# Risk Group Demographics in Simulated STI Epidemics

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## Contents



### Key Contributions

1. Formalize a mathematical framework for risk group demographics
2. Describe methods for deriving risk group demographic parameters from common data sources
3. Illustrate differences in modelled projections for different implementations of risk group demographics, using an example sexually transmitted infection

# 1 Background

** R O U G H **

- key factors in risk of HIV acquisition
- intro HIV modelling, prior work showing importance of heterogeneity
- comments on applicability of these concepts to non-HIV transmissible diseases (other STI, non-S TI)
- prior work on turnover, comment on need for "equilibration" / "burn-in" period

What do we mean by "risk group dynamics"?

1. inclusion of risk groups at all (yes / no)
2. inclusion of turnover among these groups (yes / no, how?)
3. consideration of how groups are re-balanced given differential attributable death – subject of future work

From Eaton and Hallett (2014) [3]: *Two behavioral parameters – the rate of transition from higher- to lower-risk groups and* [...] *– were particularly important for simulating the observed prevalence trend in many different ways, as well as determining the intervention impact.*

From SR by Mishra et al. (2012) [7]: N = 107 models included behavioural heterogeneity, while N = 88 did not.

From SR by Ronn et al. (2017) [8]: N = 34 included risk heterogeneity, while N = 11 models had none.

Some papers to include in Table 1:

# 2 The System

This section introduces a system of compartments, flows between them, and equations which can be used to describe risk group dynamics.

We denote the variable representing the size of risk group $i \in [1, \dots, G]$ as $x_i$ and the vector of all $x_i$ as $\boldsymbol{x}$. The total population size is denoted $N = \sum_i x_i$,[1] and the proportions represented by each group by $\hat{x}_i = x_i N^{-1}$. The rate of population entry for all groups is denoted by $\nu$, and the rate of exit by $\mu$. We do not consider disease-attributable death, which may vary by group, though this will be the subject of future work. All rates have units *per year* ($\text{yr}^{-1}$). The proportion of the entering population who are in group $i$, which may not be equal to the proportion of the current population in group $i$, is denoted $\hat{e}_i$. Since the rate of entry $\nu$ is typically expressed as a proportion of the total population size $N$,we model the theoretical entering population $\boldsymbol{e}$ as also having size $N$, so that $e_i = \hat{e}_i N$.

Turnover transitions can occur between any two groups, in either direction; therefore we denote the turnover rates as a $G \times G$ matrix $\zeta$, where $\zeta_{ij}$ corresponds to the transition $x_i \to x_j$. An explicit definition is given in Eq. (2.1), where the diagonal elements are denoted $*$ since they represent transitions from a group to itself, which is inconsequential.

$$\zeta = \begin{bmatrix} * & x_1 \to x_2 & \cdots & x_1 \to x_G \\ x_2 \to x_1 & * & \cdots & x_2 \to x_G \\ \vdots & \vdots & \ddots & \vdots \\ x_G \to x_1 & x_G \to x_2 & \cdots & * \end{bmatrix} \tag{2.1}$$

These transition flows and the associated rates are summarized for $G = 3$ in Figure 1.

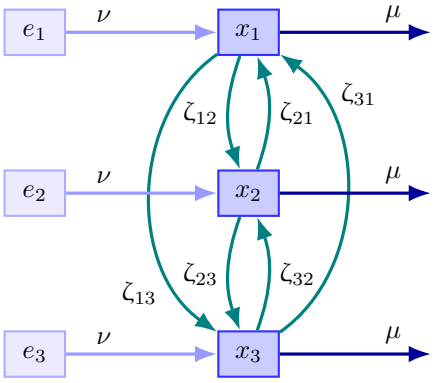


Figure 1: System of compartments and flows between them for $G = 3$

Some key assumptions of this work:

- The health states of individuals moving between risk groups due to turnover is proportional to the health states of the group overall.
- Disease-attributable death has negligible impact on risk-group proportions.
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## 2.1 Parameterization

Next, we explore methods for estimating the values of parameters in the system described above ($\nu$, $\mu$, $\hat{\boldsymbol{x}}$, $\hat{\boldsymbol{e}}$, and $\zeta$) directly from some commonly available sources of data.

In most cases, there will not be sufficient data to directly estimate all parameters, especially $\zeta$. The next section outlines additional methods to solve for these values.

