# Supplementary Material to "Individual-based model for the control of Bovine Viral Diarrhea spread in livestock trade networks"

## S1: Simulation Control Measures

## S2: Spot Testing

"Spot testing" methodology based on a hypergeometric distribution sampling as outlined in [3]. In case of a positive result, an antigen test (regular blood test) is scheduled for each animal in the farm that has not been tested already to identify the source of transient infection and search for PI animals.

### S3.1: Single Farm Dynamics

We assume a minimal example of how the system should behave in terms of infectious states and population in figures 1a, 1b and 1c respectively. The simulation runs for the same settings as in the multi-farm frame without any intervention strategy, as calibrated for the case of Germany in [2] and with no PI animals originating from the source farm. The population of the single farm is set to 1,000 animals to achieve well-mixed conditions for the epidemic dynamics and to diminish finite-size effects. Since there is an inherent supply-and-demand mechanism to equalize the imbalance caused by demographic factors in the system, the minimum working setup requires the source and the drain farms as well. We notice therefore that the population fluctuates around the initial value of 1,000.

Moreover, the peak of infection is highly pronounced, when only a single farm is considered, as can be seen in figure 1b. This effect is typical of SIR dynamics and depends on the involved infectious and recovery rates [4]. The spatial structure may then shift the outbreak peak in value and time depending on the exact heterogeneities (farm size distribution) and connectivity (supply and demand) of the farm-nodes involved in the simulation.

### S3.2: Effect of PI introduction from the Source Farm

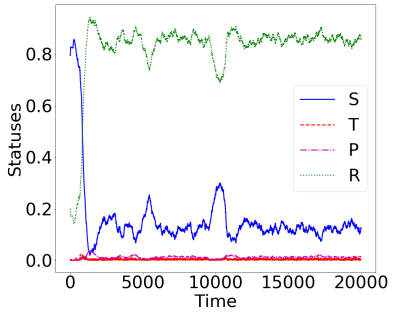
For the single farm with 2% probability of introduction of PI animals through the source farm, the PI peak is over twice higher than in the former case and

| **Control Measure** | **Description** |
|---|---|
| Trade control on animal level | Trade is only allowed, if the animal has tested BVD-negative |
| Trade control on herd level | If a PI animal is detected, the farm will go under quarantine for 40 days. No animals are allowed to leave the farm. Moreover, no pregnant cow can be moved before having given birth to a calf that has tested negative for BVDV. |
| Testing and removal: ear notch | All calves are tested for BVDV within seven days after birth. Animals with a positive test result will be traded to the slaughterhouse. Positive animals may be retested to exclude a transient infection after a maximum number of days, (which can be specified) in the model. Moreover there is the percentage of positive animals that will be retested. |
| Testing and removal: blood test | All cattle must be tested for BVDV before they can be traded. Animals with a positive test result are traded to the slaughterhouse. BVDV-positive animals may be retested to exclude a transient infection after a maximum number of days, which can be specified in the model. Moreover, there is a parameter included on the percentage of positive animals that will be retested. |
| Antibody testing: spot testing | Spot testing is included in the model. Animals in a certain age (specified in the model) are tested with a certain frequency A sample of young animals in the farm is tested. If at least one animal that tests positive for BVDV, all animals of the farm will be tested by blood testing (see above). |
| Vaccination | All cattle in a farm will be vaccinated against BVDV. Since there are several vaccines (modified live vaccines as well as inactive vaccines) we simplified the model by summarizing all combinations of vaccination. As "vaccination" in our model might be a combination of different vaccines, the overall efficacy is termed "vaccine working probability". |

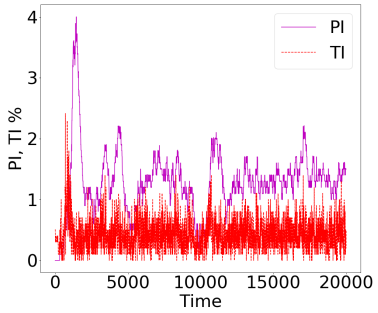
Table 1: Summary of the simulation control measures (S1).

