# Enzymatic reduction of fatty acids and acyl-CoAs to long chain aldehydes and alcohols

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*Summary.* The properties of enzymatic systems involved in the synthesis of long chain aldehydes and alcohols have been reviewed. Fatty acid and acyl-CoA reductases are widely distributed and generate fatty alcohols for ether lipid and wax ester synthesis as well as fatty aldehydes for bacterial bioluminescence. Fatty alcohol is generally the major product of fatty acid reduction in crude or membrane systems, although reductases which release fatty aldehydes as products have also been purified. The reduction of fatty acid proceeds through the ATP-dependent formation of acyl intermediates such as acyl-CoA and acyl protein, followed by reduction to aldehyde and alcohol with NAD(P)H. In most cases, both the rate of fatty acid conversion and acyl chain specificity of the reaction are determined at the level of reduction of the intermediate. The reduction of fatty acids represents the major pathway for the control of the synthesis of fatty aldehydes and alcohols. Several other enzymatic reactions involved in lipid degradation also release fatty aldehydes but do not appear to play an important role in long chain alcohol synthesis.

*Key words.* Fatty acid; long chain alcohol; aldehyde; acyl-CoA; dehydrogenase; ether lipid; wax ester.

## A) *Introduction*

Long chain aliphatic aldehydes and alcohols have been detected as components of lipids from bacteria[55,77], insects[31,93] plants[37] and animal tissues[21,90,103]. Fatty alcohols and aldehydes play important roles in the metabolic pathways of a number of organisms since they can generate fatty acids along with formation of the reduced forms of enzyme cofactors in a reaction involving large favorable free-energy changes. Free and esterified fatty alcohols are very abundant in marine organisms where they represent an important storage form of energy[59]. Similarly, germinating seeds also contain high levels of esterified fatty alcohols which serve as an essential source of energy for plant growth[54]. In luminescent bacteria, fatty aldehydes are substrates for the luciferase reaction[106], for which they provide an essential source of chemical energy for light emission[49]. Unsaturated long chain aldehydes and alcohols are major components of many insect sex pheromones[53] and thus play an important role in species recognition and attraction.

The reduction of fatty acids represents the main pathway for the synthesis of fatty aldehydes and alcohols although several other enzymatic reactions that produce fatty aldehydes have also been identified. Despite the fact that fatty aldehyde synthesis from acyl-CoA had been detected in vitro more than 25 years ago[96], only recently has a fatty acid reductase been purified to apparent homogeneity and resolved into distinct constituants[73,74]. Studies on its structure and mechanism have assisted in providing a more comprehensive view of the enzyme systems involved in fatty acid reduction. Their properties are reviewed in this paper.

## B) *Organism and tissue distribution*

The enzymatic reduction of fatty acids or long chain acyl-CoAs to aldehydes and alcohols has been demonstrated in a wide variety of cell-free systems (table 1). In most cases, the reduction of fatty acids requires ATP, CoA and either NADH or NADPH. For acyl-CoA, the fatty acid is already activated and only NAD(P)H is necessary for reduction to aldehyde or alcohol.

These activities have been identified in several mammalian tissues such as brain, heart and harderian glands which contain high levels of ether-linked glycerolipids[27,46,71]. In these tissues, fatty alcohols are precursors of the alkyl and alkenyl moieties of ether lipid[48,79,80,105]. Fatty alcohols are also esterified to form waxes in mammalian tissues[23,102]. Neoplasms, in which the levels of fatty alcohols, ether lipids and wax esters are elevated, also contain high levels of acyl-CoA reductase[45,46,80]. For example, the specific activity of acyl-