[1] In many models, "total population" actually refers to an age-constrained range.

### 2.1.1 Total Population Size

The model of total population size over time is defined by entry and exit rates, $\nu$ and $\mu$, as in:

$$N(t) = N_0\big(1 + \mathcal{G}(t)\big)^t \tag{2.2a}$$
$$\mathcal{G}(t) = \nu(t) - \mu(t) \tag{2.2b}$$

and we note that the average duration of an individual in the model at time $t$ is given by:

$$\delta(t) = \mu^{-1}(t) \tag{2.3}$$

Variation in rate of entry across risk groups is captured in $\hat{\boldsymbol{e}}$, and we generally do not stratify rate of exit by activity group (besides disease-attributable death); therefore, we can assume that $\nu$ and $\mu$ do not vary across risk groups, which allows us to derive them with $N(t)$, independent of the population proportions $\hat{\boldsymbol{x}}$, $\hat{\boldsymbol{e}}$, and turnover $\zeta$.

The simplest approach assumes a constant population size $N(t) = N_0$, or a growth rate of zero, yielding $\nu = \mu$. However, this does not reflect the true positive population growth of most contexts, and may result in underestimated incidence, due to the relative reduction in inflow of susceptibles.

Another approach is to fix $\mathcal{G}(t)$ as some constant. When using this approach, extra care should be taken to ensure the resulting $N(t)$ matches any available population size estimates to a reasonable degree.

Typically, data will be available for the total size of the population over time $N(t)$, so the growth rate for each time interval $t_i$ can be derived by rearranging Eq. (2.2a):

$$\mathcal{G}(t_i) = \left(\frac{N(t_{i+1})}{N(t_i)}\right)^{-(t_{i+1}-t_i)} - 1 \tag{2.4}$$

All of these approaches help define $\mathcal{G}(t)$, but leave one degree of freedom, since any choice of $\mu(t)$ can be compensated by $\nu(t)$ to yield the desired $\mathcal{G}(t)$. However, we can usually leverage the known duration of individuals in the model $\delta(t)$ to choose $\mu(t)$ as in Eq. (2.3). This can come from an assumed duration of sexual activity, or a constant, predefined age range relevant to parameterization. Then, we can solve for $\nu(t)$ using Eq. (2.2b).

### 2.1.2 Turnover

Next, we assume that $\nu(t)$ and $\mu(t)$ are known, and we focus on resolving $\hat{\boldsymbol{e}}(t)$ and $\zeta(t)$. Similar to above, we will first formulate the problem as a system of equations; then we will consider which data and assumptions we can leverage to solve the system.

We begin by defining the "conservation of mass" equation for a given group $x_i$, where that the rate of change of the group is simply the sum of flows in / out of the group:

$$\frac{d}{dt}x_i = \nu\, e_i + \sum_j \zeta_{ji}\, x_j - \mu\, x_i - \sum_j \zeta_{ij}\, x_i \tag{2.5}$$

While Eq. (2.5) is written in terms of absolute population sizes $\boldsymbol{x}$ and $\boldsymbol{e}$, it is equivalent to divide through by $N$, yielding a system in terms of proportions $\hat{\boldsymbol{x}}$ and $\hat{\boldsymbol{e}}$, which is often more useful, since $N$ need not be known.

We further assume that the average proportions of each group $\hat{x}_i$ do not change over time. Therefore, the desired rate of change for risk group $i$ will be equal to the growth of the risk group, $\mathcal{G}x_i$. Substituting this into Eq. (2.5), and simplifying, we have:

$$\nu\, x_i = \nu\, e_i + \sum_j \zeta_{ji}\, x_j - \sum_j \zeta_{ij}\, x_i \tag{2.6}$$

Now, depending on the number of risk groups, we have $G$ and $G(G-1)$ unknowns in $\boldsymbol{e}$ and $\zeta$, totalling $G^2$ variables to resolve. We denote these variables as the vector $\boldsymbol{\theta} = [\boldsymbol{e}, \boldsymbol{z}]$, where $\boldsymbol{z} = \text{vec}_{i\neq j}(\zeta)$; this allows us to define a system of linear equations of the form:

$$\boldsymbol{b} = A\,\boldsymbol{\theta} \tag{2.7}$$

where $A$ is a $G \times G^2$ matrix and $\boldsymbol{b}$ is a $G$-length vector, representing the right-hand side and left-hand side of Eq. (2.6), respectively. In this form, we can use $A^{-1}\boldsymbol{b} = \boldsymbol{\theta}$ to solve for $\boldsymbol{\theta}$.

