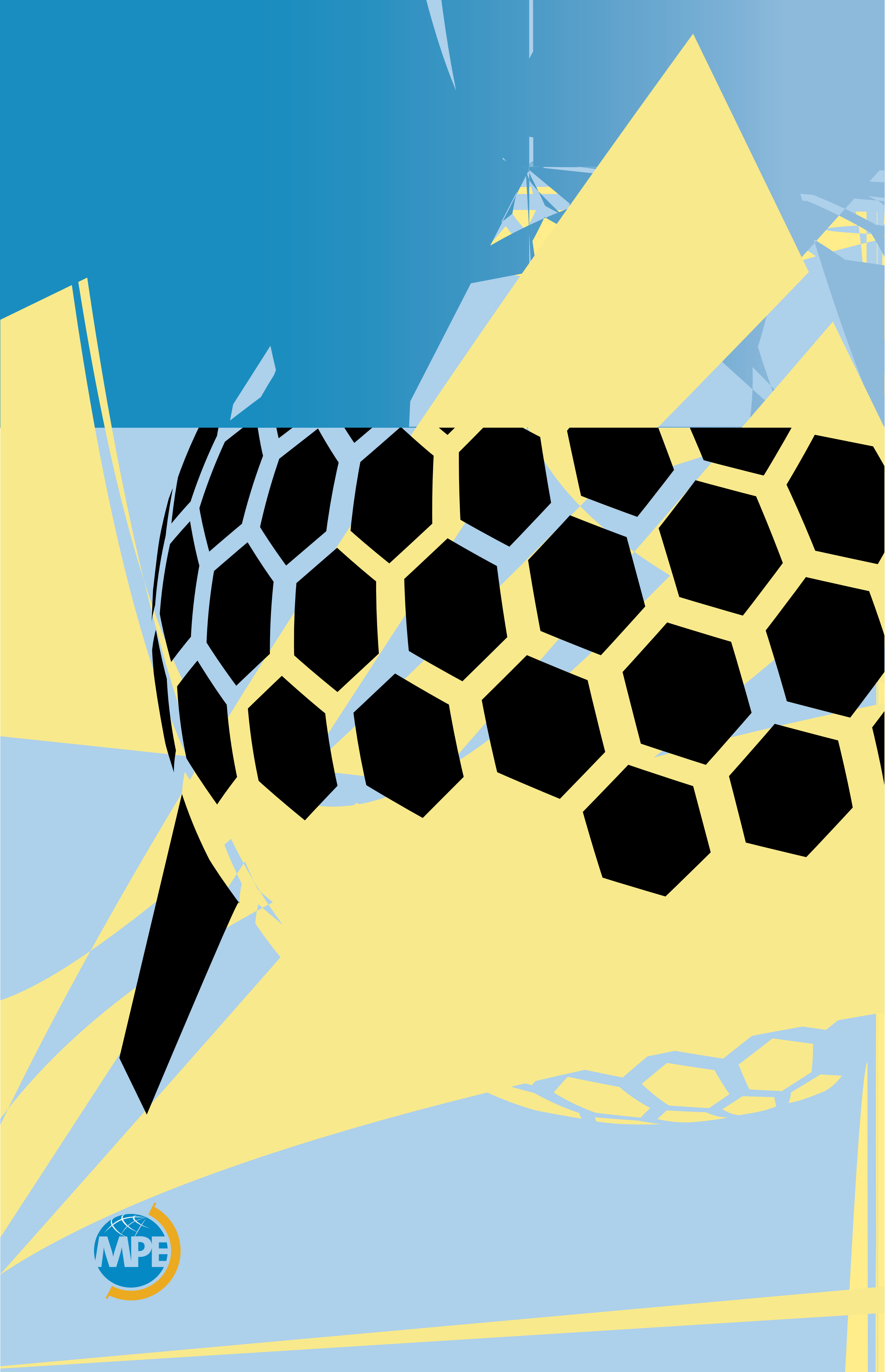
MPE

Chapter 6
Stochastic Population Kinetics and Its Underlying Mathematicothermodynamics

Hong Qian

Abstract Ba ed d ffe e a ca , ca ca ec a c e e e a a d e f fea e e a e a d e e e . C e de eo e eac f c a a ge be f e a deg ee f feed e f a , e ec , e c.; e be a f e e a ge b eo e e a e f e c e a e f da f c e ca e c e e a ba ed c a c a e a c . S c a c a e c a e e fi a d e ea c e e e a f e b g ca d. T c a e d ce e a e a ca de g a d g a d e e e ce f a dde e d a c c e da g a c a c ea e c de f a - a b g ca e . T e a e a c e d a c e e ed e age e a a f J. W. G bb c e ca e d a c f e b c e ca eac e , a e e ge e a e .

6.1 Introduction

F a Jac b (1920 2013), e f e ead g eo a b g . f e e e ce , a ed b T e P be a d e Ac a [13] a We e a ad ad ca c a ged ce e Re g a ce f b g e e e e ea d. O e ca fac e e e a ed a e a c a a c a ge f e f e e a e . T e a e g a f a e a ca ce ce a a e e e e e ea d e f a e a c .

C e e e a a c a be ee e a e a ca de , e e , c a d b g . W e e a e Ne e a f a a e T de e a c d , e d e a e c a e e f c fide ce f e a e a ca de b g .

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I Ne a ec a c , e a a d e e e ed b a e a d de d bed b e e e . Eac a , e.g., a Ne a a c e, a a e a d e c . T e a a d acc d g c e , e d, c f de ca ec e ade f a . W e eac d d a ec e a c c a c , e.g., a ec a d d a [4] d e e a c , a e ec e f a ca a e a e e e (b), deg ada (dea), a a d ffi (g a), a e a (c a ac e c g), a d d ac . S c a f a eac e c e a a e V, c a b c e ca eac e c a ge ce , ca be g ea ed d f a ege - a ed, c - e Ma ce de d b g ea be a , c g e ec e a d e eac , e a a e.

P a d a c b g a g bee de d bed d f ea d ffe e a e a [17]. Ma f e e a a e e a ab a e e c e a f c e ca eac . I c a d , e a d ce a g fa e a e a f a e e e d f e e a a g e a d e P ce . We a a e e f d ffe e a e a f a d a c a a a e a ca f da e e f bab a d Ma ce e .

Af d c g e c a c a e a ca e e e a f a e c , e Sec . 6.9 f e c a d, e e e a ece d c ed d a a e a ca c e a e a Ma a e c . T c e a a e a ab e e e b a ce e e f d d a c , fi de e ed e e ee ce b c . dea g ea e c a c f a a d ec e . T d g e a e a ca c e e c a c a e c f e b ec fi c , e c ed e d , c e a a ca d ce c a c ed e , e -d e e , e d c , fee e d g d a , e c. We a d e a : T e fi c c ed e ba a ce f a fee e d g e fi c , a d e ec d c c d ed c d a c ed a c .

F a , a e a c , c f a a a b c e , a d e c c g ce b g a e a ea e e a ca e a ed - ab a d add e- de b fi ca e f e → ∞ a d e e V → ∞ [12, 26].

6.2 Probability and Stochastic Processes: A New Language for Population Dynamics

T e a e fi da e a e f a e a ca de g: (a) e e e g ce fic da a d f a e a ca f a e a a d (b) de d b g a e be a (a a e g e ed, ca b g ca , e ec c, c e ca , ec ca , ç a , …) ba ed e g, e ab ed f a a d e a . F ac f be g , e a ca e f a d e a . N e, acc d g Ka P (1902 1994) a d f ç e ce, e eg a e ç e fic ac fa f g a e : a e e fi f a e a e , c e e g f a e da a (e.g., ca e) a d e e g a ec a (e.g., de g); a d (b) de e g ed c fi a e , c a f f g ca , a e a ca , ded c .

Le e a ead d ed, de ed a f e c a b e be ca . I C a . 1 H e a d Le d ced e g a e g a g ce : f a a g e 100 da , e e a e e e 50 da , a d a f a e 25 da . I fac , e g a e .

$$= \lim_{\Delta \to 0} \frac{P(+ \Delta) - P( )}{\Delta}.$$

I a a e a e (fl) e f e a c ce f Ne ca ! B d e a e e e a f a g ? A a f f a , e e f a ? C ea e ca be e e e Δ a : *population change* ca a e ege be .

Sec d, a a e e ee c a eg a a g e ac e fi 100 da , a d a e e 100 da ? I a e e f a a a a age .

I deed, *discreteness* a d *probability* a e fi da e a e a a- d a c . B a e bee g ed e d ffe e a e a -ba ed de f a d a c . We a a d g a e c a e be . M f e a a a e a e fi [1, 19, 20, 22, 23, 28, 31].