Table 1. Cell-free systems catalyzing the reduction of fatty acids or acyl-CoAs to long chain aldehydes or alcohols

| Source | | Subcellular localization | Reductant | References |
|---|---|---|---|---|
| Mammals | Rat brain | Microsomes[a] | NADPH | 3, 4, 57, 58 |
| | Mouse brain | Microsomes[a] | NADPH | 7 |
| | Mouse preputial gland tumor | Microsomes[a] | NADPH | 81, 104 |
| | Rabbit harderian gland | Microsomes[a] | NADPH | 72 |
| | Bovine cardiac muscle | Soluble fraction[b] | NADH | 30 |
| Birds | Uropygial glands | Microsomes | NADPH | 40, 41 |
| Fish | Gourami roe | Microsomes[a] | NADPH | 22 |
| | Gourami caecum | Microsomes[a] | NADPH | 91 |
| Plants | Jojoba cotyledons | Wax pads | NADPH | 63 |
| | Broccoli leaves | Soluble fraction[b] | NADH | 38 |
| Algae | *Euglena gracilis* | Microsomes[a] | NADH | 34–36, 39 |
| Bacteria | *Mycobacterium* | Microsomes | NADPH | 100 |
| | *Photobacterium* and *Vibrio* | Microsomes | NADPH | 9, 52, 67–70, 73, 95 |
| | | Soluble[a,b] | | |
| | *Clostridium* and *Acenitobacter* | Soluble[b] | NADH | 11, 12, 15 |

[a] These systems have been shown to catalyze the reduction of fatty acids. In addition to NAD(P)H, fatty acid reduction requires ATP and CoA, except in luminescent bacteria where the reaction appears to be CoA-independent. All the other systems catalyze only the reduction of fatty acyl-CoAs. [b] Fatty acid or acyl-CoA reductase which release fatty aldehydes as reaction products have been characterized from these soluble extracts. Fatty alcohol is generally the major product of reduction in the other systems although aldehydes have also been detected in most cases.

CoA reductase in mouse preputial gland tumors is 20-fold higher than in rat brain[104].

The reduction of fatty acids also supplies fatty alcohols which serve as precursors in the synthesis of wax esters in plants[63], fish[22, 59] and microorganisms[39, 100]. Fatty acid reduction also provides the fatty aldehyde substrate for luciferase in bioluminescent bacteria[68]. The physiological significance of fatty acyl-CoA reduction in the nonluminescent *Clostridium butyricum*, which does not appear to contain wax esters nor the elements for the ether lipid pathway, still remains unclear[12].

C) *Reaction mechanism*

The major product obtained from reduction of fatty acid or fatty acyl-CoA in crude or partially purified enzyme preparations is generally the alcohol. However, low levels of fatty aldehydes have been detected in most of these reactions and exogenous aldehydes have also been shown to be reduced to fatty alcohols. Furthermore, for some of the soluble fatty acid and acyl-CoA reductases that have been partially purified from different sources and resolved from distinct aldehyde reductases, only the fatty aldehyde was obtained as a reaction product[12,30,32,38,69]. These results indicate that distinct enzymes are involved in the reduction of fatty acid to aldehyde and from aldehyde to alcohol in many, if not all, of these systems. In membrane systems, fatty aldehydes do not appear to be released as free intermediates since aldehyde-trapping agents and excess exogenous aldehyde have little effect on the reduction of labeled acyl-CoA to the alcohol[4]. However, studies on the solubilization and purification of the membrane enzyme systems are necessary to establish if fatty aldehydes are channelled between different enzyme systems or are products of a multifunctional enzyme complex which can synthesize both aldehyde and alcohol.

The membrane-bound acyl-CoA reductases are very sensitive to inhibition by detergents[4,35] and solubilization has only been achieved for the acyl-CoA reductase from *E. gracilis* microsomes in high salt[35]. The solubilized enzyme has been partially resolved from microsomal fatty acid synthetase and fatty acyl-CoA transacylase. However, aggregation occurred upon salt removal and the enzyme has not been subjected to further characterization.