Unfortunately, for any $G > 1$, the system is underdetermined by a factor of $G(G-1)$, meaning there are many combinations of $\boldsymbol{e}$ and $\zeta$ which satisfy Eq. (2.6). Therefore, we now resume our task of leveraging data and assumptions to define a unique solution.

Our first tool is another equation. We note that the duration of time spent in a particular group $\delta_i$ is the inverse of all efferent flow rates:

$$\delta_i = \left(\mu + \sum_j \zeta_{ij}\right)^{-1} \tag{2.8}$$

These durations could be derived from survey data, including for key populations, or they could be assumed. Rearranging Eq. (2.8), we obtain ${\delta_i}^{-1} - \mu = \sum_j \zeta_{ij}$, which yields an additional $G$ equations in our linear system – i.e. rows of $A$ and $\boldsymbol{b}$. For $G = 2$, this provides enough constraints to fully determine the system, as shown in Appendix A Example Systems, but for larger $G$, still more constraints are needed.

The simplest additional constraints can be elements in $\boldsymbol{\theta}$ which are directly specified – i.e. elements of of $\boldsymbol{e}$ or $\zeta$. For example, the proportion of individuals who move from one risk group to another each year ($\zeta_{ij}$) may be assumed or derived from data. Similarly, the distribution of individuals across risk groups in the entering population $\hat{\boldsymbol{e}}$ may be approximated using the proportions among the lowest age group for which data are available. In each case, the value specified is appended to $\boldsymbol{b}$, and a row appended to $A$ of the form: $[0, \ldots, 1, \ldots, 0]$, with 1 in the position of the element in $\boldsymbol{\theta}$.

There are, however, two notable caveats to this approach. First, not all combinations of specified elements will add an equal number of constraints. Specifying all elements of $\boldsymbol{e}$ will only add $G-1$ (not $G$) constraints, since $\sum \hat{\boldsymbol{e}} = 1$, so the final element adds no new information. Similarly, specifying all elements of $\zeta_{ij}$ for a given $i$ as well as the duration for the group $\delta_i$ will only add $G-1$ (not $G$) constraints, since Eq. (2.8) must hold. Second, not all combinations of specified values will yield a valid solution,[2] and it is unfortunately difficult to anticipate problematic combinations.

Finally, we note that additional constraints may be avoided altogether if we pose the problem as an optimization problem, namely:

$$\boldsymbol{\theta}^* = \arg\min f(\boldsymbol{\theta}), \quad \text{subject to: } \boldsymbol{b} = A\,\boldsymbol{\theta};\ \ \boldsymbol{\theta} \geq 0 \tag{2.9}$$

where $f$ is a function such as $||\cdot||_2$. However, the choice of $f$ implies a prior on the values of $\boldsymbol{\theta}$, and so introduces bias in the solution.

## 2.2 Previous Approaches

In this section, we will examine previous approaches to modelling risk groups in simulated HIV epidemics, and the assumptions inherent to these methods. Box 1 summarizes the most common assumptions regarding the dynamics of these risk groups, while Table 1 summarizes previous works with respect to these assumptions.

Many of the previously proposed models of HIV transmission follow Assumption 1.1. and do not consider heterogeneity in risk of acquisition within major demographic groups, such as heterosexual men / women, and MSM. This is a significant assumption, and may lead to large discrepancies with models which do consider risk heterogeneity, as explored in Section 3. Moreover, this assumption precludes any consideration of turnover, since there is only one risk group, $G = 1$.

* (discussion of each assumption in turn)

[2] Even rank-deficient systems be inconsistent.

Box 1: Common assumptions regarding the dynamics of risk groups

1. **Risk Groups:** Major demographic groups are stratified by risk of HIV acquisition.
   1.1. **No:** $G = 1$; Major demographic groups are homogeneous in risk of HIV acquisition.
   1.2. **Yes:** $G > 1$; Heterogeneity in risk of HIV acquisition within major demographic groups is considered.
2. **Turnover:** Individuals may move between risk groups.
   2.1. **No:** $\zeta = 0$; Individuals do not move between risk groups.
   2.2. **Constant:** $\zeta > 0$; Individuals move between risk groups at a constant rate.
3. **Population Growth:** Increase in the total $N$ over time.
   3.1. **No:** $\nu = \mu$; Population size $N$ is constant.
   3.2. **Yes:** $\nu > \mu$; Population size $N$ increases, at some constant or data-driven rate.