| N | $\leq 10$ | $\leq 20$ | $\leq 40$ | $\leq 80$ | $\leq 160$ | $> 180$ |
|---|---|---|---|---|---|---|
| n | 8 | 10 | 12 | 13 | 13 | 14 |

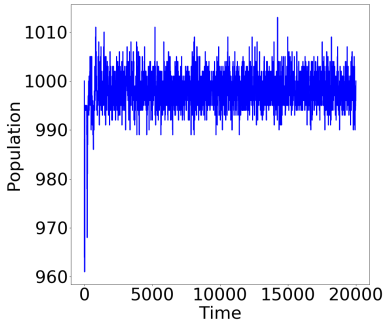
Table 2: Sample sizes given a farm population according to the spot testing of young cattle. Population sizes (N) and the corresponding samples (n) needed to be tested negative so that the prevalence of the infected animals in the population will not exceed 20% with a confidence of 95%.




(a) Evolution of all states.

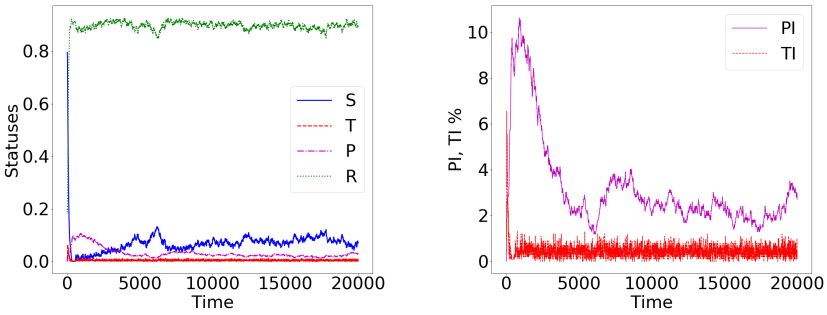



(b) Evolution of the infectious states.




(c) Demographic evolution.

Figure 1: Single farm dynamics with an initial PI population but without subsequent PI introduction from the source farm during the simulation: Panel 1a: time series of the S, TI, PI and P states. Panel 1b: enlargement for infectious states TI and PI. Panel 1c: evolution of the farm's population without intervention strategy. Initial conditions: S, TI, R, PI levels: 79%, 0.5%, 20.5%, 0%; here: 790, 5, 205 and 0 out of 1,000 animals, respectively.




(a) All states' evolution.

(b) Infectious states' evolution.

Figure 2: The respective evolution plots of figure 1 but for a probability of a PI introduction from the source farm of 2%.

| $p(\mathrm{PI_{in}})$ (%) | $\bar{t}_{\max \mathrm{PI}}$ | $\overline{\mathrm{PI}}_{\max}$ | $\langle \mathrm{PI_{eq.}} \rangle$ |
|---|---|---|---|
| 0 | 1,420 | 0.025 | 0.012 |
| 1 | 870 | 0.029 | 0.015 |
| 2 | 710 | 0.037 | 0.015 |
| 5 | 645 | 0.058 | 0.017 |
| 10 | 640 | 0.075 | 0.018 |
| 20 | 890 | 0.113 | 0.023 |

Table 3: Sensitivity of PI-infectious metrics for single farm dynamics (PI introduction probability as the control variable): Mean value of the first occurrence peak time $\bar{t}_{\max \mathrm{PI}}$ and peak height $\overline{\mathrm{PI}}_{\max}$ for the PI prevalence (average over 10 realizations) and its average value $\langle \mathrm{PI_{eq.}} \rangle$ for the last 5,000 time steps, i.e. $t \in [15000, 20000]$, (quasi equilibrium) normalised for different probability of PI introductions from the source farm. Initial condition as in figure 1.

therefore the recovered (R) class of animals remains consistently at high levels, without much fluctuation. The demographic time series is virtually identical to the one for no PI animals entering the system through the source farm 1c. The settings remain always as those in the main text without any intervention strategy.

