Supplementary Table S1. Elementary reaction probabilities and transition probabilities for the two-state reaction scheme (*RS* 1 in Figure 1C).

Elementary reaction probabilities	Transition probabilities
$\boldsymbol{a} = \dfrac{\boldsymbol{k_{A,i+1}}}{\boldsymbol{k_{A,i+1}} + \boldsymbol{k_{UF,i}}}$	$P(F_i \rightarrow F_{i+1}) = \dfrac{d}{1 - bc}$
$\boldsymbol{b} = \dfrac{\boldsymbol{k_{UF,i}}}{\boldsymbol{k_{A,i+1}} + \boldsymbol{k_{UF,i}}}$	$P(F_i \rightarrow U_{i+1}) = \dfrac{ca}{1 - bc}$
$\boldsymbol{c} = \dfrac{\boldsymbol{k_{FU,i}}}{\boldsymbol{k_{A,i+1}} + \boldsymbol{k_{FU,i}}}$	$P(U_i \rightarrow F_{i+1}) = \dfrac{bd}{1 - bc}$
$\boldsymbol{d} = \dfrac{\boldsymbol{k_{A,i+1}}}{\boldsymbol{k_{A,i+1}} + \boldsymbol{k_{FU,i}}}$	$P(U_i \rightarrow U_{i+1}) = \dfrac{a}{1 - bc}$

Supplementary Table S2. Elementary reaction probabilities and transition probabilities for the on-pathway reaction scheme (*RS* 2 in Figure 1C).

Elementary reaction probabilities	Transition probabilities
$\boldsymbol{a = \frac{k_{A,i+1}}{k_{A,i+1} + k_{UI,i}}}$	$P(F_i \to F_{i+1}) = \frac{k[1 - cb]}{1 - cb - de}$
$\boldsymbol{b = \frac{k_{UI,i}}{k_{A,i+1} + k_{UI,i}}}$	$P(F_i \to U_{i+1}) = \frac{eca}{1 - cb - de}$
$\boldsymbol{c = \frac{k_{IU,i}}{k_{A,i+1} + k_{IU,i} + k_{IF,i}}}$	$P(F_i \to I_{i+1}) = \frac{eh}{1 - cb - de}$
$\boldsymbol{d = \frac{k_{IF,i}}{k_{A,i+1} + k_{IF,i} + k_{IU,i}}}$	$P(U_i \to F_{i+1}) = \frac{bdk}{1 - cb - de}$
$\boldsymbol{e = \frac{k_{FI,i}}{k_{A,i+1} + k_{FI,i}}}$	$P(U_i \to U_{i+1}) = \frac{a(1 - de)}{1 - cb - de}$
$\boldsymbol{h = \frac{k_{A,i+1}}{k_{A,i+1} + k_{IU,i} + k_{IF,i}}}$	$P(U_i \to I_{i+1}) = \frac{bh}{1 - cb - de}$
$\boldsymbol{k = \frac{k_{A,i+1}}{k_{A,i+1} + k_{FI,i}}}$	$P(I_i \to F_{i+1}) = \frac{dk}{1 - cb - de}$
N/A	$P(I_i \to U_{i+1}) = \frac{ca}{1 - cb - de}$
N/A	$P(I_i \to I_{i+1}) = \frac{h}{1 - cb - de}$

Supplementary Methods

Functional forms of the series representing the transition probabilities.

In the Methods Section of the main text we illustrated how to calculate the transition probability $\boldsymbol{P(I_i \rightarrow F_{i+1})}$ for the off-pathway reaction scheme. Here, for the sake of completeness, we show how the other eight transition probabilities can be calculated for that reaction scheme.

$$P(F_i \rightarrow F_{i+1}) = k + edk + ededk + ecbdk + edededk + edecbdk + ecbdedk + ecbcbdk + \cdots \quad \text{[S1]}$$

$$= k + k\sum_{j=0}^{\infty}\sum_{l=0}^{j}\binom{j}{l}[de]^{j+1-l}[cb]^{l} \quad \text{[S2]}$$

$$= \frac{k[1-cb]}{1-cb-de}. \quad \text{[S3]}$$

Eq. S1 represents the contribution of the different pathway probabilities to the total transition probability of the system starting in state F_i and transitioning to state F_{i+1} without first populating states U_{i+1}or I_{i+1}. For example, the system could make this transition in one step, with probability k; it could do it in three steps, with a probability equal to the product edk; and so on up to an infinite number of steps. The functional form of the series in Eq. S1 can be expressed as shown in Eq. S2. The sum of series is finite and equals Eq. S3. The calculations for the other transitions are shown below.

$$P(F_i \rightarrow U_{i+1}) = eh + edeh + ecbh + ededeh + edecbh + ecbcbh + ecbdeh + \cdots$$
$$= eh + eh\sum_{j=1}^{\infty}\sum_{l=0}^{j}\binom{j}{l}[de]^{j-l}[cb]^{l}$$
$$= \frac{eh}{1-cb-de}. \quad \text{[S4]}$$

$$P(F_i \rightarrow I_{i+1}) = eca + edeca + ecbca + ededeca + edecbca + ecbdeca + ecbcbca + \cdots$$
$$= eca + eca\sum_{j=1}^{\infty}\sum_{l=0}^{j}\binom{j}{l}[de]^{j-l}[cb]^{l}$$
$$= \frac{eca}{1-cb-de} \quad \text{[S5]}$$