Table 1: Summary of prior work with respect to modelled risk group dynamics.

| Ref. | Year | Author | Risk Groups $G$ | Mortality $\phi$ | Dynamic Rebalance $RB$ | Turnover $\zeta$ |
|---|---|---|---|---|---|---|
| [6] | 2008 | Hallett et al. | 3 | Yes | None | None |
| [1] | 2012 | Barnighausen et al. | 1 | Yes | None | N/A |
| [4] | 2012 | Estill et al. | 1 | Yes | None | N/A |
| [2] | 2013 | Cremin et al. | 3 | Yes | None | None |
| [3] | 2014 | Eaton and Hallett | 3 | Yes | None | Constant |

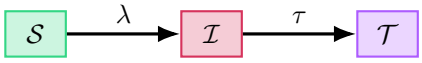


Figure 2: Modelled health states

# 3 Experiment

We have described an approach to parameterizing models of risk group dynamics which hopefully highlights the *feasibility* of including such model components based on available data. Next, we will explore the *importance* of including these components through comparison of projected model outputs across different implementations of risk group dynamics. First, we will compare major structural variants involving population growth, risk groups, and turnover. Second, we will investigate the impact of turnover sparsity – that is, only modelling certain transitions, such as in [3].

## 3.1 Model & Simulations

We use a simple deterministic model of heterosexual HIV transmission, including three health states: susceptible $\mathcal{S}$, infected $\mathcal{I}$, and on treatment $\mathcal{T}$, as shown in Figure 2, and up to three levels of sexual activity (risk groups $G$): high $H$, medium $M$, and low $L$. Individuals of sex $k$ in risk group $i$ are assumed to form sexual partnerships at a rate $C_{ki}$ with individuals of the opposite sex k. The probability of partnership formation with a partner of sex k in risk group i is assumed to follow the formulation proposed by Garnett and Anderson [5]:

$$\rho_{ki\mathrm{ki}} = (1-\epsilon)\psi_{ki\mathrm{ki}} + (\epsilon)\pi_{ki\mathrm{ki}} \tag{3.1}$$

where $\epsilon$ is a parameter controlling the dominance of assortative $\psi$ ($\epsilon = 0$) versus proportional $\pi$ ($\epsilon = 1$) mixing.

Transmission of HIV from infected $\mathcal{I}$ to susceptible $\mathcal{S}$ individuals is assumed to occur with probability $\beta_{k\mathrm{k}}$ per partnership. Individuals on treatment $\mathcal{T}$ are not considered infectious. The force of infection for susceptibles of sex $k$ in risk group $i$ is therefore modelled using the following equation:

$$\lambda_{ki} = C_{ki} \sum_{\mathrm{ki}} \rho_{ki\mathrm{ki}}\, \beta_{k\mathrm{k}} \frac{\mathcal{I}_{\mathrm{ki}}}{N_{\mathrm{ki}}} \tag{3.2}$$

Infected individuals are assumed to be diagnosed and begin treatment at a rate $\tau$ (per year). As described in Section 2, individuals enter the model at a rate $\nu$, exit at a rate $\mu$, and transition between risk groups at rates $\zeta_{ij}$. The default parameters for this base model are summarized in Table 2.

Using this model (and its variants), simulated epidemics are initialized in $t = 1975$ with $N_0 = 1000$ individuals, distributed proportionally according to $\hat{\boldsymbol{x}}$. Among these individuals, 6 are infected, and the remainder are susceptible; for $G = 3$, this corresponds to one infected person in each sex-risk group, while for $G = 1$, this corresponds to three infected people in each sex. Simulated epidemics run until $t = 2025$, and are solved numerically using Euler's method with a time step of $dt = 0.5$ years.