What stands out in figures 2a and 2b in comparison with their counterparts 1a and 1b (the demographics are statistically identical in both cases and are therefore skipped in figure 2) of no introduction of PI animals from the source farm is the epidemic outbreak peak value and the effect this has on the immune, R class of animals.

A sensitivity analysis of the effect of the introduction of PI animals is shown in tables 3 and 4. The tables show that within a farm the PI level is related to the probability of introduction of PI animals through the source farm.

| $p(\mathrm{PI_{in}})$ (%) | $\bar{t}_{\mathrm{PI,first}}$ | $\bar{t}_{\mathrm{PI,last}}$ | $\bar{t}_{\mathrm{tr.,first}}$ | $\bar{t}_{\mathrm{tr.,last}}$ | $\langle\sum \mathrm{PI,in}\rangle$ | $\langle\sum \mathrm{tr.,in}\rangle$ |
|---|---|---|---|---|---|---|
| 0 | None | None | 7.5 | 19,961.7 | 0 | 1,122 |
| 1 | 1,195.4 | 18,425.2 | 7.5 | 19,924.6 | 12 | 1,141 |
| 2 | 46 | 18,890.7 | 7.5 | 19,965.2 | 25 | 1,115 |
| 5 | 8.2 | 19,352.7 | 7.5 | 19,932.3 | 61 | 1,119 |
| 10 | 8.2 | 19,694.3 | 7.5 | 19,941.4 | 115 | 1,117 |
| 20 | 7.5 | 19,801.4 | 7.5 | 19,931.6 | 229 | 1,135 |

Table 4: Single farm descriptive statistics of the PI and arbitrary animal trades averaged over 10 realisations (PI introduction probability as the control variable). Mean value of the first introduction time of a PI, $\bar{t}_{\mathrm{PI,first}}$, mean value of the last introduction time of a PI, $\bar{t}_{\mathrm{PI,last}}$, mean value of the first animal trade time $\bar{t}_{\mathrm{tr.,first}}$, mean value of the last animal trade time $\bar{t}_{\mathrm{tr.,last}}$, mean value of the total PI introductions $\langle\sum \mathrm{PI,in}\rangle$ and mean value of the total animal introduction $\langle\sum \mathrm{tr.,in}\rangle$.

| | | $\beta_{\mathrm{TI}}$ | | | |
|---|---|---|---|---|---|
| | | 0.01 | 0.03 | 0.05 | 0.1 |
| $\beta_{\mathrm{PI}}$ | 0.1 | 11 | 12 | 12 | 21 |
| | 0.5 | 210 | 305 | 317 | |
| | 0.8 | 278 | | | |

Table 5: Final number of persistently infected animals as a function of $\beta_{\mathrm{TI}}$ and $\beta_{\mathrm{PI}}$.

# S4: Description of the model behavior for multiple farms

## S4.1: Infectious Sensitivity on Farm Size Distribution

We observed a constant PI prevalence in the simulation for large farm animal populations and relatively small numbers of farms (as typical for the federal state of Thuringia, data not shown). However, the PI prevalence decreased slightly over time when using a farm size distribution that reflected Germany (figure 3).

## S4.2: Influence of transmission rates on the model

Table 5 shows the influence of the transmission rates $\beta_{\mathrm{TI}}$ and $\beta_{\mathrm{PI}}$ on the number of PI animals in the population at the end of the simulation. When changing the infection transmission parameter $\beta$, we observed that $\beta_{\mathrm{PI}}$ is mainly influencing the number of PI animals as per table 5.