$$P(U_i \rightarrow F_{i+1}) = dk + dedk + cbdk + dededk + decbdk + cbdedk + cbcbdk + \cdots$$
$$= dk + dk\sum_{j=1}^{\infty}\sum_{l=0}^{j}\binom{j}{l}[de]^{j-l}[cb]^{l}$$
$$= \frac{dk}{1-cb-de} \quad \text{[S6]}$$

$$P(U_i \rightarrow U_{i+1}) = h + cbh + deh + cbcbh + cbdeh + dedeh + decbh + \cdots$$
$$= h + h\sum_{j=1}^{\infty}\sum_{l=0}^{j}\binom{j}{l}[cb]^{j-l}[de]^{l}$$
$$= \frac{h}{1-cb-de} \quad \text{[S7]}$$

$$P(U_i \rightarrow I_{i+1}) = ca + cbca + deca + cbcbca + cbdeca + dedeca + decbca + \cdots$$
$$= ca + ca\sum_{j=1}^{\infty}\sum_{l=0}^{j}\binom{j}{l}[cb]^{j-l}[de]^{l}$$

$$= \frac{ca}{1-cb-de} \quad [S8]$$

$$P(I_i \rightarrow U_{i+1}) = bh + bcbh + bdeh + bcbcbh + bcbdeh + bdecbh + bdedeh + \cdots$$
$$= bh + bh\sum_{j=1}^{\infty}\sum_{l=0}^{j}\binom{j}{l}[de]^{j-l}[cb]^{l}$$
$$= \frac{bh}{1-cb-de} \quad [S9]$$

$$P(I_i \rightarrow I_{i+1}) = a + bca + bdeca + bcbca + bcbcbca + bcbdeca + bdecbca + bdedeca + \cdots$$
$$= a + a\sum_{j=0}^{\infty}\sum_{l=0}^{j}\binom{j}{l}[bc]^{j+1-l}[de]^{l}$$
$$= \frac{a[1-de]}{1-cb-de} \quad [S10]$$

In the same fashion the transition probabilities for reaction schemes 1 and 2 can also be calculated (Tables S1 and S2).

Derivation of Equation 5 in the main text.

From Eq. 4 in the main text we have that

$$P_{F,i} = P_{F,i-1}P(F_i \rightarrow F_{i+1}) + P_{I,i-1}P(I_i \rightarrow F_{i+1}) + P_{U,i-1}P(U_i \rightarrow F_{i+1}). \quad [S11]$$

Based on the conservation of probability we can write

$$P_{I,i-1} = 1 - P_{F,i-1} - P_{U,i-1}. \quad [S12]$$

Substituting Eq. S12 into S11 we have

$$P_{F,i} = P_{F,i-1}P(F_i \rightarrow F_{i+1}) + P(I_i \rightarrow F_{i+1}) - P_{F,i-1}P(I_i \rightarrow F_{i+1}) - P_{U,i-1}P(I_i \rightarrow F_{i+1})$$
$$+P_{U,i-1}P(U_i \rightarrow F_{i+1}). \quad [S13]$$

Eq. S13 can be rearranged and written as

$$P_{F,i} = P_{F,i-1}[P(F_i \rightarrow F_{i+1}) - P(I_i \rightarrow F_{i+1})] + P_{U,i-1}[P(U_i \rightarrow F_{i+1}) - P(I_i \rightarrow F_{i+1})]$$
$$+P(I_i \rightarrow F_{i+1}). \quad [S14]$$

To make the notation more compact let $A_i \equiv P(F_i \rightarrow F_{i+1}) - P(I_i \rightarrow F_{i+1})$; $B_i \equiv P(U_i \rightarrow F_{i+1}) - P(I_i \rightarrow F_{i+1})$; and $C_i \equiv P(I_i \rightarrow F_{i+1})$. Substituting these definitions into Eq. S14 we have

$$P_{F,i} = P_{F,i-1}A_i + P_{U,i-1}B_i + C_i \quad [S15]$$

To find the recursive relationship expressed by Eq. 5 of the main text we write down Eq. S15 for the specific cases of $i = 1, 2$ and 3:

$$P_{F,1} = P_{F,0}A_1 + P_{U,0}B_1 + C_1, \quad [S16]$$

$$P_{F,2} = P_{F,1}A_2 + P_{U,1}B_2 + C_2, \quad [S17]$$

$$P_{F,3} = P_{F,2}A_3 + P_{U,2}B_3 + C_3. \quad [S18]$$

The initial conditions at nascent chain length $i = 1$ are $P_{F,0} = 0$, $P_{I,0} = 0$ and $P_{U,0} = 1$, therefore Eq. S16 equals

$$P_{F,1} = B_1 + C_1. \quad [S19]$$

Substituting Eq. S19 into S17, and S17 into S18 we have, for $P_{F,3}$

$$P_{F,3} = B_1A_2A_3 + C_1A_2A_3 + P_{U,1}B_2A_3 + C_2A_3 + P_{U,2}B_3 + C_3 \quad [S20]$$

The recursive pattern in the series written in Eq. S20 can be expressed, for a nascent chain containing i residues, as

$$P_{F,i} = \sum_{j=0}^{i-1} P_{U,j}B_{j+1}\prod_{l=j+2}^{i} A_l + \sum_{j=1}^{i} C_j \prod_{l=j+1}^{i} A_l \quad [S21]$$

where we define $A_{l>i} \equiv 1$. Substituting the definitions of A_j, B_j, and C_j in terms of the transition probabilities into Eq. S21 yields Eq. 5 of the main text.