A a g a c ea a e a a bab de fi c (df) ( ):

$$\int_{-\infty}^{\infty} ( )\mathrm{d} = 1, \quad ( ) \geq 0. \tag{6.1}$$

T e ea g f e ( ) : f fi e a d , e bab f b g $\in (, + \mathrm{d}]$, $( )\mathrm{d}$:

$$\Pr\{ < \leq + \mathrm{d} \} = ( )\mathrm{d} . \tag{6.2}$$

T e , e α a e babi d b f . defi ed a

$$F\;(\;)=\mathrm{P}\{\;\le\;\}=\int_{-\infty}\;(\;)\mathrm{d}\;,\;\mathrm{a\ d}\;(\;)=\frac{\mathrm{d}F\;(\;)}{\mathrm{d}}. \tag{6.3}$$

T e ea (e ec ed a e) a d a a ce f e a d a ab e e a e

$$\langle\;\rangle=\mathbb{E}[\;]=\int_{-\infty}^{\infty}\;(\;)\mathrm{d}\;, \tag{6.4}$$

$$\mathrm{Va}[\;]=\mathbb{E}\big[(\;-\;)^2\big]=\int_{-\infty}^{\infty}\big(\;-\;\big)^2\;(\;)\mathrm{d}\;, \tag{6.5}$$

c e a e de ed $\mathbb{E}[\;]$ b . T a e a e f a d a ab e a g ea a e a e e e a a d a , a ca ed Ga a . T e f a e a da d f

$$(\;)=\lambda\;^{-\lambda}\;,\quad\ge 0,\;\lambda>0, \tag{6.6}$$

ea a d a a ce be g λ^{-1} a d λ^{-2}; e a a a a da d f

$$(\;)=\frac{1}{\sqrt{2\pi}\sigma}\;^{-(\;-\;)^2/2\sigma^2}, \tag{6.7}$$

ea a d a a ce σ^2.

Ga a a d b de d α ed; c d g a e [11]. I de d a a c e e ce f e *central limit theorem*. I a a ca a e g g a a ge c ec f de ca , de e de a . I e f g ec , e a a f d a ca ce e g a , e a c e , b e a f e a a ca a : e e a d b ed e be ee a e e e . I c a c de g f a d a c , e a f α e a d be f d d a a a a α a e; a e e a d e f e e e e a c a ge e be f d d a b e.

T e be d e e, ega - a ed a d a ab e a e Be , b - a , P , a d ge e c [30].

Le e e e d ffe e a e a

$$\frac{\mathrm{d}}{\mathrm{d}}=-\lambda\;, \tag{6.8}$$

e $\lambda > 0$. T e a a bee d ced a a a e a ca de f e e a g ac f a ad ac e a a a e

$$\frac{(\ )}{(0)} = {}^{-\lambda}\ . \tag{6.9}$$

If a e a c c e *identical and independent,* e

$$\Pr\{a\ c\ e\ \ e\ a\ g\ ad\ ac\ e\ a\ \ e\ \} = {}^{-\lambda}\ . \tag{6.10}$$

H e f T e a d e a c e e e f ad ac e deca c ,
e

$$\Pr\{a\ c\ e\ \ e\ a\ g\ ad\ ac\ e\ a\ \ e\ \} = \Pr\{T \geq \ \}. \tag{6.11}$$

T a - ega e ea - a ed a d a ab e a e bab d b $F_T(\ ) = \Pr\{T \leq \ \} = 1 - {}^{-\lambda}$ a d bab de fi c $f_T(\ ) = \mathrm{d}F(\ )/\mathrm{d}\ = \lambda\ {}^{-\lambda}$.

W a e f be , e ec e ce a d ec a , g e e e e a d b ed a g e? W a ? A g d d a d g f e e e de e eade a dee d - a d g f e a e a ca f da f a d a c , a e ge a ca a f ee g a d be a f a a ge a f d d a [15].

6.2.2.1 Rare Event

Le T be e a d e a c a ca a e e c . If e c e ce f c a e e de e de e a [1, 2] a d [2, 3], a d c ce f e (e.g., e e a d e e a e a a), e

$$\Pr\ b.\ f\ \ e\ e\ \ c\ \ g\ \ [0,\ \ + \Delta\ ] = \tag{6.12}$$

$$\Pr\ b.\ f\ \ e\ e\ \ c\ \ g\ \ [0,\ \ ] \times \Pr\ b.\ f\ \ e\ e\ \ c\ \ g\ \ [\ ,\ \ + \Delta\ ].$$

T a ,

$$\Pr\{T > \ + \Delta\ \} = \Pr\{T > \ \} \times \Pr\ b.\ f\ \ e\ e\ \ c\ \ g\ \ [\ ,\ \ + \Delta\ ].$$

N f e bab f e c e e c g e e a [, + Δ]. a Δ , a d e bab f e a e e e $\propto (\Delta\ )$, e

$$\Pr\{T > \ + \Delta\ \} = \Pr\{T > \ \} \times \Big(1 - \lambda\Delta\ + (\Delta\ )\Big). \tag{6.13}$$

T e ,

$$\frac{d}{d} P\{T > \} = -\lambda P\{T > \}, \implies F_T( ) = \, ^{-\lambda} . \quad (6.14)$$

E a e: T e a g e f e fi e c g a e e g a eg a da .

6.2.2.2 Memoryless

O e f e a , fac defi g, e fe e a d b ed a g e .

$$\frac{P\{T \geq \ + \tau\}}{P\{T \geq \ \}} = \frac{ ^{-\lambda(+\tau)}}{ ^{-\lambda}} = \, ^{-\lambda\tau} . \quad (6.15)$$

E a e: Y a d a b d ge e . b e e ea e f a e e a d b ed e e . E e g b a c g e a e a a a , e g a c bee ac e a ea ! M e e g , e e d d a a a , e fa e e e e co . I a e a ca : f a $T \sim \lambda \, ^{-\lambda}$ a d e e de e de d b ed, e $T^* = \ (T_1, T_2, \cdots, T \ )$ a a a e e a d b

$$P\{T^* > \} = P\{T_1 > , \cdots, T > \}$$
$$= P\{T_1 > \} \times P\{T_2 > \} \times \cdots \times P\{T > \} = \, ^{-} , \quad (6.16)$$

e $= \lambda_1 + \lambda_2 + \cdots + \lambda$. T , $f_{T^*}( ) = \ ^{-}$.

6.2.2.3 Minimal Time of a Set of Non-Exponential i.i.d. Random Times

N c d a e f a d e $\{T\}$. T e e *identical, independently distributed* (.d.) a d e df $f_T( )$ a d a e bab d b $F_T( )$. T e $T^* = \ (T_1, T_2, \cdots, T \ )$ a d b

$$P\{T^* > \} = \Big(1 - F_T( )\Big) . \quad (6.17)$$

N , d g ca ed $\hat{T}^* = \ T^*$ a d c d g be a ge, d b .

$$P\{\hat{T}^* > \} = \Big(1 - F_T\Big(-\Big)\Big) \simeq \Big(-\frac{F'_T(0)}{} + O(^{-2})\Big) \to \, ^{-F'_T(0)} . \quad (6.18)$$

T ef e f $F_T'(0) = j_T(0)$ fi e, e b a a e e a d b ed e.
We e e a e a ca c d $j_T(0) > 0$: a a ca , e a e e ca e , ed e ec a f e co e ce f a e e e a de f ag de fa a e e ca e e .

I e e ec , e a e d ed e e e a d b ed a g e ba ed e e e e a a c c g (1) e ge e a d (2) de e de . F e, Sec . 6.2.2.3, e a e a f - e e a T, a g a $j_T(0) \neq 0$, e f a ge c ec f .d. T be e e a . T . a g a g e f e ca e, a a a e e ca e, e e a e (6.8) de a d a c .

6.2.3.1 Khinchin's Theorem

Le c d a e a e g b b . O e b g a a ge b f e g b b , a d e a ea e b b a g de ca de e de d b ed fe e df j ( ). F eac g -b b c e , e a e b b e e d e b . T e e e e ce 0, $T_1, T_2, \cdots, T$, $\cdots$ ca ed a *renewal process*, c $T = \sum_{\ell=1}$ $^{(\ell)}$, e e $^{(\ell)}$ d ff e ℓ a e .d. a d a ab e d a f e d b j ( ). N f e e e e, e a e de ca de e de e e a ce e . T e e e e ce f b b c a g g f a *superposition* f e e e a ce e [3], a a ed E g. 6.1.
F a g e e e a ce e e a e d b j ( ), e c e- d g c g ce , e.g., e b f e e a co ed bef e e , N, a e d b

$$\Pr\{N \geq \} = \Pr\{T \leq \} = F_T(\ ) = \int_0 j_T(\ )d\ . \qquad (6.19)$$

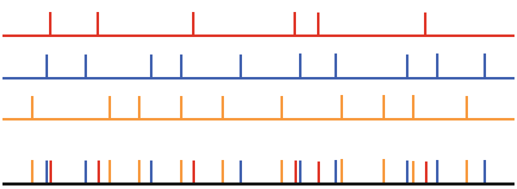

Fig. 6.1 If e ed, a ge, a d b e ce e e e e e e a e e f g b b f 3 d ff e c e , e e f ec b ed ce f a e b b c a ge I e e f e ee d d a ce e . W e a d c e , a a ca a e ge

T eref re,

$$\Pr\left\{N = \right\} = F_{T}() - F_{T\ +1}(). \tag{6.20}$$

N f e a d c a e , a d e T^* be e a g e f e e e e a , T^* a e d a e e e a e . I d b d ffe e f $\jmath$ ( ). I fac , e a

$$\begin{aligned}\Pr\{T^* \le \ \} &= \sum_{\ell=0}^{\infty} \Pr\left\{N = \ell\right\} \Pr\left\{T_{\ell+1} \le \ + \ \right\}\\ &= \sum_{\ell=0}^{\infty} \Big(F_{T_\ell}() - F_{T_{\ell+1}}()\Big) F_{T_{\ell+1}}(+). \end{aligned} \tag{6.21}$$

T eref re, e bab de fi c f e a a T^*

$$\jmath_{T^*}() = \frac{\mathrm{d}}{\mathrm{d}} \Pr\{T^* \le \ \}. \tag{6.22}$$

$D\kappa$

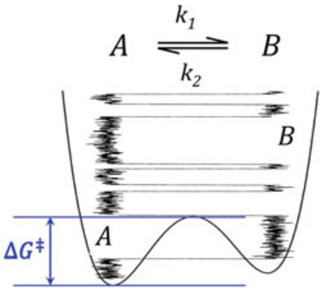

Fig. 6.2 T e a e a ca de d f a c e ca eac f a ge eo e. I a e e ge a ca a f a ge be f d e e, c a c eac $\ 1 \propto\ ^{-\Delta G\ /\ _B T}$

We a e d o ed $\frac{d}{d} = -\lambda$ e λ: ad ac e deca . A d d e ee a a a d o ca be a ed $\frac{d}{d} =$ a e , e a f f a a d a c .

