TABLE II

PREVALENCE OF SPECIFIC mRNAs IN RODENT LIVER ESTIMATED FROM PROTEIN SYNTHESIS RATES[a]

1	2	3	4	5	6	7	8	9	10	11
Number	Protein	EC number	Molecular weight ($\times 10^{-3}$)		From indirect calculation of k_s				From direct measurement of relative k_s	
			Protein	Subunits	Fraction of total protein[b] ($\times 10^4$)	A_0: Molecules of each subunit per cell[c] ($\times 10^{-5}$)	$T_{1/2}$[d] (h)	Molecules of each mRNA per cell[e]	Relative k_s: Fraction of total protein synthesis[f] ($\times 10^4$)	Molecules of each mRNA per cell[g]
1	RNA polymerase II	2.7.7.6	464 to 534[h1] (30, 31)	8 kinds, av = 50[h1] (30,31)	0.22 (30[i,h3], 32[k])	0.026	10[n] (33, 34)	1.8		
2	NAD glycohydrolase B	3.2.2.5	87 (35, 36)		2.5[j] (35, 37)	1.7	430[o,r] (37)	2.7		
3	Acetyl CoA carboxylase	6.4.1.2	215 (38)	118 and 125 (38)	1.5[j,m1] (38, 40, 41)	0.38	55[p] (39, 40)	4.8	1.3[r,m1] (39, 40[n])	15
4	NAD glycohydrolase A	3.2.2.5	77 (35, 36)		5.0[j] (35, 37)	3.9	430[o,r] (37)	6.3		
5	RNA polymerase I	2.7.7.6	412 or 473[h1] (31, 42)	5 or 6 kinds, av = 80[h1] (31, 42)	0.31 (32[k], 42[i,h1])	0.020	1.3[s] (34)	11		
6	Alanine aminotransferase	2.6.1.2	114 (43)	57 (43-45)	2.9 (43[i,m2], 44[i,l], 46[k,i,m2])	3.1	84 (26[p], 46[o], 47[n])	25	0.35[r,k] (46)	18
7	Serine dehydratase II	4.2.1.13	64 (49)	34 (49)	0.48[i,m3] (49, 50)	0.85	20[q2] (52[o], 53[n])	29	0.60[r,u] (52[m4], 54[m3])	46
8	Ribosomal proteins		1730[h2] (29)	70 kinds, av = 25 (29[h2], 55[h1], 56[h2], 57)	2.6[e]	6.5	120[p] (58)	37		
9	Xanthine oxidase	1.2.3.2	300 (59)	150 (59)	18[i,m5] (60)	7.2	96[o] (60)	52		
10	NADPH cytochrome *c* reductase		58[h3] (61)	58 (23, 61[h3])	5.5[j] (25, 61[h2], 62)	5.7	70[p] (23, 25, 62-64)	56	0.74[r] (23, 25)	37
11	Ornithine aminotransferase	2.6.1.13	140 (65, 66)	38 (66, 67)	2.5[p] (65[j,m6], 66[i,m6], 67[j], 68[j], 69[j])	4.0	48[p] (68, 69)	58	1.2[r] (54[m3], 67[m1])	90
12	Glucose 6-phosphate dehydrogenase	1.1.1.49	120 (70[h4], 71-73, 74[h5])	63 (70[h4], 73, 74[h5], 75)	7.1 (71[i,m8], 73[j,m8], 74[j,h5], 71[j], 76[j])	6.8	70[p,q] (76)	67	3.0[r] (76, 77[m8])	140
13	α-Glycerophosphate dehydrogenase	1.1.2.8	62 (78-81[h6])	31 (78-81[h6])	5.7[j] (79, 80)	11	96[n,o] (82)	79		
14	Glucokinase	2.7.1.2	48 (83)	48 (83)	1.1[q] (83)	1.4	12[n] (84, 85)	81		
15	Aspartate aminotransferase, cytoplasmic	2.6.1.1	95 (86[h6], 87[h4], 88[h8])	50 (86[h6], 88[h8])	7.7[j] (86[h5], 87[h6], 88[h6])	9.3	75[p] (47[t2], 89)	86		
16	Pyruvate kinase L	2.7.1.40	210 (90-92)	105[w,h9] (91)	5.6[j,m9] (90)	3.2	24[o,t4] (93)	90		
17	Cytochrome *c*		14[h11] (94)	14[h11] (94)	6.9[j] (95, 95[h10], 96)	30	210[p] (96-99)	99		
18	Tryptophan oxygenase	1.13.11.12	172 (100, 101)	43 and 43 (101)	0.55 (100[j,l,m10], 101[j,l,m10], 102[k,m11,12], 103[k], 104[k])	0.38	2.5 (102[p], 107[o], 108[n], 109[n])	100	1.2[r] (102[k,m12], 104[t])	60
19	Nucleoside diphosphatase		80 (110, 111[h6])		6.0[j] (110, 111[h6], 112)	4.5	30[p] (112)	100		