The requirement of CoA for fatty acid reduction suggests that the reaction proceeds via the formation of acyl-CoA. The presence of long chain acyl-CoA synthetase [fatty:CoA ligase (AMP-forming)] in mammalian microsomal fractions and in a wide variety of organisms[24, 47] as well as fatty acyl-CoA reductases in most preparations also support this conclusion. It should be recognized that alternate intermediates such as acyl-ACPs, acyl-AMP or acylated enzymes are also possible. However, very limited information is available on the reduction of these acylated derivaties. Long chain alcohol synthesis from stearoyl-ACP has been shown in wax pads of jojoba cotyledons[63] while palmitoyl-ACP was not reduced by a partially purified acyl-CoA reductase from *Clostridium butyricum*[12].

An acyl-protein intermediate has been identified in the fatty acid reductase reaction of *P. phosphoreum*[70, 74]. This fatty acid reductase has been shown to be an enzyme complex which can be resolved into two distinct activities referred to as acyl-protein synthetase and acyl-CoA reductase. The acyl-protein synthetase catalyses the formation of acyl-protein in a reaction that requires cleavage of ATP to AMP but which appears to be independent of the presence of coenzyme A[70]. This synthetase has been purified to homogeneity and shown to be associated with a polypeptide of mol. wt of 50,000 (as analyzed by SDS-polyacrylamide gel electrophoresis) which becomes acylated with fatty acids in the presence of ATP. The purified acylated protein functions as an immediate substrate for the acyl-CoA reductase, being reduced to the aldehyde in a NADPH-dependent reaction[74]. These results indicate that fatty acid reduction in *P. phosphoreum* occurs via an acyl-protein rather than an acyl-CoA intermediate although exogenous acyl-CoA can also serve as substrate for the reduction reaction. They also raise the possibility that acyl-CoA reductases detected in other biological systems (table 1) might not have their activities restricted to only acyl-CoAs.

D) *Thermodynamics and kinetics*

In all systems, the reduction of fatty acids appears to proceed via their activation to acylated derivatives followed by reduction with NADPH or NADH. A reaction implicating acyl-CoA and aldehyde as intermediates could be catalyzed by the sequential reactions of acyl-CoA synthetase, acyl-CoA reductase and aldehyde reductase (reactions 1–3) as outlined below:

$$RCOO^- + ATP + CoASH \rightarrow RCO{-}SCoA + AMP + PPi \quad (1)$$

$$RCO{-}SCoA + NAD(P)H + H^+ \rightarrow RCHO + NAD(P)^+ + Co\ ASH \quad (2)$$

$$RCHO + NAD(P)H + H^+ \rightarrow RCH_2OH + NAD(P)^+ \quad (3)$$

The acyl-CoA synthetase reaction (reaction 1) requires ATP. The free energy provided by the cleavage of ATP is similar to that of acyl-CoA hydrolysis; acyl-CoA synthetase reactions are thus freely reversible with equilibrium constants near unity[47]. Similarly, ATP hydrolysis is also required for the activation of fatty acids to acyl-ACPs[66] and acyl proteins[70, 73]. This step appears to be rapid compared to the rate of fatty acid (and acyl-CoA) reduction and thus is not rate limiting in the reaction[3,22,65].

Once activated at the acyl-CoA, the conversion with the aldehyde is freely reversible, with an equilibrium constant ($K_{eq}$) for reaction 2 of $8.3 \times 10^3$ determined for the NADH-dependent reduction of acetyl-CoA to acetaldehyde[8]. The equilibrium between the acyl-CoA and aldehyde is affected by the $H^+$ concentration, being in favor of aldehyde oxidation at neutral pH ($K_{eq} = 8.3 \times 10^{-4}$ $M^{-1}$ at pH 7.0).