T e a be e b f d: e d ea e b a a e e ! T e a g e f e e b e ec ed be e e a . F e, e a e e ec ed be a e be f d d a e (E e 1.2), a ( ). T ef e, *on average the growth is 1 additional person in* $\left(\ \mathbb{E}[\ \ ]\right)^{-1}$ *time*:

$$\frac{d}{d}\mathbb{E}[\ \ (\ )] = \ \mathbb{E}[\ \ (\ )]. \tag{6.25}$$

Dea a e e , b a e e , a e a a e e . M b g ca d a c ab c g e a , a d ab b g ca e e a ead c a g g a . S c a c e g f e a e e . T J. D. M a a ed [17] a c g de f a ec e a e a e e e a c a e a :

$$\frac{d}{d} = b\ \ - \text{dea}\ \ + \ \text{g a}\ \ , \tag{6.26}$$

e ( ) e a de .

D e e a e c e Ma ce e e e e ca ed a Ma a , Q- ce e , a g fi d ced A e Je e 1954 b *A Distribution Model, Applicable to Economics* a d e b Da d F eed a 1971 b *Markov Chains*. I f e bab f a e a e , ( ), e a

$$(\ +d\ ) - \ (\ ) = \left(\sum_{\ell=1}^{N} \ \ _\ell(\ )\ \ _\ell\right) d\ , \tag{6.27}$$

e $_\ell$ d e a ba f a e ℓ e fi e a e a d . E . (6.27) ca ed a *master equation*. I fi da e a $\mathbf{P}(\ ) = \ ^{\mathbf{Q}}$, e e $\mathbf{Q}$ a a ff-d ag a e e e ≥ 0 a d

$$= -\sum_{\ne} \ . \tag{6.28}$$

T ef e, **Q** a eac a d e f e . I f e efed a fi e a a ae a . I ea a ca e, e

$$\sum_{=1}^{N} \ (\ )$$

de e de f e . T e a bab c ed e . N e e a a d ffe e ce be ee E . (6.26) a d (6.27): T e f a e a f a *density* ( ) e e a a e a f e bab f a *size* ( ) ≡ P{N( ) = }; e g - a d de f f a a ea fi c f e e a ece ea . T e d e f e a ODE e , e c g a e f .

6.2.5.1 Kolmogorov Forward and Backward Equations

I a f , E . (6.27) ca be e e ed a $\frac{d}{d} = \mathbf{Q}$, e = ($_1, \cdots,$ $_N$) a ec . T e a ca ed *Kolmogorov forward equation*. N e c ea g e f a d e a ab e bab d b (a ec), b ab e a bab a (fi da e a) **P**( ) a a e **P**(0) = **I**. M e e g ,

$$\frac{d}{d}\mathbf{P} = \mathbf{PQ} = \left(\ \mathbf{Q} \right) \mathbf{Q} = \mathbf{QP}. \quad (6.29)$$

T a d ffe e d ffe e a e a :

$$\frac{d}{d} = \sum_{\ell=1}^{N} \ \ell \ \ell, \quad (6.30)$$

c ca ed *Kolmogorov backward equation*. If {π } a a a bab d b , e.g., e

$$\sum_{\ell=1}^{N} \pi_\ell \ \ell = 0, \quad = 1, 2, \cdots, N,$$

e e e bac a d e a , ( ) a e a f

$$\sum_{=1}^{N} \ (\ )\pi$$

be g de e de f e , e.g., ac ed a .

T e . ı e K g f a d a d bac a d e ı a . a . a e a e a e . Le ( ) a d ( ) be . ı . a f a d e ı a d ffe e a d b (0) a d (0). T e

$$\frac{d}{d} \sum^{N}_{=1} ( ) \left(\frac{( )}{( )} \right) \leq 0. \qquad (6.31)$$

O e . e a ca e f , c de e c ce f ( ) $= \pi$, f $\pi > 0 \,\forall$.

S a , e ı a K g bac a d e ı a , ( ) a d ( ) d ffe e a c d (0) a d (0), e ec e , a e

$$\frac{d}{d} \sum^{N}_{=1} \left(\pi \quad ( ) \right) \left(\frac{( )}{( )} \right) \leq 0. \qquad (6.32)$$

O e . e a ca e f e c g ( ) $\equiv$ 1. T e ı a E . (6.32) ca ed a *H*-fi c ; e ı a E . (6.31) ca ed e a e e , K bac Le b d e ge ce f a e , ee e g ca c e - . T e e e ı a e a dee ca f e ec d a f d a c .

6.3 Theory of Chemical and Biochemical Reaction Systems

A ge a e e e a f c e c e ca eac . . e .

$$\nu_{1} \quad _1 + \nu_{2} \quad _2 + \cdots \nu \quad \longrightarrow \kappa_{1} \quad _1 + \kappa_{2} \quad _2 + \cdots \kappa \quad . \qquad (6.33)$$

$1 \leq \quad \leq$. T e a e . e e a d eac . ($\nu \quad -\kappa$) a e ca ed *stoichiometric coefficients*, e e a e a . e e . e eac . I a b ade . e . e, a eac . ı . a e f e e . .

Beca . e f e c . a f a ,

$$\frac{d}{d} = \sum_{=1} \left(\kappa \quad - \nu \quad \right) \hat{\varphi} \quad (\mathbf{x}) \qquad (6.34)$$

e e . e c ce a f c e ca . e e. , 1 ≤ ≤ , a d

$$\hat{\varphi}\ (\mathbf{x}) = \ \ {}_{1}^{\nu\ 1}\ {}_{2}^{\nu\ 2} \cdots \ {}^{\nu} \qquad (6.35)$$

. ca ed e . a a e . fl f e eac . $\mathbf{x} = (\ _1,\ _2, \cdots,\ )$. E . (6.34) . ca ed a e e a . , a d E . (6.35) . ca ed *the law of mass action* (LMA).

Le . c de ba . ca e d . d e e, d d a e. e . f e . b e eac . E . (6.33), e a a e. T e DGP a . e. a e . eac co . f g a e e a d . b ed a g e, a e a a e d

$$\varphi\ (\mathbf{X}) = \ \ V \prod_{\ell=1} \left(\frac{\ \ell!}{(\ \ \ell - \nu\ \ell)!V^{\nu\ \ell}} \right), \qquad (6.36)$$

e e eo a . be . f c e ca . e e. be g . N e $\varphi\ (\mathbf{X})$ a . e d e f [e]$^{-1}$. C ea 1 e

$$= \int^{\infty} \lambda \quad ^{-\lambda} \quad \prod_{\ell=1,\ell\neq} \left(\int^{\infty} \lambda_{\ell} \quad ^{-\lambda_\ell \ell} \mathrm{d} \ell \right)$$

$$= \left(\frac{\lambda}{\lambda_1 + \cdots + \lambda} \right) \quad ^{-(\lambda_1+\cdots+\lambda \;)} . \qquad (6.39)$$

T ea e f g a fac : e a e a g $\{T \}$ g e a d ab e : $T^* \equiv$ $\{T \}$ a d $^* \equiv$ a g $\{T \}$; e a e T^* a d e de * a e a ca de e de .

6.3.3.1 Poisson Process

A a da d P ce ( ) a ega - a ed, c - e Ma ce d b

$$\mathrm{P}\left\{ \; (\;) = \; \right\} = \frac{}{!} \; ^{-} . \qquad (6.40)$$

A P ce a b a *point process* e e e a , $T_1, T_2, \cdots, T$, a d a *counting process* e e e a ( ). T e f a a e ea - a ed, d e e- e Ma ce de e de e e , a d $T_{+1} - T$ e e a d b ed a e 1.