20	ATP citrate lyase	4.1.3.8	500 (113)	125 (114)	7.9[j,m13] (113, 115, 116)	3.8	24[o] (117)	110		
21	Arginase	3.5.3.1	118 (118)	31 (118, 119)	8.0[j] (118, 120[m14], 121)	16	96[p] (120)	120		
22	Fatty acid synthetase		500 (122-124)	240 (124-126[h12])	50 (125[k], 126[j], 127[i,m15], 128[j], 129[j])	12	70[p] (122, 129, 131, 132)	120	20[u] (126[r], 129[r], 131[r,m15])	150
23	Cytochrome b_5, microsomal[x]		17[h10] (136)	17 (23)	5.0 (25[j], 62[j], 137[j], 138[j])	18	110[p] (23, 25, 62-64, 99, 112, 139)	120	0.55[r,u] (23, 25)	93
24	Acetanilide hydrolysing esterase			63 (140)	20[j] (140)	19	96[p] (139)	140		
25	Phosphoenol pyruvate carboxykinase, cytoplasmic	4.1.1.32	74 (141)	65 (142)	3.3 (141[i,m16], 142[k], 143[j])	3.1	13[p] (143, 146)	160	7.0[r] (142, 147)	310
26	Fructose 1,6-diphosphatase	3.1.3.11	140 (148[h10], 149[h10], 150[h6], 151[h13])	38 (151[h13], 152[h10])	5.2[j] (148[h10]152[h10], 153)	8.3	36[p] (154)	160		
27	δ-Aminolevulinate dehydratase	4.2.1.24	270 (155-157[h6])	38 (23, 156, 157[h6])	20[j,m17] (155, 158)	32	130[p] (23, 158)	170	3.3[r] (23, 158[m17])	250
28	Hydroxymethylglutaryl CoA reductase	1.1.1.34	220 (159)	68 (160)	1.1[j,m18] (159)	0.98	3 (162[n,o], 163[o], 164[o], 165[n,o])	230		
29	Malate dehydrogenase, cytoplasmic	1.1.1.40	66[h5,h6] (169)	35 (170[h2])	20[j] (168)	34	96[n,o] (77)	240		
30	Lactate dehydrogenase 5		125 (171)	35 (23)	24[j] (24, 172)	41	115[p] (172)	250	3.7[r] (24)	270
	Young animal				95[j] (173)	160	125[o] (23, 173)	880	50[r] (23, 173)	1100
	Old animal				13[j] (174, 175)	22	420[o] (174, 175)	36		
31	Pyruvate kinase M	2.7.1.40	230 (176[h14], 177[h15])	115[o] (91[h9], 92, 176[h14])	11 (90[k,m7], 177[j,h15])	5.8	15[p] (90)	270		
32	Cytochrome *P*-450		350 (178)	4 kinds, av = 51 (179, 180, 181[h10], 182[h10])	40[j] (182-186)	12	31 (186[p], 187[o], 188[p])	270		
33	Glyceraldehyde 3-phosphate dehydrogenase	1.2.1.13	130[h14] (189-191)	36[h14] (189-191)	20[j] (172, 192, 193[h10])	38	85[p] (172, 192)	310		
34	Tyrosine aminotransferase	2.6.1.5	118 (194, 195)	30[r] (194, 195)	0.57 (194[j,m19], 197[j], 198[j,m19], 199[j], 199[j,m20])	1.1	2.0 (197[p], 199[p], 202[n], 203[o,r])	380	7.2[r] (197, 199)	690
35	Catalase	1.11.1.6	245 (204, 205)	59 (23, 205)	55[j] (206, 207[j,m21])	56	60[p] (23, 209-211)	640	1.5[r] (23, 210)	730
36	Cytochrome oxidase	1.9.3.1	230[h16] (212)	110 (90, 212[h16], 213[h16])	230[j] (68)	130	135[p] (68)	640		
37	Thymidilate kinase	2.7.1.21	75 (214-216[h18])	75 (214)	3.9[j,m22] (215)	3.1	2.6[s] (218)	820		
38	Ferritin		460[h17] (219-221)	20 (23, 220, 221)	17[j] (222-224)	51	36[p] (23, 225)	980	6.6 (23[r], 223[r], 226[r], 227[t])	960
39	Aldolase	4.1.2.31	160 (228, 229)	40 and 40 (228-230)	150 (172[j], 231[j])	110	75[p] (172, 192[h10])	1000		
40	Ornithine decarboxylase	4.1.1.17	130 (232[h19], 233)	75 (232[h19])	0.37[j,m23] (233)	0.3	0.2[n] (235, 236)	1000		