Aldehyde reduction to the corresponding alcohol occurs by reversal of the alcohol dehydrogenase reaction (reaction 3). The equilibrium constant ($K_{eq}$) for this

reaction is on the order of $10^{11}$ $M^{-1}$ [62, 64, 88]; the equilibrium being in favor of aldehyde reduction at physiological pH. The oxidation and reduction reactions have different pH dependencies with the rate of alcohol oxidation being higher at alkaline pH (pH 8–10) while aldehyde reduction occurs more efficiently near neutrality (pH 5–8[42, 89, 97, 98]. Similarly, the rate of fatty acid reduction to alcohol is also optimal near neutral pH[22,38,39,41,91,104]. However, the interpretation of the results on sequential reactions is complicated by the possibility that the differences in nucleotide specificity and pH dependence could reflect different rate-limiting steps. The rates of alcohol oxidation to aldehyde and acyl-CoA reduction to aldehyde (i.e. the biosynthesis of fatty aldehyde) appear to be the slowest steps in the interconversion of fatty acids and alcohols, which is consistent with the observation that aldehydes are usually detected in very low amounts upon fatty alcohol oxidation or fatty acid reduction.

E) *Pyridine dinucleotide specificity*

The microsomal or membrane fatty acid and acyl-CoA reductases show a remarkably high specificity for NADPH with the only clear exception being the NADH-dependent system from *E. gracilis* (table 1). In contrast, the soluble systems are generally NADH specific with the exception in this case being the NADPH specific fatty acid reductase complex from luminescent bacteria. However, it is possible that this system may be weakly associated with the membrane and is released on lysis of the cells. Alternatively, it may be reflective of the need for producing free aldehyde for the luminescence reaction rather than channeling into wax esters or other lipids.

Only the same soluble systems from the luminescent bacteria have been reported to reduce fatty acid whereas the other soluble systems analyzed to date, have only been capable of reducing an activated form of the fatty acid (i.e. acyl-CoA). This result may simply reflect decoupling of the fatty acid activating and reducing enzymes on solubilization either due to dissociation upon dilution or a membrane localization of the fatty acid activating enzymes. In contrast, many of the membrane or microsomal systems have the capacity to reduce free fatty acids. Unfortunately, studies on solubilized or purified fatty acid reductase activity have not yet been accomplished for the membrane systems and only the soluble fatty acid reductase from luminescent bacteria has been characterized (see section C).

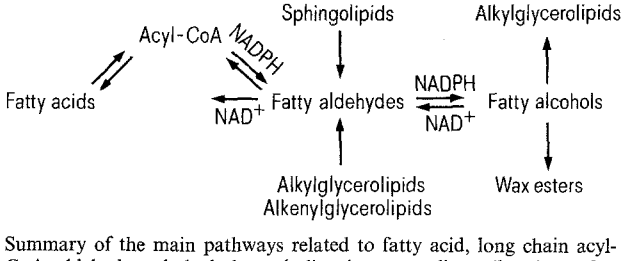
The reduction of fatty aldehydes by aldehyde reductases or alcohol dehydrogenases in soluble systems can be either NADH- or NADPH-dependent[6, 12, 14, 32, 38, 69, 85, 89] and may or may not differ from the specificity of the acyl-CoA reductase. In mammalian tissues, the reduction of fatty aldehyde in soluble and microsomal fractions is mainly NADPH-specific, as in the case of the acyl-CoA reductase. Fatty aldehyde reduction in rat brain microsomes, appears to be catalyzed by different enzyme(s) than that involved in acyl-CoA reduction since the fatty alcohol was exclusively labeled from the B side hydrogen of the nicotinamide ring of [$^3$H] NADPH when palmitoyl-CoA was used as substrate while exogenous palmitaldehyde was labeled from both A and B side hydrogens of NADPH[4]. The reduction of fatty aldehyde in brain microsomes, as in soluble fractions from mammalian tissues, appears to be mainly catalyzed by aldehyde reductases of broad specificity involved in the reduction of various metabolites and xenobiotic aldehyde[13,98].