6.3.3.2 Random Time Changed Poisson Representation

I f P ce e , e c a c a ec f a DGP e e e g e ega b f e ea e a e ,

$$(\;) = \quad (0) + \sum_{=1} \left(\kappa \quad - \nu \; \right) \quad \left(\int_0 \varphi \; \left(\mathbf{X}(\;) \right) \mathrm{d} \; \right) \qquad (6.41)$$

c φ (**X**) g e (6.36). We a e ab ed e a a b e b f a e f ea e, a E . (6.33), a d b e eac e . We ee a e f $\mathbf{X} \to \infty$ a d $V \to \infty$,

$$\varphi \; (\mathbf{X}) \to \quad V \prod_{\ell=1} \left(\frac{\ell}{V} \right)^{\nu \; \ell} = \quad V \prod_{\ell=1} \; {}_{\ell}^{\nu \; \ell} = V \hat{\varphi} \; (\mathbf{x}). \qquad (6.42)$$

φ (**X**) a ca ed e *propensity* f e eac .

6.3.4.1 One-Dimensional System

C de e c a c a e c f a g e ece . Le ( ) be e bab f a g d d a e a a e . T e ( ) a fie e a e e a

$$\frac{\mathrm{d} \quad (\ )}{\mathrm{d}} = \quad {}_{-1} \quad {}_{-1} - \quad (\quad + \quad) + \quad {}_{+1} \quad {}_{+1}, \tag{6.43}$$

c a d a e e b a e a d dea a e f e a e ac d d a . T e a a d b E . (6.43) ca be b a ed:

$$\frac{}{\ {}_{-1}} = \frac{\ {}_{-1}}{}. \tag{6.44}$$

T e ef e,

$$= \ {}_{0} \prod_{=1} \left(\frac{\ {}_{-1}}{} \right), \tag{6.45}$$

c $_{0}$ be de ed b a a .
E . (6.43) e DGP c e d g e ea a d a c f a g e ece b a d dea a e ˆ( ) a d ˆ( ), ( ) ≡ $\frac{(\ )}{V}$,

$$\frac{\mathrm{d}}{\mathrm{d}} = \hat{}(\ ) - \hat{}(\ ), \tag{6.46}$$

e,

$$\hat{}(\ ) = \ {}_{V\to\infty} \frac{\ V}{V}, \quad \hat{}(\ ) = \ {}_{V\to\infty}$$

V

C de a a b a x = (1, 2, ··· ,), a ≥ 0. I e ab e ce f g a f ede e e ca a g a e = − , e

$$\frac{d}{d} = . \quad (6.48)$$

F c , e a a e a b e ca ab a e a d dea a e a e c a . T e e e ca a g a e f e e e a , c a e ea e ca a g a e,

$$- = \frac{\sum_{=1} \frac{d}{d}}{\sum_{=1}} = \frac{\sum_{=1}}{\sum_{=1}}, \quad \geq 0. \quad (6.49)$$

T e ,

$$\frac{d^{-}(\mathbf{x})}{d} = \left[\frac{\sum_{=1} {}^2}{\sum_{=1}} - \left(\frac{\sum_{=1}}{\sum_{=1}} \right)^2 \right]. \quad (6.50)$$

We e a e e de [···] e g - a d de e ega e:

$$\frac{\sum_{=1} {}^2}{\sum_{=1}} - \left(\frac{\sum_{=1}}{\sum_{=1}} \right)^2 = \frac{\sum_{=1} \left(- ^{-} \right)^2}{\sum_{=1}} \geq 0. \quad (6.51)$$

I fac e ac e a ce f a g e ffe e b a . T e ef e, a a e f e e a e a a a g . T a e a ca e a a f e dea f b Ada S , ec c , a d C a e Da , e a a e ec . I fac , e [···] E . (6.50) a bee de fied b R. A. F e , e B a c a d e a b g , a e g f fi e . d e a a e ec [6]. He e a e f S *magnum opus* A I e Na e a d Ca e f e Wea f Na (1776):

> A e d d a , e f e, e dea a c a e ca b e ca a e f d e c d , a d d ec a d a d ce a be f e g ea e a e; e d d a ece a ab e de e a a e e e f e ce a g ea a e ca . He ge e a deed, e e d e e b c de , c e g . B efe g e f d e c a f f e g d , e e d eo ; a d b d ec g a d c a a e a d ce a be f e g ea e a e, e d ga , a d e , a a e ea e , ed b a be a d e a e d c a a f e . N a a e e f e ce a a a f . B g e e f e e e a f e ce e effec a a e e ea e d e . I a e e c g d d e b e affec ed ade f e b c g d . I a affec a deed, c a g e c a , a d e fe d eed be e ed d ad g e f .

6.5 Ecological Dynamics and Nonlinear Chemical Reactions: Two Examples

Le ( ) be e a de f a eda a e a d ( ) be e a de f a e a e a e e. T e e e eda - e d a c [17]

$$\begin{cases} \frac{d}{d} = \alpha \quad - \beta \quad , \\ \frac{d}{d} = -\gamma \quad + \delta \quad . \end{cases} \tag{6.52}$$

T e de a ed a a f e ea d a c ca be f d a e b a e a ca b g d ffe e a e a [17].

Le c de e f g c e ca eac e :

$$A + \quad \xrightarrow{1} 2 \quad , \quad + \quad \xrightarrow{2} 2 \quad , \quad \xrightarrow{3} B. \tag{6.53}$$

T e acc d g e LMA, e c ce a f a d , fi ed c ce a- f A a d B be g a d :

$$\frac{d}{d} = \ _1 \quad - \ _2 \quad , \quad \frac{d}{d} = - \ _3 \quad + \ _2 \quad . \tag{6.54}$$

T ef e, e ee a d a c f a ec g ca eda - e e e a - ab e a a f a c e ca eac e a ca a [16]: e fi eac (6.53) e e a e g g a a ca a f e eac $A \rightarrow$. A e e a a ea e b de f a c e ca eac ca ed a *catalyst*.

Le c de a de d ed ec g ca d a c c e- [17]:

$$\begin{cases} \frac{dN_1}{d} = \ _1 N_1 - \ _1 N_1^2 - \ _{21} N_1 N_2, \\ \frac{dN_2}{d} = \ _2 N_2 - \ _2 N_2^2 - \ _{12} N_2 N_1. \end{cases} \tag{6.55}$$

Ca e de g a . . e f c e ca eac . a e d. a de ca . . e f d ffe e a e a ? W . . f ge e a , e . a. e a $_{12} > _{21}$.

$$A + \xrightarrow{1} 2 , + \xrightarrow{2} B, A + \xrightarrow{3} 2 ,$$
$$+ \xrightarrow{4} B, + \xrightarrow{5} B, + \xrightarrow{6} + B, \tag{6.56}$$

c , acc d g e LMA,

$$\begin{cases} \frac{d}{d} = (_1) - _2 {}^2 - _5 , \\ \frac{d}{d} = (_3) - _4 {}^2 - (_5 + _6) . \end{cases} \tag{6.57}$$

If e de f , N_1, N_2, a d

$$(_1) \leftrightarrow _1, _2 \leftrightarrow _1, _5 \leftrightarrow _{21}, (_3) \leftrightarrow _2, _4 \leftrightarrow _2, (_5 + _6) \leftrightarrow _{12},$$

e (6.57) e . a e a. (6.55). N e a e a eac , $+ \rightarrow + B$. d ced e e. e $_{12} > _{21}$.

A c . e . ec f e . e f c e ca eac . (6.56) d ca e. a e . e a eac . $2A \rightarrow B$. S ce eac a d e. e eac e. e b e, e ca be c e ca e b . Ra e, e . e e e a eac e. a *nonequilibrium steady state* c e . a c . , . e a c e ca fl c . e g $2A$ B.

We d g . e . e. e -de . Le . c de a c e c e ca eac . . e ,

$$A + \xrightarrow{1} 2 , + \xrightarrow{2} B. \tag{6.58}$$

I . ea . ee a e ODE acc d g e LMA,

$$\frac{d}{d} = \left(1 - \frac{}{K}\right) , = _1 , K = \frac{}{_2}, \tag{6.59}$$

. e ce eb a ed *logistic equation* a d a c. . I e ec g ca c e , . a. e e ca a g a e e ab. e ce f a-. ec e. c e ; a d K . a. *carrying capacity*.

c de ed b e a c c e f a e e, e.g., a e g . $_B$ B a c a , a d T e a e Ke . T e e G bb ee e g f e f (6.62) e f e c e ca e a

$$G = \sum_{=1} \nu \left(\quad + \ _B T \quad \right). \tag{6.65}$$

W e e eac eac e e b , e a e a c e ca e a be g e a b de :

$$\sum_{=1} \left(\nu - \kappa \right)\left(\quad + \ _B T \quad \right) = 0. \tag{6.66}$$

T e

$$\prod_{=1} \left(\quad \right)^{\nu - \kappa} = \ ^{-\frac{(\nu - \kappa)}{_B T}} = \frac{-}{+}, \tag{6.67}$$

$$\Delta G = \left(\sum_{=1} \kappa \quad \right) - \left(\sum_{=1} \nu \quad \right) = \ _B T \quad \left(\frac{-}{+}\right). \tag{6.68}$$

T a e - f a a ca be f d e c ege c e e b .