[a] Data refer to proteins in rodent liver, except where otherwise specified. Where more than one value of a given parameter is cited, the listed one is the approximate average. Agreement is most often within a factor of 2. Averages based on exceptionally diverse values are indicated in the footnotes.

[b] The fraction of the total cell protein comprising the protein of interest is calculated from direct measurement or from purification data. When the total protein content was not explicitly measured (as in the majority of the cases), the value used for the calculation was based on the following assumptions, derived from the literature: The liver is 20% protein by (wet) weight; 50% of the protein in a whole cell (or mitochondria) homogenate is included in a low-speed supernatant; 40% is included in a high-speed supernatant and 10% of the protein is included in mitochondrial and microsomal preparations. Precipitation of proteins with acetone is assumed to be quantitative, and solubilization of proteins from such preparations is assumed to be 50%. Where the concentration of the protein is not determined in the normal animal, it is corrected to that in the normal state, as detailed in the footnotes, by the measured differences in enzyme activities, or enzyme content.

[c] The protein content in mouse and rat liver is taken as 1 ng cell^{-1}. This is based on a protein to DNA ratio of about 125, as summarized in (11), and a DNA content calculated to be about 8.2 pg cell^{-1} (12, using 7.3 pg as the DNA content of human liver cells). Where the subunit molecular weights of low molecular weight proteins are not known, they are assumed to be monomeric.

[d] Uncertainties associated with various methods of measuring protein degradation rates have recently been reviewed (19). We relied mainly on measurements made at steady state in normal animals by methods utilizing the isolation of radiolabeled protein. For our purposes measurements based on the kinetics with which the protein activity appears during induction seem more accurate than measurements made during deinduction.

TABLE II—*Continued*

In any case, as detailed for several instances in the footnotes, the $T_{1/2}$ for proteins measured at steady state in the normal animal is usually equal to or longer (though by less than a factor of 2) than the $T_{1/2}$ measured during induction or deinduction, or at steady state in animals under abnormal conditions.

[e] The steady-state concentration of mRNA is calculated from the protein synthesis rate, k_s, assuming a translation efficiency of 10^3 molecules of protein mRNA^{-1} h^{-1} (22). k_s is calculated from the values of A_0 (column 7) and from k_d (= $0.69/T_{1/2}$), calculated from the data of column 8, by use of Eq. [2].

[f] The relative k_s of a protein is measured as the fraction of the total instantaneous protein synthesis attributable to that protein, i.e., the ratio of radioactivity in the particular protein to the radioactivity in total protein. Measurements made *in vitro* utilize protein synthesis systems programmed with polysomes or various RNA fractions. Glass and Doyle (23) report only relative specific activities, and their data have been converted to relative k_s using the fraction of total protein listed in column 6. Postmitochondrial RNA preparations, whether or not derived from purified polysomes, are assumed to include 50% of the total mRNA (27). Measurements made *in vivo* utilize relatively short (20 min to 4 h) pulses of radioactive amino acids. One exception is a 60-s pulse used by Kuehl (24). Here, where necessary, it is assumed that soluble protein has the same specific activity as total protein and that the protein fractionation is that detailed in footnote *b* above. Although not noted in all labeling conditions, a *decline* in total protein specific activity is often observed after about 30 min of labeling (24–26). This is usually attributed to the export of a large fraction of the labeled liver proteins occurring after the rapid exhaustion of the radioactivity in the amino acid pool (25, 26). We have used the data of Kim (26) to correct the reported total protein radioactivity for losses due to export. Expressed as the fraction of the radioactivity in total newly synthesized protein which can still be observed in liver proteins at various times after the beginning of labeling, this is 0.75 at 30 min, 0.55 at 60 min, 0.33 at 120 min, and 0.30 at 240 min. For the experiments reported here the magnitude of this correction should be essentially independent of the actual kinetics of amino acid pool labeling.