Table 2: Base model parameters. All rates have units year$^{-1}$ and durations are in years.

| Symbol | Description | Value |
|---|---|---|
| $\beta$ | transmission probability per partnership: men $\rightarrow$ women, women $\rightarrow$ men | [0.1 0.05] |
| $\epsilon$ | mixing parameter where: 1 $\rightarrow$ proportional and 0 $\rightarrow$ assortative [5] | 1.0 |
| $\tau$ | rate of treatment initiation among infected | 0.1 |
| $N_0$ | initial population size | 1000 |
| $\hat{\boldsymbol{x}}$ | proportion of system individuals: high, medium, low activity | [0.04 0.20 0.76] |
| $\hat{\boldsymbol{e}}$ | proportion of entering individuals: high, medium, low activity | [0.04 0.20 0.76] |
| $\boldsymbol{\delta}$ | average duration spent in: high, medium, and low activity groups | [5 15 25] |
| $C$ | rate of partner change among individuals: high, medium, low activity | [25 5 1] |
| $\nu$ | rate of population entry | 0.05 |
| $\mu$ | rate of population exit | 0.03 |

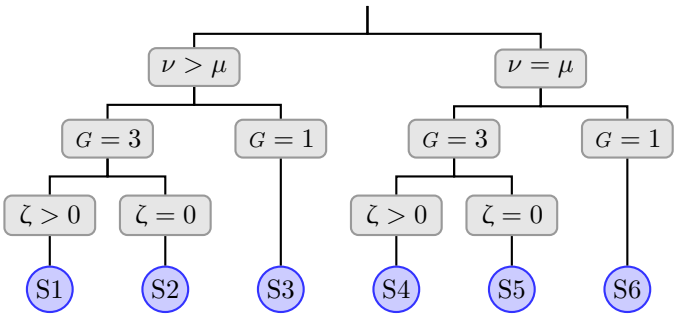


Figure 3: Summary of 6 structural model variants with respect to simulated risk group dynamics. $\nu$: rate of population entry, $\mu$: rate of population exit, $G$: number of risk groups, $\zeta$: rates of population turnover

Table 3: Model parameters for structural variants. All rates have units year$^{-1}$ and durations are in years.

| Parameter | S1 | S2 | S3 | S4 | S5 | S6 |
|---|---|---|---|---|---|---|
| $\hat{\boldsymbol{x}}$ | [0.04 0.20 0.76] | [0.04 0.20 0.76] | [1.0] | [0.04 0.20 0.76] | [0.04 0.20 0.76] | [1.0] |
| $\hat{\boldsymbol{e}}$ | [0.04 0.20 0.76] | [0.04 0.20 0.76] | [1.0] | [0.04 0.20 0.76] | [0.04 0.20 0.76] | [1.0] |
| $C$ | [25 5 1] | [25 5 1] | [2.76] | [25 5 1] | [25 5 1] | [2.76] |
| $\delta$ | [5 15 25] | [33 33 33] | [33] | [5 15 25] | [33 33 33] | [33] |
| $\zeta_{HL}$ | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 |
| $\nu$ | 0.05 | 0.05 | 0.05 | 0.03 | 0.03 | 0.03 |
| $\mu$ | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |

## 3.2 Structural Variants

Drawing on the most common assumptions outlined in Box 1, we define a series of six structural model variants for investigation. These variants, summarized in Figure 3, include zero versus nonzero population growth, homogeneous versus heterogeneous risk ($G = 1$ vs $G = 3$), and zero versus nonzero turnover among risk groups ($\zeta = 0$ vs $\zeta > 0$).

In order to facilitate fair comparisons across model variants with respect to parameter values, we start from the base model described above (S1 in Figure 3), and aim to make simplifications with minimal impact on system characteristics. For example, when moving from $\nu > \mu$ to $\nu = \mu$, we ensure the average duration of individuals in the model $\mu^{-1}$ is unchanged by fixing $\mu$ and reducing $\nu$ to match (S4–S6). Similarly, when collapsing the stratification of risk groups from $G = 3$ to $G = 1$ (S3,S6), we define the homogeneous partner change rate $C$ as the weighted average of the previously risk-stratified $C$. Finally, considering rates of turnover $\zeta$ (which are only applicable for S1,S4) we fully determine the system, as outlined in Section 2.1.2, by specifying the average duration of individuals in each group $\boldsymbol{\delta}$, as well as the distribution of individuals entering the model $\hat{\boldsymbol{e}}$, and the proportion of high activity individuals moving to the low activity group each year $\zeta_{HL}$. The resulting parameter values for each scenario are summarized in Table 3.