F g E . (6.34) a d (6.35), e a e

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}} &= \sum_{=1} \left(\kappa - \nu \right)\left(\hat{\varphi}^{+} - \hat{\varphi}^{-}\right) \\ &= \sum_{=1} \left(\kappa - \nu \right)\hat{\varphi}^{-} \left\{ \mathrm{e} \quad \left[\sum_{\ell=1} \left(\kappa_{\ \ell} - \nu_{\ \ell}\right) \quad \left(\frac{\ell}{\ell}\right) \right] - 1 \right\} \\ &= \sum_{=1} \left(\kappa - \nu \right)\hat{\varphi}^{+} \left\{ 1 - \mathrm{e} \quad \left[\sum_{\ell=1} \left(\nu - \kappa \right) \quad \left(\frac{\ell}{\ell}\right) \right] \right\}. \end{aligned} \tag{6.69}$$

E a (6.69) a e $\ell =$ ℓ, e e $[\cdots] = 0$ a d e e $\{\cdots\} =$ 0 a e , f e e . T e ef e, e e c e a (6.69) c e e c e ca e b acc d g e d a c , e.g., E . (6.66) a d (6.67). I e e g , ece a a b ad c c e c a (6.69) a d e b e d a c Sec . 6.6.1 a e c . e e ce f a c a c e c de d f a eac e [10].

We a e ab e f a a ea c e ca eac a a e V a b f e e , A, B, a d C b f A, B, a d C:

$$A + B \underset{-}{\overset{+}{\rightleftharpoons}} C. \tag{6.70}$$

We e a e $A + C$ a d $B + C$ d c a ge e eac . He ce e ca de e $A + C =$ A a d $B + C =$ B a e a a f A a d B, c d g e C, a e a e. N f e e C a e - ega e ega - a ed a d a ab e de be e c a c c e ca e c , e ea c e ca eac , acc d g DGP a e-d e a b - a d-dea ce , a e-de e de b a d dea a e. $= {}^{+}$ A B a d $= {}_{-}$ C. T e , acc d g E . (6.45), e a e a e b d b $( ) = \Pr\{ \; C = \; \}$:

$$\frac{\;(\;+1)}{\;(\;)} = \frac{{}^{+}(\;A - \;)(\;B - \;)}{{}^{-}(\;+1)V}, \tag{6.71}$$

c $A = \; A(0) + \; C(0)$ a d $B = \; B(0) + \; C(0)$. T e ef e,

$$(\;) = \frac{\Xi^{-1}\; A!\; B!}{!(\;A - \;)!(\;B - \;)!}\left(\frac{+}{-V}\right) \;, \tag{6.72}$$

e Ξ a a fac

$$\Xi(\lambda) = \sum_{=0}^{(\;A,\;B)} \frac{\;A!\; B!\,\lambda}{!(\;A - \;)!(\;B - \;)!}, \quad \lambda = \left(\frac{+}{-V}\right). \tag{6.73}$$

M e a , b g $A + \; B + \; C = \; {}^{0}_{A} + \; {}^{0}_{B} - \; C$,

$$-\quad (\;C)$$

$$= - \left[\frac{\lambda^{\;C}}{C!(\;A - \;C)!(\;B - \;C)!}\right] + c \; .$$

$$= {}_A \left(\frac{A}{V}\right) - {}_A + {}_B \left(\frac{B}{V}\right) - {}_B + {}_C \left(\frac{C}{V}\right) - {}_C - {}_C \left(\frac{+}{-}\right)$$

$$= {}_A \; {}_A + {}_B \; {}_B + {}_C \; {}_C + {}_C \left(\frac{{}_C - {}_A - {}^0_B}{{}_B T}\right) - ({}_A + {}_B + {}_C)$$

$$= \sum_{\sigma=A,B,C} {}_\sigma \left(\frac{\sigma}{{}_B T} + {}_\sigma - 1\right). \qquad (6.74)$$

T . ag ee E . (6.65).

I c a. ca c e ca e c , f a g e $\mathbf{x}( )$, e Idea fi c f e c e ca eac e .

$$G \; [\mathbf{x}( )] = \sum_{\sigma=1} {}_\sigma \left({}_\sigma + {}_B T \; {}_\sigma - {}_B T \right). \qquad (6.75)$$

T e , f g E . (6.34), a g eac a d e. e eac e. e b e a e c a $^+$ a d $^-$,

$$\frac{\mathrm{d}}{\mathrm{d}} G \; [\mathbf{x}( )] = \sum_{=1} \frac{\mathrm{d}}{\mathrm{d}} \left(\; + {}_B T \; \right)$$

$$= {}_B T \sum_{=1} \sum_{=1}$$

a e g c d e d a c . W e a c e ca eac e a a ed ce a d d ffe e c e ca e a , ca eac a c e ca e b . Ra e eac e a *nonequilibrium steady state* (NESS).

Le c de e f g e a e , e Sc g de f b ab [34] a d Sc a e be g de f ea c a [17, 25, 35].

6.6.4.1 Schlögl Model

$$A + 2 \underset{1}{\overset{+}{\rightleftharpoons}} 3 \quad , \quad \underset{2}{\overset{+}{\rightleftharpoons}} B, \tag{6.78}$$

c e c ce a (c e ca e a) f A a d B a e a ed b a e e a age . T eac a *Schlögl model*, e d a c ca be de bed b e d ffe e a e a

$$\frac{\mathrm{d}}{\mathrm{d}} = {}^{+}_{1} {}^{2} - {}^{-}_{1} {}^{3} - {}^{+}_{2} + {}^{-}_{2} = J(\ ), \tag{6.79}$$

c a d- de a . I ca e b b ab a d add e- de b fi ca e e . A f e co de e c , e $_A \neq \ _B$. N e e c e ca e b : $_A = \ _A + \ _B T \quad = \ _B + \ _B T$, a d

$$\left(- \right) = \frac{{}^{+}_{1}\ {}^{+}_{2}}{{}^{-}_{1}\ {}^{-}_{2}}. \tag{6.80}$$

D ffe e a e a (6.79), a a e ${}^{+}_{1}\ {}^{+}_{2} = {}^{-}_{1}\ {}^{-}_{2}$, a e g - a d- de

$$\begin{aligned} J(\ ) &= {}^{+}_{1} {}^{2} - {}^{-}_{1} {}^{3} - {}^{+}_{2} + {}^{-}_{2} \\ &= {}^{+}_{1} {}^{2} - {}^{-}_{1} {}^{3} - {}^{+}_{2} + \frac{{}^{+}_{1}\ {}^{+}_{2}}{{}^{-}_{1}} \\ &= \left({}^{2} + \frac{{}^{+}_{2}}{{}^{-}_{1}} \right) \left({}^{+}_{1} - {}^{-}_{1} \right). \end{aligned} \tag{6.81}$$

T e ef e, e $J(\ )$ a a e fi ed a $= \frac{{}^{+}_{1}}{{}^{-}_{1}}$, e c e ca e b . I ge e a , e (6.78) ca e b c e ca b ab ; b b e e A a d B a e a ffi e a ge c e ca e a d ffe e ce, e.g., *a chemostat*.

M e e e g , e a d a f g (6.80), e DGP f e be f , ( ) aga a e-d e a b -a d-dea ce ,

$$= \frac{{}_1^+ \ (\ -1)}{V} + {}_2^- \ V = \frac{{}_1^+}{V}\left(\ (\ -1) + \frac{{}_2^+ V^2}{{}_1^-}\right), \quad (6.82)$$

$$_{+1} = \frac{{}_1^-(\ +1) \ (\ -1)}{V^2} + {}_2^+(\ +1)$$

$$= \frac{{}_1^-(\ +1)}{V^2}\left(\ (\ -1) + \frac{{}_2^+ V^2}{{}_1^-}\right).$$

T e ef e, e a a d b , acc d g E . (6.45),

$$= C \prod_{\ell=0}^{-1} \frac{{}_1^+ \ /V}{{}_1^-(\ell+1)/V^2} = \frac{\lambda}{!} {}^{-\lambda}, \quad \lambda = \left(\frac{{}_1^+ \ V}{{}_1^-}\right). \quad (6.83)$$

T a P d b , e ec ed a e be g $\mathbb{E}[\ ] = \lambda$. T e ef e, e e ec ed c ce a (${}_1^+ / {}_1^-$).

6.6.4.2 Schnakenberg Model

S a ,

$$A \underset{{}_1^-}{\overset{{}_1^+}{\rightleftharpoons}} \ , \quad B \xrightarrow{\ {}_2\ } \ , \quad 2 \ + \ \xrightarrow{\ {}_3\ } 3 \ , \quad (6.84)$$

a *Schnakenberg model*, e d a c f

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}} = {}_1^+ - {}_1^- - {}_3 \ ^2 = (\ , \ ), \\ \frac{\mathrm{d}}{\mathrm{d}} = {}_2 - {}_3 \ ^2 = (\ , \ ). \end{cases} \quad (6.85)$$

T e ca e b c c e c a a d H f b fi ca . I e f e DGP, e b a a a d ffi . We efe e eade [25, 35] f a -de a a f e de .