[g] This calculation of mRNA frequencies per cell assumes that the fraction of mRNA for a particular protein is equivalent to the fraction of protein synthesis devoted to the protein. It was not possible to apply corrections for possible differences in translational efficiencies, either *in vivo* or *in vitro*, though at least *in vitro* translational efficiencies could differ considerably. The calculations of total cell RNA content (33 pg) and poly(A)mRNA content (1% of the total RNA) are detailed in footnote *f* to Table I. The total mRNA content is approximately 2.2% of the total cell RNA. This is estimated from the fraction of total cell RNA in polysomes, 70% (27, 28); the mass of rRNA per ribosome, 7300 nucleotides (29); the weight average number of ribosomes per polysomal mRNA, 10 (28); and the weight average length of mRNA, 2500 nucleotides (1–3). From these data about 3.2% of the polysomal RNA appears to be mRNA, or 0.73 pg cell^{-1}. The number of mRNA molecules is calculated using the subunit molecular weights given (column 5) and a 1 to 10 ratio of protein mass to the mass of mRNA for which it codes.

[h1] Mouse lymphoma.

[h2] Rabbit reticulocyte.

[h3] Pig heart.

[h4] Rat mammary gland.

[h5] Pig liver.

[h6] Cow liver.

[h7] Rat brain.

[h8] Sheep liver.

[h9] Rat kidney.

[h10] Rabbit liver.

[h11] Mammalian tissue.

[h12] Rat cultured liver cells.

[h13] Rabbit kidney.

[h14] Rabbit muscle.

[h15] Mouse ascites cells.

[h16] Cow heart.

[h17] Horse spleen.

[h18] Cow thymus.

[h19] Rat prostate.

[i] Calculated as the inverse of the *n*-fold purification.

[j] Based on measurements by enzymatic, chemical, immunochemical, or other standard separation procedures.

[k] As in *j* above, but the calculation made here requires the specific activity of the pure protein (see *l*).

[l] This reference contains a specific activity for the pure protein utilized in determining protein concentrations in reports designated by footnote *k*.

[m1] Acetyl CoA carboxylase activity increases 2.5-fold with fat-free diet after fasting and decreases 3-fold with fasting and 10-fold with high-fat diet (39, 40). The $T_{1/2}$ is the same at steady state with all diets except during fasting, where it decreases 2-fold (40).

[m2] Glucocorticoid treatment increases alanine aminotransferase activity 5-fold (26, 47, 48). The steady state $T_{1/2}$ remains about the same (26).

[m3] Form II is the only serine dehydratase activity in the normal state. With high-protein diet it increases 5-fold and form I reaches an equivalent activity (49) such that the total activity increases 10-fold (49, 51). The calculations are not affected if both forms are transcribed from the same gene.

[m4] Total serine dehydratase activity decreases 10-fold with starvation and increases 10-fold with glucocorticoid treatment (49, 52). Form II is probably the principal activity in both cases (49).

[m5] Xanthine oxidase activity increases 10-fold with a change from an 8 to a 23% protein diet. The enzyme was purified to the same specific activity from animals on both diets (60).

[m6] A high-protein diet increases ornithine aminotransferase activity 3.5-fold (51, 67–69). At steady state, the $T_{1/2}$ is the same regardless of diet; during dietary shifts in activity the $T_{1/2}$ declines somewhat less than 2-fold (69).

[m7] A 12% protein diet decreases ornithine aminotransferase activity 2.5-fold (67), a 0% protein diet about 5- to 10-fold (66, 67).

[m8] The amount of glucose 6-phosphate dehydrogenase does not change with the diet, although its activity appears to (76). The $T_{1/2}$ of the enzyme remains essentially the same at any steady-state level or during induction or deinduction (76).

[m9] There is a 3-fold increase in pyruvate kinase L activity with a high-carbohydrate diet, while M activity remains the same (90, 92).

[m10] Simultaneous treatment with tryptophan and glucocorticoid in the intact rat increases tryptophan oxygenase activity 10-fold, with a further increase to 15-fold with repeated treatment; there is an additional 2-fold increase in young rats (100).

