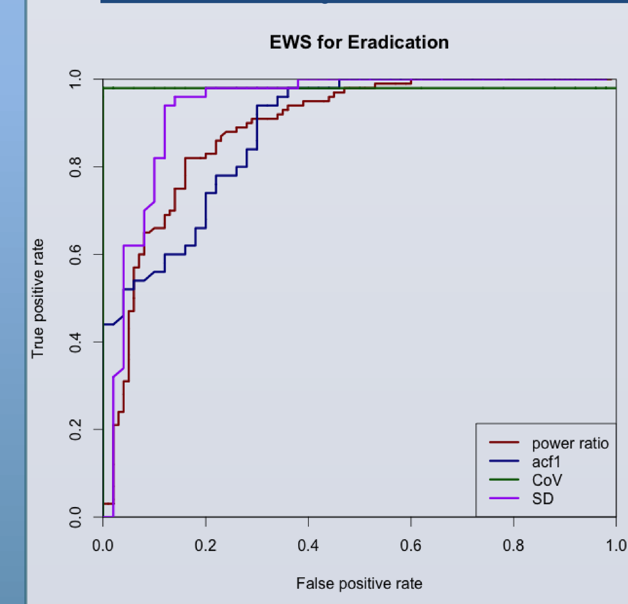

Fig. 6) ROC curves for detecting eradication with 100% reporting. Fig.3 explains how to interpret ROC curves. AUC values for power ratio, autocorrelation at lag-1 (acf1), coefficient of variation (CoV), and standard deviation (SD) were 0.87, 0.86, 0.98, and 0.91, respectively. SD decreases as the crit. trans. is approached, in contrast to the other EWS which increase prior to the crit. trans.. The power ratio was found to increase non-linearly as the crit. trans. is approached.

Detecting eradication with under-reporting

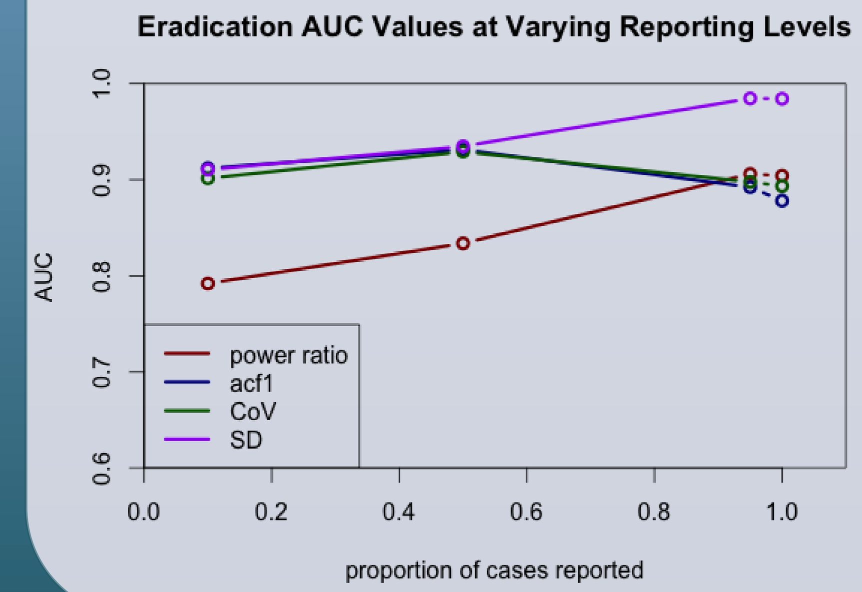

Fig. 7) AUC values for prediction of eradication threshold at varying levels of case reporting. For determining when diseases have crossed the crit. trans. for eradication, the power ratio is not as reliable as other EWS.

Detailed Methods

Emergence:
- Stochastic simulations (n=100) increase as crit. pop. is reached
- Power ratio=$\text{power}_{Freq=64}/\text{power}_{Freq=4}$ calculated across timeseries

Eradication:
- Simulations (n=100) forced to extinction due to an asymptotically increasing vaccination up to 96% coverage
- Residuals=$\text{data}_{actual} - \text{data}_{smooth}$ (local polynom. regression fitting)
- Power ratio=$\text{power}_{Freq=256}/\text{power}_{Freq=8}$ calculated across timeseries

Under-reporting:
- Reporting levels determined using binomial random sampling from the 100% reporting level simulation

Analysis:
- Morlet wavelets (complex exponentials x Gaussian window) used
- Acf1, SD, CoV used moving window=0.25; no prior detrending
- AUC/ROC input=amount of linear increase before crit. trans.

Main Conclusions & Future Directions

- Wavelet plots clearly show an increase in low frequency powers as the crit. trans. is approached for both disease emergence and eradication (fig. 2b & 5b)
- Power ratio is a reliable predictor for disease emergence events (fig. 3). Previous studies, using other EWS, found that emergence events were difficult to predict[5]
- Even as percentage case reporting drops, the power ratio remains highly reliable at predicting emergence events (fig. 4)
- For the disease simulated, smallpox, the wavelet plot was able to to detect a periodicity around 5-6 years, which is consistent with literature of historic dynamics[6]. Wavelet analysis was not impacted by annual variability in transmission for this specific simulation.
- The power ratio increases non-linearly as the crit. trans. is approached for disease eradication
- For detecting crit. trans. in diseases going towards eradication, the power ratio is less accurate than SD and CoV (fig. 6)
- Future studies should test the reliability of power ratios on other infectious disease systems; especially ones which are impacted by annual seasonal fluctuations (i.e. influenza)

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