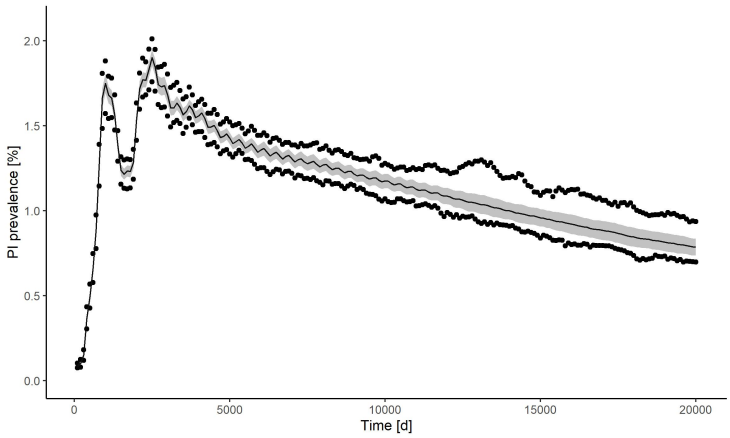



Figure 3: Mean PI prevalence over time without control. The variance results from different simulation runs for the farm size distribution of Germany (scaled down). The line represents the mean prevalence, the dots the minimum and maximum prevalence, while the grey area the standard deviation.

## S4.3: Sensitivity of infections to the test

We tested the influence of the sensitivity and specificity of the virus test on the PI prevalence in figure 4 and table 6. A declining trend in PI prevalence was observed for an increasing sensitivity of the test.

## S4.4: Sensitivity of infections to vaccination

We tested the effect of it on the PI prevalence by varying the working probability of vaccination from zero to one. Figure 5 shows that the increase of the vaccine working probability (VWP)[1] had a dwindling effect on the PI prevalence. Nevertheless, up to a VWP of 30%, there was no noticeable difference between the baseline scenario (no measure) and vaccination.

[1]We remind the reader that as per the simulation settings in section 2 this refers to the probability to successfully immunize a susceptible animal.

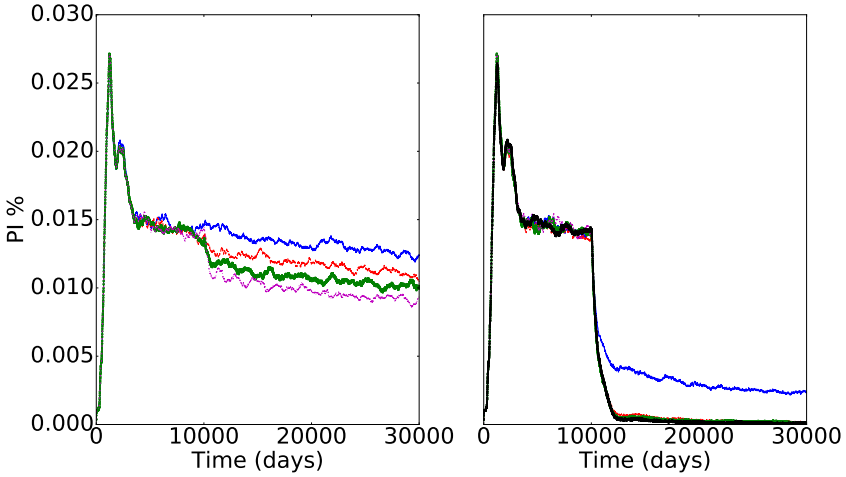



Figure 4: New regulation (i.e. from 2016, ear-notch testing with 40-day quarantine of the farm in case of positive result) strategy for different test accuracy probabilities ranging from 0 to 1 in both panels, see table 6 for details. The effect of the ear notch test protocol is enforced from day 10,000 onward.

| Probability | Style (Position) |
|---|---|
| 0 | Solid, blue (left) |
| 0.1 | Dashed, red (left) |
| 0.2 | Dotted-dashed, green (left) |
| 0.3 | Dashed, dotted, magenta (left) |
| 0.8 | Solid, blue (right) |
| 0.98 | Dashed, red (right) |
| 0.99 | Dotted-dashed, green (right) |
| 0.998 | Dashed, dotted, magenta (right) |
| 1 | Dotted, black (right) |

Table 6: Probabilities of the test's sensitivity for the new regulation (i.e. from 2016, ear-notch testing with 40-day quarantine of the farm in case of positive result).