[m11] In the adrenalectomized rat, simultaneous treatment with tryptophan and glucocorticoid increases tryptophan oxygenase activity 7-fold above normal (106). Tryptophan induces about a 6-fold increase in tryptophan oxygenase activity and content in the intact rat (104–106). This is due at least in part, to a large increase in the $T_{1/2}$ of the enzyme during induction (102, 108).

[m12] Adrenalectomization decreases tryptophan oxygenase activity and the content of enzyme protein by less than 1.7-fold (105, 106).

[m13] A high-carbohydrate diet following a fast increases ATP citrate lyase activity about 10-fold (115, 117).

[m14] Arginase activity varies about 2-fold with changes in diet protein, but there is little difference in the $T_{1/2}$ at steady state (120).

[m15] Fatty acid synthetase activity and content increase about 6-fold above normal when the rat is fed a fat-free diet after fasting (128–130). The $T_{1/2}$ is the same in both cases, but apparently declines somewhat less than 2-fold with fasting (131).

[m16] Phosphoenolpyruvate carboxykinase activity increases 3-fold with fasting (141, 142, 144). The $T_{1/2}$ at steady state is independent of diet but declines 2-fold during induction or deinduction (142, 144–146).

[m17] Lv^a/Lv^a strains are used; δ-aminolevulinate dehydratase activity in Lv^b/Lv^b strains is about 2.5-fold lower (158).

[m18] There is a diurnal activity change in hydroxymethylglutaryl CoA reductase activity, with a 5-fold increase in activity at night over the

daytime level (161–165). It is assumed that the enzyme purification in (159) was initiated in the daytime, so no correction has been applied.

[m19] Glucocorticoids increase tyrosine aminotransferase activity 6-fold (196, 197). The $T_{1/2}$ is reported to increase 2-fold during induction (197).

[m20] Tyrosine increases the tyrosine aminotransferase activity 8-fold (200, 201).

[m21] Female rate livers have approximately 0.7 times the catalase activity of those of males (208).

[m22] The regenerating liver contains about 12 times the normal thymidylate kinase activity (217, 218).

[m23] Thioacetamide induces a 2.5-fold increase in ornithine decarboxylase activity (234).

[n] Measurement of the kinetics of activity loss following administration of a protein synthesis inhibitor.

[o] Measurement of the kinetics of increase or decrease of enzyme activity following experimental treatment resulting in induction or deinduction.

[p] Measurement of the kinetics of accumulation or decay of radioactivity in isolated protein measured under steady state conditions.

[q] As in *p*, but not under steady-state conditions, i.e., during induction or deinduction.

[r] Measured *in vivo*.

[s] Measured *in vitro*.

[t1] Measured for the microsomal NAD glycohydrolase (which may be both A and B), but both microsomal and plasmalemal enzymes have similar decay constants (37).

[t2] The decay of prelabeled serine dehydratase enzyme studied during moderate amino acid induction in (52) is probably form II (49); both forms are synthesized during induction with a high-protein diet (49) which is used in (53). The $T_{1/2}$ of prelabeled enzyme declines 4-fold during glucose repression (52).

[t3] The kinetics of total aspartate aminotransferase activity increase was measured but only the cytoplasmic form responds to glucocorticoid treatment (89).

[t4] The kinetics of total pyruvate kinase activity increase was measured, but only the L form increases with a high-carbohydrate diet (90, 92).

[t5] As has been shown in cow kidney (166) and pig heart (167), the majority of malate dehydrogenase activity is probably due to the cytoplasmic enzyme in rat liver (168).

[u] The relative k_s is calculated using the acetyl CoA carboxylase concentrations indicated in the purification protocol in (40).

[v] The number of ribosomes per cell is calculated from the RNA content per cell (33 pg; see footnote *f* to Table I) and assuming that 80% of the RNA is ribosomal (27) with a combined molecular weight of 2.4×10^6 per ribosome (29).

[w] It is reported that the molecular weight of at least the major liver M form of pyruvate kinase is one-half that listed for the M form (92).

[x] This may be the same as mitochondrial cytochrome b_5 (133) but the mitochondrial form comprises less than about one-third the total in rat and pig liver (134, 135) and turns over one-half as rapidly as the microsomal form in the rat liver (99). Thus, the mRNA concentration would be less than 1.3 times higher than that of the microsomal form alone.

[y] There is approximately a 4- to 5-fold difference between the values reported in the cited references.

[z] Recent analysis of tyrosine aminotransferase newly synthesized in cultured rat hepatoma cells suggests a subunit size of 55,000 molecular weight (240, 241).