The high specificity of NADPH for the reduction of fatty acids and aldehydes is in marked contrast to the reverse reactions involving long chain alcohol and aldehyde dehydrogenases which are to a large extent NAD specific[22, 43, 44, 78, 81, 91]. This difference is consistent with the biosynthetic pathways being NADPH-dependent and the degradative pathways being NAD-dependent in biological systems.

Because of this difference in pyridine dinucleotide specificity, it has generally been inferred that different enzyme systems are involved in fatty acid (acyl-CoA) reduction and long chain alcohol oxidation. These results on partially purified systems should be interpreted with caution since different rate limiting steps and pH optima are involved in the reactions (see section D). Furthermore, studies on the purified aldehyde dehydrogenase (acyl-CoA reductase) from *V. harveyi* have shown that marked differences in pyridine dinucleotide specificity are observed according to the direction of the reaction[5,9]. More studies on enzyme fractionation and reaction kinetics are required to establish the individuality and specificity of the enzymes involved in the interconversion of fatty acids and alcohols.

F) *Fatty acid and acyl-CoA specificity*

Maximal rates of fatty acid reduction (to alcohol) in microsomes from gourami roe[22] and *Euglena gracilis*[39] are obtained for $C_{14:0}$ and $C_{16:0}$ acids with lower rates of conversion being observed for fatty acids of shorter or longer chain lengths. Fish roe microsomes also reduce unsaturated fatty acids [e.g. oleic acid ($C_{18:1}$) and linoleic acid ($C_{18:2}$)] at about half the rate of palmitic acid[22]. Homogenates from mouse preputial gland tumors show maximal rates of alcohol synthesis from saturated fatty acids of 14 to 18 carbons and slightly lower rates from elaidic ($C_{18:1}$ trans) and linoleic acids. Other fatty acids are reduced at a rate of less than 10% of that of palmitic acid (linolenic, $C_{18:3}$ ~ arachidonic, $C_{20:4}$, > oleic > lauric > decanoic > behenic > $C_{22:0}$)[104]. Fatty acid reduction by rat brain microsomes shows a clear preference for $C_{16:0}$, $C_{18:0}$ and $C_{18:1}$ acids




Summary of the main pathways related to fatty acid, long chain acyl-CoA, aldehyde and alcohol metabolism in mammalian cells. The preferred dinucleotide for each reaction characterized (generally in crude systems) is given. Additional details concerning the number of enzymes involved in these conversions, their mechanism and subcellular localization are given in the text.

with a much lower activity for fatty acids of other chain lengths or having more than one cis double bond. A similar chain length specificity was also observed for reduction of acyl-CoAs except with a higher efficiency in reduction of $C_{12:0}$ and $C_{14:0}$ acyl-CoAs[4, 58]. These differences may reflect the relative stabilities of the acyl-CoA with different enzyme preparations (e.g. variations in esterase, transferase or other interfering activities) or assay conditions (i.e. acyl-CoAs can react with various reducing agents[87] as well as adsorb at the air/water interface of solutions[2].

The specificities of fatty acid or acyl-CoA reductases for saturated or monounsaturated compounds in *E. gracilis* and rat brain are consistent with the chain lengths of the alcohol moieties found in the wax esters of *E. gracilis*[39] and with the acyl chain length composition of alkylglycerolipids of rat brain[4, 58]. However, the situation appears different in gourami roe where the specificity of fatty acid reduction does not seem to account for the alcohol composition of the wax esters[22]. Other factors, such as the availability of fatty acids, could also be involved in determining the alkyl composition in these cases. Specific thioesterases which have been shown to be associated with fatty acid synthetases and involved in chain termination of fatty acid synthesis[75, 76] could also influence the composition of fatty acids directly available for the fatty acid reductase. Coupling of the reduction of fatty acids with soluble[72] or microsomal[34, 35] fatty acid synthetases has also been reported, with the absence of reduction of exogenously supplied fatty acids in certain cases[72].