6.7 The Law of Large Numbers—Kurtz's Theorem

S a g e a e e a (6.43), e c de a a a d ffe e a e a (PDE) f a c de fi c $J(\ ,\ )\mathrm{d}\ = \ _V(\ )$ e e $= \frac{}{V}$, d $= \frac{1}{V}$, e

$$\frac{\partial J(\ ,\ )}{\partial}= V\frac{\mathrm{d}\ _V(\ )}{\mathrm{d}}$$
$$= \frac{1}{\mathrm{d}}\Big(J(\ -\mathrm{d}\ ,\ )\hat{}(\ -\mathrm{d}\ ) - J(\ ,\ )\big(\hat{}(\ ) + \hat{}(\ )\big)$$
$$+ J(\ +\mathrm{d}\ ,\ )\hat{}(\ +\mathrm{d}\ )\Big)$$
$$= \frac{\partial}{\partial}\Big(J(\ +\mathrm{d}\ /2,\ )\hat{}(\ +\mathrm{d}\ /2) - J(\ -\mathrm{d}\ /2,\ )\hat{}(\ -\mathrm{d}\ /2)\Big)$$
$$\approx \frac{\partial}{\partial}\left\{\frac{\partial}{\partial}\left(\frac{\hat{}(\ )+\hat{}(\ )}{2V}\right)J(\ ,\ ) - \big(\hat{}(\ ) - \hat{}(\ )\big)J(\ ,\ )\right\} + \cdots \tag{6.86}$$

c

$$V^{-1}\ _V\ = \hat{}(\ ),\quad V^{-1}\ _V\ = \hat{}(\ ), \tag{6.87}$$

a $V \to \infty$.

T e ef e e f $V \to \infty$,

$$\frac{\partial J(\ ,\ )}{\partial} = -\frac{\partial}{\partial}\big(\hat{}(\ ) - \hat{}(\ )\big)J(\ ,\ ), \tag{6.88}$$

c c e d e d a d ffe e a e a

$$\frac{\mathrm{d}}{\mathrm{d}} = \hat{}(\ ) - \hat{}(\ ), \tag{6.89}$$

a defi e e c a ac e c e f (6.88).

N c de e ce

$$( ) = \frac{( ) - V\ ( )}{\sqrt{V}}, \tag{6.90}$$

c c ac e e de a f $\frac{( )}{V}$ ( ). I e f $V \to \infty$, df J (,) a fie a ea PDE e- a g c effic e

$$\frac{\partial J\ (,)}{\partial} = \frac{\partial}{\partial}\left\{\frac{\partial}{\partial}\left(\frac{\hat{}(\ ( )) + \hat{}(\ ( ))}{2}\right) J\ (,) - \left(\hat{}'(\ ( )) - \hat{}'(\ ( ))\right) J\ (,)\right\}. \tag{6.91}$$

T ef e, ( ) a c e, ea - a ed, e- ge e Ma ce . N e e PDE (6.91) d ffe e f PDE (6.86). T e a e c a ea e K a M a e a a d a Ka e Ω-e a , e ec e [32]. T e f e a ed e ce a e e .

T ca g e E . (6.86) af e ec d de a a a d b

$$- \ \hat{J}\ ( ) = 2V \int \left(\frac{\hat{}( ) - \hat{}( )}{\hat{}( ) + \hat{}( )}\right) \mathrm{d}\ . \tag{6.92}$$

O e a d, e a g e (6.45),

$$= \ _0 \prod_{=1} \left(\frac{\ _{-1}}{}\right),$$

e f $V \to \infty$ $V^{-1}\ _V = \hat{}( )$, $V^{-1}\ _V = \hat{}( )$, a d $V^{-1} = \mathrm{d}$, e d

$$- \ _V = -\sum_{=1} \left(\frac{\ _{-1}}{}\right) + C \leftrightarrow - \ J\ ( ) = V \int \left(\frac{\hat{}( )}{\hat{}( )}\right) \mathrm{d}\ . \tag{6.93}$$

I be E . (6.92) a d (6.93) a e ac a e a e? We ce a b a e de ca ca e e a:

$$\frac{d}{d}\left(- \quad (\ )\right) = 2V\left(\frac{\hat{}(\ ) - \hat{}(\ )}{\hat{}(\ ) + \hat{}(\ )}\right) = 0 \implies \hat{}(\ ) = \hat{}(\ ). \tag{6.94}$$

I fac , e a a e a a ca e e de ca :

$$\left[\frac{d^2}{d^{\ 2}}\left(- \quad (\ )\right)\right]_{\hat{}=\hat{}} = 2V\left(\frac{\hat{}'(\ ) - \hat{}'(\ )}{\hat{}(\ ) + \hat{}(\ )}\right) = V\left(\frac{\hat{}'(\ ) - \hat{}'(\ )}{\hat{}(\ )}\right)$$

$$= \left[\frac{d^2}{d^{\ 2}}\left(- \quad (\ )\right)\right]_{\hat{}=\hat{}}. \tag{6.95}$$

H e e ca be , a a e a e, a e g ba ca be d ffe e [20, 37]! T e a K a e M a e a a a d a a f c a c e c e ab . C e, ea - a ed Ma ce e a e a ca ed *diffusion processes*. T e ab e e a e a e g ba a d d ffi a a f c a c a e c ge e a .

6.8 The Logic of the Mechanical Theory of Heat and Nonequilibrium Thermodynamics

I de e e e a e ece e Sec . 6.9

T e a g be ee B a e a d e e b d a c . I add e c e a , e de G -Ma a ac a e e e *entropy balance equation* [5],

$$\frac{\mathrm{d}S}{\mathrm{d}} = + J_S, \tag{6.96}$$

a e f fi da e a e e , e e e d c a e a d J_S e a e f e ed a e b d g . T e ec d a f d a c , e.g., C a e a , d c a e a ≥ 0. U f a e , B a ec a ca e f ea ab e d e a e a e (6.96) f a Ha a d a c e g add a a ba ed a *stosszahlansatz*.[1] A e ee f Sec . 6.9, e , Ma d a c ab e de ce a e a e (6.96). A c a c d a c a ac e b d a c ab e fi g c ga , a a fi de a ed b B g a a d Leb 1955 [2].

T ee e d, a g a e e ed e e a a e a a a ca e (e.g., a) a d c e e eed f g (e.g., e a), f e Ne a ec a c c ca be e e e ed a e a ca f a Ha a e

$$\frac{\mathrm{d}}{\mathrm{d}} = \frac{\partial H(\, , \,)}{\partial}, \quad \frac{\mathrm{d}}{\mathrm{d}} = -\frac{\partial H(\, , \,)}{\partial}. \tag{6.97}$$

O e f e a e c ce g e E . (6.97) e d a c a a ce f $H(\,(\,),\,(\,))$:

$$\frac{\mathrm{d}}{\mathrm{d}} H(\,(\,), \,(\,)) = \frac{\partial H}{\partial} \Big($$

N , e a e a e Ha a fi c c a a e e a a a e e , $H(, , V, N)$ e V e b e f a ec a ca e a d N e b f a c e e b , e e e e c a a ed a e a a g a , b e e g c a bee e e e d ed : W a e g- e be a f e e a a fi c f V, N, a d a a e ?

A Ha a e , e e , fi da e a d ffe e f e ea e e e a e d ed, c a e a ac e fi ed ( ). I fac , c ea a e g- e be a a fi c f e a c d $H\big((0), (0)\big) = E$. He a d B a (1884) ea ed a a e d a c e b a e f a ec a ca e *not a single point in the phase space, but rather, it is an entire invariant manifold* defi ed b e e e e $H(, , V, N) = E$. I a B a ge ea e a e ca defi e

$$S\big(E, V, N\big) = {}_B \;\big\{ \text{ a e ec ed b e face } H(,) = E\big\}$$

$$= {}_B \int_{H(,)\le E} \mathrm{d} \;\mathrm{d} \;. \tag{6.99}$$

S ce $S(E)$ c, e a a c fi c $E = E(S, V)$. T e

$$\mathrm{d}E = \left(\frac{\partial E}{\partial S}\right)_{V,N} \mathrm{d}S + \left(\frac{\partial E}{\partial V}\right)_{S,N} \mathrm{d}V + \left(\frac{\partial E}{\partial N}\right)_{S,V} \mathrm{d}N$$

$$= T\mathrm{d}S - \;\mathrm{d}V + \;\mathrm{d}N. \tag{6.100}$$

W a e g fica ce f E . (6.100)? E c e e ba ed e fac a a Ha a e a a *conservation of mechanical energy* H. F e, e e , c e a f e g a d f a g e Ha a e a g e a a , b a e Ha a e e e e e , a d e e a g a e e c a f Ha a e a g V a d N, a d a a e e . I bec e a a a d e a , a *the First Law of Thermodynamics*. N e, acc d g e , d a c a e e T, , a e a e a ca defi ed a E . (6.100). T e a e e ge e e a.

T a d a e ec a ca e a , g fec , a ea e c e g a d ea e a f a a . , e , a e a f c a ca ; a a a e a f B a :

$$\frac{\partial\rho(,)}{\partial} = D\frac{\partial^2\rho(,)}{\partial^2} = -\frac{1}{\eta}\frac{\partial(\hat{F}\rho)}{\partial}, \tag{6.101}$$

e e

$$\hat{F} = -\frac{\partial}{\partial}, \quad \text{a d} \quad = D\eta \quad \rho(,) = {}_B T \quad \rho(,). \tag{6.102}$$

$\hat{F}$ a *entropic force* c e , a d a c e ca e a .