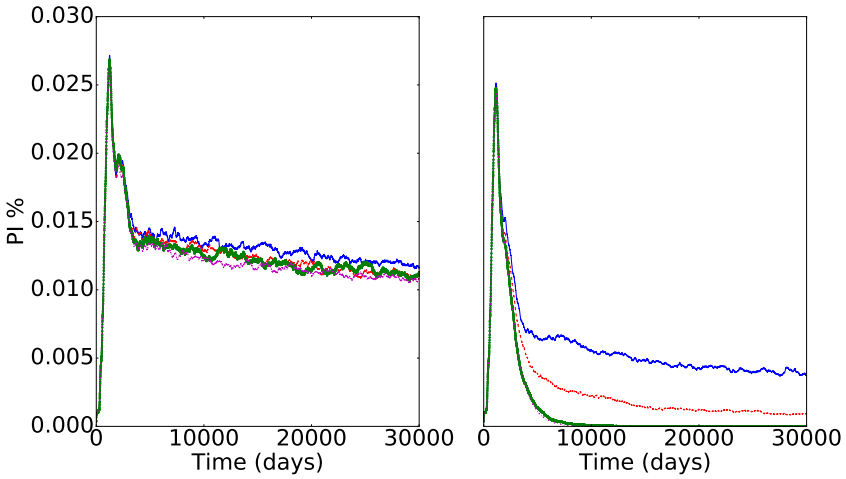



Figure 5: Non-targeted vaccination strategy for different vaccination working probabilities ranging from 0 to 1 in both panels, see table 7 for details.

| Probability | Style (Position) |
|---|---|
| 0 | Solid, blue (left) |
| 0.1 | Dashed, red (left) |
| 0.2 | Dotted-dashed, green (left) |
| 0.3 | Dashed, dotted, magenta (left) |
| 0.8 | Solid, blue (right) |
| 0.9 | Red, dashed (right) |
| 0.985 (default) | Dotted-dashed, green (right) |
| 1 | Dashed-dotted, magenta (right) |

Table 7: Vaccination working probabilities for the sensitivity of the vaccination strategy in both panels.

### S4.5: Model Infections VS Data Infections

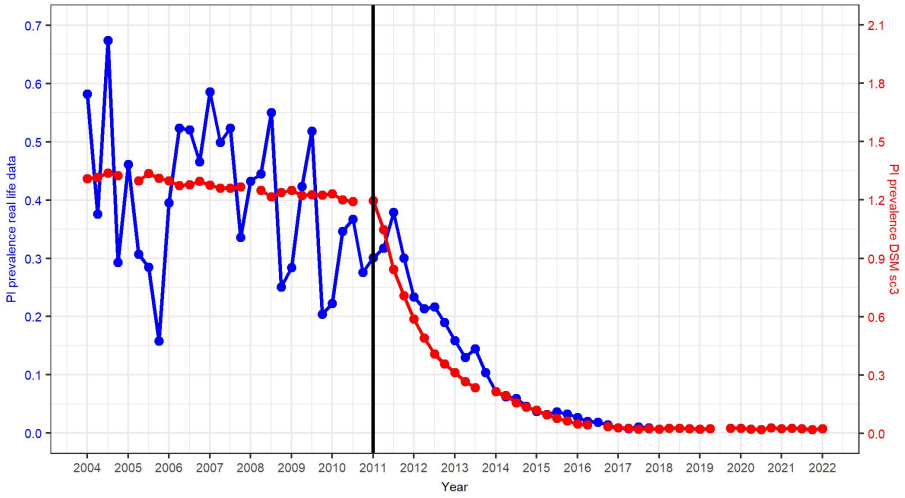



Figure 6: Comparison of the PI prevalence in reality (source: [1], blue dots corresponding to the left axis) and as simulated for the current control strategy (red dots corresponding to the right axis).

## References


[1] `https://www.hi-tier.de/`, 2020.

[2] Jason Bassett, Pascal Blunk, Thomas Isele, Jörn Gethmann, and Philipp Hövel. An agent-based model for bovine viral diarrhea. *arXiv preprint arXiv:1812.06964*, 2018.

[3] F. J. Conraths and J. Gethmann. Epidemiologische Untersuchungen in Tierpopulationen. Technical report, FLI, Greifswald - Insel Riems, August 2015.

[4] P. Rohani. *Modeling infectious diseases in humans and animals*. Princeton University Press, Princeton, 2008.