The acyl-CoA reductase from bovine cardiac muscle has been shown to be specific for palmitoyl-CoA with lower activity (20%) being measured with stearoyl-CoA[30]. No activity was detected for shorter chain saturated acyl-CoAs ($C_{14}$ or $C_{10}$) although activities of less than 10% of that obtained for palmitoyl-CoA would not have been detected with the assay used. The acyl-CoA reductase from *Clostridium butyricum* is relatively unspecific for the chain length of its substrate with less than 2-fold variation in sp. act. being measured for the $C_{16:0}$, $C_{10:0}$, $C_{12.0}$ and $C_{18:1}$ acyl-CoAs[12].

## G) *Molecular properties of fatty acyl-CoA reductases*

Acyl-CoA reductases have been partially purified from bovine cardiac muscle[30], broccoli leaves[38] and *Clostridium butyricum*[12] and their mol. wts have been estimated to 90,000, 70,000 and 50,000 respectively. The acyl-CoA reductase (acyl-protein reductase) from *P. phosphoreum* has been purified to homogeneity and shown to be an oligomeric enzyme with a mol. wt of 200,000 for the native enzyme and 58,000 for the subunits[73]. This reductase has a certain level of homology with the long chain aldehyde dehydrogenase from another luminescent bacterium, *V. harveyi*. Both enzymes are induced during development of luminescence and catalyze the reduction of fatty acyl-CoAs to aldehyde in the presence of NADPH. They also have an acyltransferase or acylesterase activity in the absence of NADPH and consist of a single polypeptide chain type with an apparent mol. wt of ~ 58,000, as analyzed by SDS-polyacrylamide gel electrophoresis[5, 9, 73, 99]. However, the two enzymes differ in the form in which they are obtained in soluble extracts after cell lysis. The *P. phosphoreum* acyl-CoA reductase is associated with other proteins in a high mol. wt fatty acid reductase complex[70, 74] while the *V. harveyi* enzyme is found as a homodimer[5]. Although the *V. harveyi* enzyme has not yet been directly implicated in fatty acid reductase activity, complementation with the fatty acid activating protein of the *P. phosphoreum* system (see section C) with either the *V. harveyi* or *P. phosphoreum* acyl-CoA reductases, result in an increase in level of fatty acid acylation of the *P. phosphoreum* protein although fatty acid reductase activity is only restored with the *P. phosphoreum* acyl-CoA reductase[9].

## H) *Alternate pathways of fatty aldehyde production*

In addition to being produced as intermediates during fatty acid reduction, fatty aldehydes are released during several enzymatic reactions involving the breakdown of carbon-carbon and carbon-oxygen bonds of certain lipids (table 2). Fatty aldehydes have been shown to be produced in plant tissues and yeast during the process of α-oxidation of saturated fatty acids. The aldehyde are oxidized to the corresponding fatty acids in a NAD-dependent reaction[16, 18, 26, 50]. In addition, the polyunsaturated fatty acids linoleic ($C_{18:2}$, and linolenic ($C_{18:3}$) are oxidized to aldehyde ($C_6$ and $C_9$) and oxoacids by plant tissues, in a reaction which involves cleavage of the $C_{18}$ fatty acids at position 9 or 12[17, 19, 20, 51].

Preparations from several mammalian tissues catalyze the enzymatic cleavage of the ether bond of alkylglycerols to long chain aliphatic aldehyde and glycerol in a reaction that requires $O_2$ and a reduced pteridine. Liver and intestine possess the highest alkylglycerol cleavage activity[61] with the enzyme from rat liver being associated with the microsomal fraction[29, 82, 92]. The released fatty aldehydes can be further converted to fatty acids and/or alcohols[61, 82, 92].

The cleavage of various alkenylglycerolipids also gives rise to long chain aldehydes. Alkenylglycerolipids (plasmalogens) are a class of phosphatidates in which the fatty acid at the 1-position is substituted by an α, β-unsaturated ether. The vinyl ether bonds of ethanolamine- or choline-containing plasmalogens are enzymatically cleaved by preparations from brain[1, 10, 62] and liver[25, 101] tissues with release of fatty aldehydes.