E a (6.100) a d e e e e $H(,) = E$ ed e g e ; a *ergodicity*. I d , e d, e e a a d e e dS a d dV e c a g g. W a a e f e c a ge e ? T e , e *Second Law of Thermodynamics* a e a

$$T\mathrm{d}S \geq \mathrm{d}Q = \mathrm{d}E - \mathrm{d} \quad , \tag{6.103}$$

c dQ e a f ea a fl e e , a d d e a f d e e e . B e a de e de , a d ca ed b e d. E . (6.103) a e C a e a . T e f *entropy production* d ced acc f e e a :

$$\frac{\mathrm{d}S}{\mathrm{d}} = \quad - \frac{}{T}, \quad \geq 0, \tag{6.104}$$

c ca ed e d c , c e ega e. $= -\mathrm{d}Q/\mathrm{d}$ ca ed ea d a . I ge a , e a e de a e. E . (6.104) a a *entropy balance equation*.

6.8.2.1 Local Equilibrium Assumption and Classical Derivation of Entropy Production

If e a e a E . (6.100) a d ca ace a d e, e e a

$$\frac{\partial (,)}{\partial} = \frac{1}{T}\frac{\partial (,)}{\partial} - \sum_{=1} \frac{\partial (,)}{\partial}, \tag{6.105}$$

c e a e a ed c e b d$V = 0$. (,), (,), a d (,) e e de , e g de , a d c ce a f e ec e .

Rea g a b e g a d a c e f c e a ace- e, e a

$$\frac{\partial (,)}{\partial} = -\frac{\partial J (,)}{\partial}, \quad \frac{\partial (,)}{\partial} = -\frac{\partial J (,)}{\partial}. \tag{6.106}$$

T e , b g e e E . (6.105), a d e a c a a f ca , e a e a

$$\frac{\partial (,)}{\partial} = \quad (,) + J_S(,) \tag{6.107a}$$

e e d c a e e

$$(,) = J \frac{\partial}{\partial}\left(\frac{1}{T}\right) - \sum_{=1} J \frac{\partial}{\partial}\left(\frac{}{T}\right) - \sum_{=1} \frac{\Delta \quad \hat{\varphi}}{T}, \tag{6.107b}$$

a d e fl

$$J_S(,) = \frac{\partial}{\partial}\left(\frac{J}{T} - \sum_{=1} \frac{J}{T}\right). \tag{6.107c}$$

Acc d g O age e [18], eac e e d c a

$$\text{a fl} \times \text{d g f ce} \tag{6.108}$$

c d be - ega e. T e e f e b d a c c ce a ce e f a d : d ffi , ea , c a ge, c e - ca , e c. M e f a e a a fl e ca be b a ed, e e g ca , f e g e g.

6.9 Mathematicothermodynamics of Markov Dynamics

We c d d e e- a e Ma e c a c d a c f c e a f bab a e ace , e.g., C a a K g e a , a e a

$$\frac{d \quad ( )}{d} = \sum_{=1}^{N} \left(\quad - \quad \right), \tag{6.109}$$

c a e e fi e a a bab a e g e (6.27).

We a f e a e g c e f B a a ed Sec . 6.8.1, de e a d a c e ba ed e ge a d a c b d c g e f e . E . (6.109) e ace e Ha a e (6.97), a d e ace f B a ce e a ed $S = \ _B \ \Omega(E)$ be e G bb -S a e :

$$S( ) = - \sum_{=1}^{N} ( ) \quad ( ). \tag{6.110}$$

T e , e a

$$\frac{dS}{d} = \quad + J_S, \tag{6.111a}$$

e e

$$( ) = \frac{1}{2} \sum_{,=1}^{N} \Big(( ) - ( ) \Big) \left(\frac{( )}{( )} \right), \quad (6.111b)$$

$$J_S( ) = \frac{1}{2} \sum_{,=1}^{N} \Big(( ) - ( ) \Big) \left(\frac{\;}{\;} \right). \quad (6.111c)$$

I ed a e b a ≥ 0 ce f e a f E . (6.111b), e a e f f (−) (/) ≥ 0. We a e e e e b a ce f (6.111b) E . (6.76).

T e ef e, e a e de ed a e ba a ce e a ba ed Ma d a c , e a f ca e b . E a (6.111b) a d (6.111c) fi g e e c e e , e { ( )}, f e e fl J_S e -ega e e d c . A e a be , e a c e e e b d a c e e c c ca e, a e ace. T e effec e a a e e e a e be g 1.

If e a E . (6.109) a a a d b = 1 ∀ , e

$$\sum_{=1}^{N} \big(\; - \; \big) = \sum_{=1}^{N} \; = 0, \quad \forall \; .$$

I ca e,

$$\frac{dS}{d} = -\sum_{=1}^{N} \left(\frac{d \;( )}{d} \right) = -\sum_{,=1}^{N} \big(\; - \; \big)$$

$$= \sum_{,=1}^{N} \left(\frac{\;}{\;} \right) \geq \sum_{,=1}^{N} \left(\frac{\;}{\;} - 1 \right)$$

$$= \sum_{=1}^{N} \left(\sum_{=1}^{N} \right) = 0. \quad (6.112)$$

We e ef e a e a e e a g a f e a a babi d b f , e e e S -ded ea g fi c f e.

If a Q ce a a a a d b = , a *detailed balance*, e

$$
\begin{aligned}
J_S( ) &= \frac{1}{2} \sum_{,\ =1}^{N} \Big(\ ( ) \ - \ ( ) \ \Big) \Big(- \Big) \\
&= \frac{1}{2} \sum_{,\ =1}^{N} \Big(\ ( ) \ - \ ( ) \ \Big) \Big(- \Big) \\
&= \sum_{,\ =1}^{N} \Big(\ ( ) \ - \ ( ) \ \Big) \qquad = - \sum_{=1}^{N} \frac{\mathrm{d} \ ( )}{\mathrm{d}} \\
&= \frac{\mathrm{d}}{\mathrm{d}} \left(\sum_{=1}^{N} \ ( ) \Big(- \ \Big) \right) = \frac{1}{T} \frac{\mathrm{d}\overline{E}}{\mathrm{d}},
\end{aligned}
\tag{6.113}
$$

c

$$
\overline{E} = \sum_{=1}^{N} \ ( ) E \ , \tag{6.114}
$$

d be de fied a e ea e g , $E = -T$ a e e g f e a e acc d g B a a . T e , E . (6.111a) bec e

$$
\frac{\mathrm{d}}{\mathrm{d}} \left(\frac{\overline{E}}{T} - S \right) = - \quad \leq 0. \tag{6.115}
$$

$F = \overline{E} - TS$ a e fee e g f a d a c e . I e ec ed ca ded ea e e a a e a ac g e b . I a e b ead a e, e fee e g eac e .

F

E c aged b e ab e e , e c de e K bac Le b e d e ge ce, a a e a e e :

$$F(\ )=\sum_{=1}^{N}\ (\ )\Big(-\qquad+\qquad(\ )\Big)=\sum_{=1}^{N}\ (\ )\quad\Big(\frac{(\ )}{\ }\Big)\geq 0. \quad (6.116)$$

O e ca ac a a dF/d $\leq$ 0 f ge e a Q- ce e de a ed ba a ce:

$$\frac{\mathrm{d}F(\ )}{\mathrm{d}}=\sum_{=1}^{N}\Big(\frac{\mathrm{d}\ (\ )}{\mathrm{d}}\Big)\quad\Big(\frac{(\ )}{\ }\Big)=\sum_{,\ =1}^{N}\Big(\qquad-\qquad\Big)\quad\Big(\frac{(\ )}{\ }\Big)$$

$$=\sum_{,\ =1}^{N}\qquad\Big(\frac{(\ )}{(\ )}\Big)\leq\sum_{,\ =1}^{N}\qquad\Big(\frac{(\ )}{(\ )}-1\Big)$$

$$=\sum_{=1}^{N}\frac{\ }{\ }\Big(\sum_{=1}^{N}\Big(\qquad-\qquad\Big)\Big)=0. \quad (6.117)$$

F

M e e g , e a e a e , ba a ce e a f e F( ):

$$\frac{\mathrm{d}F(\ )}{\mathrm{d}}=E\ \ (\ )-\ \ (\ ), \quad (6.118a)$$

e ( ) ≥ 0 g e (6.111b), a d

$$E\ \ (\ )=\frac{1}{2}\sum_{,\ =1}^{N}\Big(\ \ (\ )\ \ -\ \ (\ )\ \ \Big)\quad\Big(\frac{\ }{\ }\Big)\geq 0. \quad (6.118b)$$

See [9] f e f f e a .B E ( ) a d ( ) a e - ega e c ea a E . (6.118a) ca be e e ed a e F( ) a a ce a d a c a ge e a a E ( ), a ce e , a d d a ( ), a e . T e e a e c c c e a f e a F. E a (6.118a) e ea gfi a e E . (6.111a) c J_S d e a e a defi e g .

T e ba a ce E . (6.118a) a d e c f dF/d ≤ 0 a e e a ab e e e b a ce e fi a d e ec d a f e d a c . B e a e ea a a f a a e a ca ci e f a c a c Ma d a c .

T e a e a e a ca a e, e ca a e e. ec ,
c ec e , [9, 10, 21, 24].