## 3.3 Turnover Variants

Table 4: Model parameters for turnover variants. All rates have units year$^{-1}$ and durations are in years.

| Parameter | Z0 | Z1 | Z2 | Z3 | Z4 | Z5 | Z6 |
|---|---|---|---|---|---|---|---|
| $\zeta$: | $\begin{bmatrix} \cdot & 0 & 0 \\ 0 & \cdot & 0 \\ 0 & 0 & \cdot \end{bmatrix}$ | $\begin{bmatrix} \cdot & 0 & * \\ 0 & \cdot & 0 \\ 0 & 0 & \cdot \end{bmatrix}$ | $\begin{bmatrix} \cdot & z_1 & z_1 \\ 0 & \cdot & 0 \\ 0 & 0 & \cdot \end{bmatrix}$ | $\begin{bmatrix} \cdot & z_1 & z_1 \\ 0 & \cdot & * \\ 0 & 0 & \cdot \end{bmatrix}$ | $\begin{bmatrix} \cdot & z_1 & z_1 \\ 0 & \cdot & * \\ * & 0 & \cdot \end{bmatrix}$ | $\begin{bmatrix} \cdot & z_1 & z_1 \\ 0 & \cdot & * \\ z_3 & z_3 & \cdot \end{bmatrix}$ | $\begin{bmatrix} \cdot & z_1 & z_1 \\ z_2 & \cdot & z_2 \\ z_3 & z_3 & \cdot \end{bmatrix}$ |
| $\hat{\boldsymbol{e}}$: | $[* \ * \ *]$ | $[* \ * \ *]$ | $[* \ * \ *]$ | $[* \ * \ *]$ | $[* \ * \ *]$ | $[* \ * \ *]$ | $[* \ * \ *]$ |
| $\boldsymbol{\delta}$: | $[* \ * \ *]$ | $[\delta_1 \ * \ *]$ | $[\delta_1 \ * \ *]$ | $[\delta_1 \ \delta_2 \ *]$ | $[\delta_1 \ \delta_2 \ \delta_3]$ | $[\delta_1 \ \delta_2 \ \delta_3]$ | $[\delta_1 \ \delta_2 \ \delta_3]$ |

$z_i$, $e_i$, $\delta_i$: specified values; $(*)$: calculated values; $(\cdot)$ : inconsequential.
$z_1 = 0.085$, $z_2 = 0.0183$, $z_3 = 0.005$; $\delta_1 = 5$, $\delta_2 = 15$, $\delta_3 = 25$.

# 4 References


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# A Example Systems

## A.1 $G = 1$

$$\begin{bmatrix} \nu x_1 \end{bmatrix} = \begin{bmatrix} \nu \end{bmatrix} \begin{bmatrix} e_1 \end{bmatrix} \tag{A.1}$$

## A.2 $G = 2$

$$\begin{bmatrix} \nu x_1 \\ \nu x_2 \\ {\delta_1}^{-1} - \mu \\ {\delta_2}^{-1} - \mu \end{bmatrix} = \begin{bmatrix} \nu & \cdot & -x_1 & x_2 \\ \cdot & \nu & x_1 & -x_2 \\ \cdot & \cdot & 1 & \cdot \\ \cdot & \cdot & \cdot & 1 \end{bmatrix} \begin{bmatrix} e_1 \\ e_2 \\ \zeta_{12} \\ \zeta_{21} \end{bmatrix} \tag{A.2}$$

## A.3 $G = 3$

$$\begin{bmatrix} \nu x_1 \\ \nu x_2 \\ \nu x_3 \\ {\delta_1}^{-1} - \mu \\ {\delta_2}^{-1} - \mu \\ {\delta_3}^{-1} - \mu \end{bmatrix} = \begin{bmatrix} \nu & \cdot & \cdot & -x_1 & -x_1 & x_2 & \cdot & x_3 & \cdot \\ \cdot & \nu & \cdot & x_1 & \cdot & -x_2 & -x_2 & \cdot & x_3 \\ \cdot & \cdot & \nu & \cdot & x_1 & \cdot & x_2 & -x_3 & -x_3 \\ \cdot & \cdot & \cdot & 1 & 1 & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & 1 & 1 & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & 1 & 1 \end{bmatrix} \begin{bmatrix} e_1 \\ e_2 \\ e_3 \\ \zeta_{12} \\ \zeta_{13} \\ \zeta_{21} \\ \zeta_{23} \\ \zeta_{31} \\ \zeta_{32} \end{bmatrix} \tag{A.3}$$