Long chain aliphatic aldehydes have been detected as products of the degradation of certain sphingolipids in rat liver[33, 83–86] and guinea pig intestinal mucosa[60]. The long chain bases sphinganine (dihydrosphingosine or erythro-D-amino-1,3-octanediol), sphingosine (4-t-

Table 2. Enzymatic reactions involved in the production of long chain aldehydes

| |
|---|
| Fatty acid and acyl-CoA reduction |
| α-Oxidation of fatty acids |
| Oxidation of polyunsaturated fatty acids |
| Oxidation of the ether bond of alkylglycerolipids |
| Cleavage of the vinyl ether bond of alkenylglycerolipids |
| Degradation of sphingolipids |
| Oxidation of fatty alcohols derived from hydrocarbons and wax esters |

sphingenine) and 4-hydroxy-sphinganine are phosphorylated and cleaved to phosphorylethanolamine and long chain aldehydes. The aldehydes produced correspond to hexadecanal, 2-hexadecenal and 2-hydrohyhexadecanal, respectively. The cleavage reaction is catalyzed by a pyridoxal phosphate-dependent lyase that has been detected in microsomal[84] and mitochondrial[33] fractions from rat liver. The aldehydes released are generally oxidized to the acid although reduction to alcohol has also been observed[33, 83, 84, 86].

These studies have also shown that long chain aldehydes derived from glycerolipids and sphingolipids are mainly oxidized to fatty acids, in agreement with the presence of aldehyde dehydrogenases in soluble, mitochondrial and microsomal subfractions of mammalian cells[28, 56]. The microsomal form of aldehyde dehydrogenase is more specific toward long chain aldehyde than the cytosolic form (in rat liver) and probably catalyzes the oxidation of most of the endogenously released fatty aldehydes[56]. Alternatively, fatty aldehydes could be converted to alcohols by the aldehyde reductases of broad specificity[13, 98]. However, these enzyme do not seem to play an important role in fatty alcohol synthesis since (1) fatty aldehydes are mainly oxidized to acids and (2) the synthesis of glycerolipids is insensitive to valproate, an inhibitor of aldehyde reductases[94].

## I) *Conclusion*

A general scheme of the reactions involved in the metabolism of fatty acids, aldehydes and alcohols in mammalian cells is given in the figure. In these cells and other systems, the reduction of fatty acids represents the major pathway for the production of fatty aldehydes and alcohols required for synthetic purposes, i.e. alkylglycerolipids and wax ester synthesis, substrate for bacterial luciferase. Fatty acid reduction proceeds through the ATP-dependent formation of acylated derivatives followed by their NAD(P)H-dependent reduction to aldehyde and alcohol. In most systems, both the rate and substrate specificity are mainly determined at the level of reduction of this acylated intermediate. NADPH is generally the preferred pyridine nucleotide in these cases while $NAD^+$ is the most common requirement for the oxidation of fatty alcohols and fatty aldehydes produced during hydrocarbon assimilation and wax ester hydrolysis.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# Full Papers

## On the stability of cognitive processes

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*Summary.* An empirical and mathematical model for self-organization is proposed, based on elemental properties, on unique interaction and on the combination of hierarchical elements. In the model, higher elements are stabilized by the 'cognitive' (strong) interaction of subelements, disregarding intermediate elements. This is called 'elementary reductionism' and is illustrated by the sequence quarks – elementary particles – atoms – molecules – cells – organisms – societies. Optimal dynamic interaction of nonidentical elements is called 'cognitive stability'. This is compared with thermodynamic equilibrium. The principal differences are outlined.
*Key words.* Self-organization; cognitive processes; elementary reductionism; cognitive stability; thermodynamic equilibrium; hierarchical elements; dynamics of interaction.