T e e dc g e (6.111b) ca be e a

$$= \sum_{\text{a edge}}^{N} \left(\varphi - \varphi\right) \left(\frac{\varphi}{\varphi}\right), \quad (6.119)$$

e φ = ( ) e e- a bab fl a e . I ca be e a a a Q- ce , e ab e e e ca be e e ed a a [14]

$$= \sum_{\text{a c c e } \Gamma}^{N} \left(\varphi_\Gamma^+ - \varphi_\Gamma^-\right) \left(\frac{\varphi_\Gamma^+}{\varphi_\Gamma^-}\right), \quad (6.120)$$

c $\varphi_\Gamma^\pm$ e be f Γ c c e c e ed a e e f d a d bac d d ec . M a , f c c e $\Gamma = (\ _0, \ _1, \cdots, \ , \ _0)$

$$\frac{\varphi_\Gamma^+}{\varphi_\Gamma^-} = \frac{\ _{0\,1}\ \ _{1\,2} \cdots \ _{-1}\ \ _{0}}{\ _{1\,0}\ \ _{2\,1} \cdots \ _{-1}\ \ _{0}}, \quad (6.121)$$

c de e de f e bab e ! T ef e, $\left(\varphi_\Gamma^+/\varphi_\Gamma^-\right)$ ca a d d be de d a e e dc c c e, a d e $\left(\varphi_\Gamma^+ - \varphi_\Gamma^-\right)$ a e a c a c e be f c c e c e ed a g a a ec . A e e b d a c c a ed e (6.121); ab e c c c e [27]. If a Ma ce de ba a ced, e e dc eac a d e e c c c e.

I e ce e f A. N. K g a e a (6.121) e a f eac a d e c c e f a d f e Ma ce de ed ba a ced. T ef e, e a e a ca f *detailed balance* de a fi g de f a -d e e c e e ead a e a e b . F a d e e c e , a ea e f e c c e e a e ace Γ a ba a ced c a : $\varphi_\Gamma^+ \neq \varphi_\Gamma^-$.

F a DGP N ec e a d M eac , e F fi c d ced Sec . 6.9.4 . a fi c a f e bab d b $_V(\mathbf{n},\ )$ c . e f a fi c f e eac e e V. T e e a a a a ad c c a $V \to \infty$ a e K ? I ca be a [10]

$$\frac{F[\ _V(\mathbf{n},\ )]}{V} \underset{V\to\infty}{} = \underset{V\to\infty}{} \frac{1}{V}\sum_{\mathbf{n}} \ _V(\mathbf{n},\ ) \left[\frac{\ _V(\mathbf{n},\ )}{\ _V(\mathbf{n})}\right]$$

$$= - \underset{V\to\infty}{} \frac{1}{V}\sum_{\mathbf{n}} \ _V(\mathbf{n},\ ) \quad _V(\mathbf{n})$$

$$= G\ \left[\mathbf{x}(\ )\right], \tag{6.122}$$

c $\mathbf{n} = (\ _1,\ _2, \cdots,\ _N)$, e bd f ec e f e ec e , $\mathbf{x} = (\ _1, \cdots,\ _N)$ e c e d g bd de $\mathbf{x} = \frac{\mathbf{n}}{V}$. T e K e e Sec . 6.7 a e a e c a c a ec f a DGP, $\mathbf{n}_V(\ )$,

$$\underset{V\to\infty}{} \frac{\mathbf{n}_V(\ )}{V} = \mathbf{x}(\ ), \tag{6.123}$$

e $\mathbf{x}(\ )$ e e de c, ea a e e a (e.g., E . (6.89)). M e g , acc d g e ge de a c e fi e e f bab , e e ead a e bab $_V(\mathbf{n})$ c ge a D ac- δ fi c a bab a a a ce e .

$$- \underset{V\to\infty}{} \frac{\ _V(\mathbf{n})}{V} = - \underset{V\to\infty}{} \frac{\ _V(V\mathbf{x})}{V} = G\ (\mathbf{x}). \tag{6.124}$$

T ead a e ge de a a e fi c $G\ (\mathbf{x})$ ca be de fied a a ge a ed G bb fi c f e b c e ca eac e . I ca be a

$$\frac{\mathrm{d}}{\mathrm{d}\ } G\ \left[\mathbf{x}(\ )\right] = \left(\frac{\mathrm{d}\mathbf{x}(\ )}{\mathrm{d}\ }\right) \cdot \nabla_{\mathbf{x}} G\ (\mathbf{x}) \leq 0. \tag{6.125}$$

T a ge a a f e e a E . (6.77). See [10] f e f.

6.10 Summary and Conclusion

T c a e e a e de g a ad g f b g ca e a d - ce e a c f e a f d d a , eac a fi e a a deg ee f eed . T e d d a a e g ed b a .

a d a e a ca e e e ed b a ca be a f b , dea , g a , a d a e c g. We a e a e c f ea d a d ff e a e a (ODE) de e ed a e a ca b g fi da e a a c a c e c e . T c a c a e c e e e a f b g ca ea ca be d ced e g , de e c fide ce e c c d a f a e a ca a a . We ca ed f a *Delbrück-Gillespie process*. I e a ge a , T. G. K e e , a a f a ge b , e d a e f ea a e e a a c e e a d a ODE . I Sec . 6.9, ece e e c c e b d a c a d c e d g a c c e b d a c a e e e ed. T ge e ee a , (1) c a c e c f DGP, (2) de c ea d a c f ODE , a d (3) e a e a c d a c , de a c e e e a e a ca e f a de a ge f b g ca e a d ce e f b c e ec g .

6.11 Exercises: Simple and Challenging

1. C e e e ec ed a e a d e a a ce f a e e a d b ed a d a ab e a e λ.

2. Le $_1, \cdots,$ be .d. e e a a d a ab e a e λ. Le $^* =$ { $_1,$ $_2, \cdots,$ }. S a $_{T^*}( ) =$ λ $^{-}$ λ .

3. If a e f .d. a d e a d b $_T( ), _T(0) = 0$ b $'_T(0) \neq 0,$ a e d b f $T^* =$ $\{T_1, T_2, \cdots, T\}$ e f $\to \infty$?

4. C de a c g f de ca a d de e de d d a ga - , eac a e e a d b ed e f g g b , a e λ, a d g g dea , a e .

( ) N e e a a e ac d d a , a e bab d b f e a g e e e b ? W a e bab d b f e a g e e e dea ? W a e bab d b f e a g e e e b dea e e ?

( ) Le ( ) be e babi f a g e ac d d a e a
a e :

$$\sum_{=0}^{\infty} ( ) = 1.$$

W a e f d ffe e a e a d ( ) a f ?
( ) T e ea a a e defi ed a

$$\langle \ \rangle( ) = \sum_{=0}^{\infty} ( ).$$

Ba ed e e f d ffe e a e a b a ed ( ), a

$$\frac{d}{d}\langle \ \rangle = \left(\lambda - \ \right)\langle \ \rangle.$$

5. T e 3- a e Ma e ,

$$A \underset{-1}{\overset{1}{\rightleftharpoons}} B \underset{-2}{\overset{2}{\rightleftharpoons}} C \underset{-3}{\overset{3}{\rightleftharpoons}} A, \tag{6.126}$$

a bee de ed b c e de e c f a a c a ge f a
g e e eo e de g g g ee d ffe e a e A, B, a d
C. F e a e, A -ac e, B a a ac e, a d C fi ac e.

( ) T e bab e f e a e , $\mathbf{p} = (_A, _B, _C)$, a fie a d ffe e a
e a

$$\frac{d}{d}\mathbf{p}( ) = \mathbf{p}( )\mathbf{Q},$$

e e $\mathbf{Q}$ a 3×3 a . W e e $\mathbf{Q}$ f e . S a e
feac a d e e . D o bab c e , a e
ea g f e ?

( ) C e e ead a e bab e $_A$, $_B$, a d $_C$, a d a
e ead a e, e e (bab c) fl f a e A B,

$$J_{A\to B} = \ _1 \ _A - \ _{-1} \ _B,$$

e a ea e e fl f a e $B \to$ a e C, a d a e e fl f
$C \to A$. S ce e a e a e a e ca ed e ead a e fl J f
e b c e ca eac c c e (6.126).

( ) W a e c d e f a e , f $J = 0$?

6. C da a g e e e E e ea f b a e ea e S. T e M c ae Me e e c

$$E + S \underset{-1}{\overset{1}{\rightleftharpoons}} ES \xrightarrow{2} E^* + P. \quad (6.127)$$

Beca e e a g e e e ea e g, e c ce a f S ca be a ed a a a c a , a e a e $_S$.

W e e d ff e a e a f e bab f e e e be g a e E, ES, a d E^*: $_E(\ )$, $_{ES}(\ )$, a d $_{E^*}(\ )$.

G e a c d $_E(0) = 1$, $_{ES}(0) = 0$, a d $_{E^*}(0) = 0$, e $_{E^*}(\ )$.

I c ea a e e f ee e e f a e E E^* c a c. Le T be e a d e. W a e bab d b f T, $_T(\ )$? H e a ed $_{E^*}(\ )$?

C e e ec ed a e $\mathbb{E}[T]$. C a e e e M c ae Me e f a.

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